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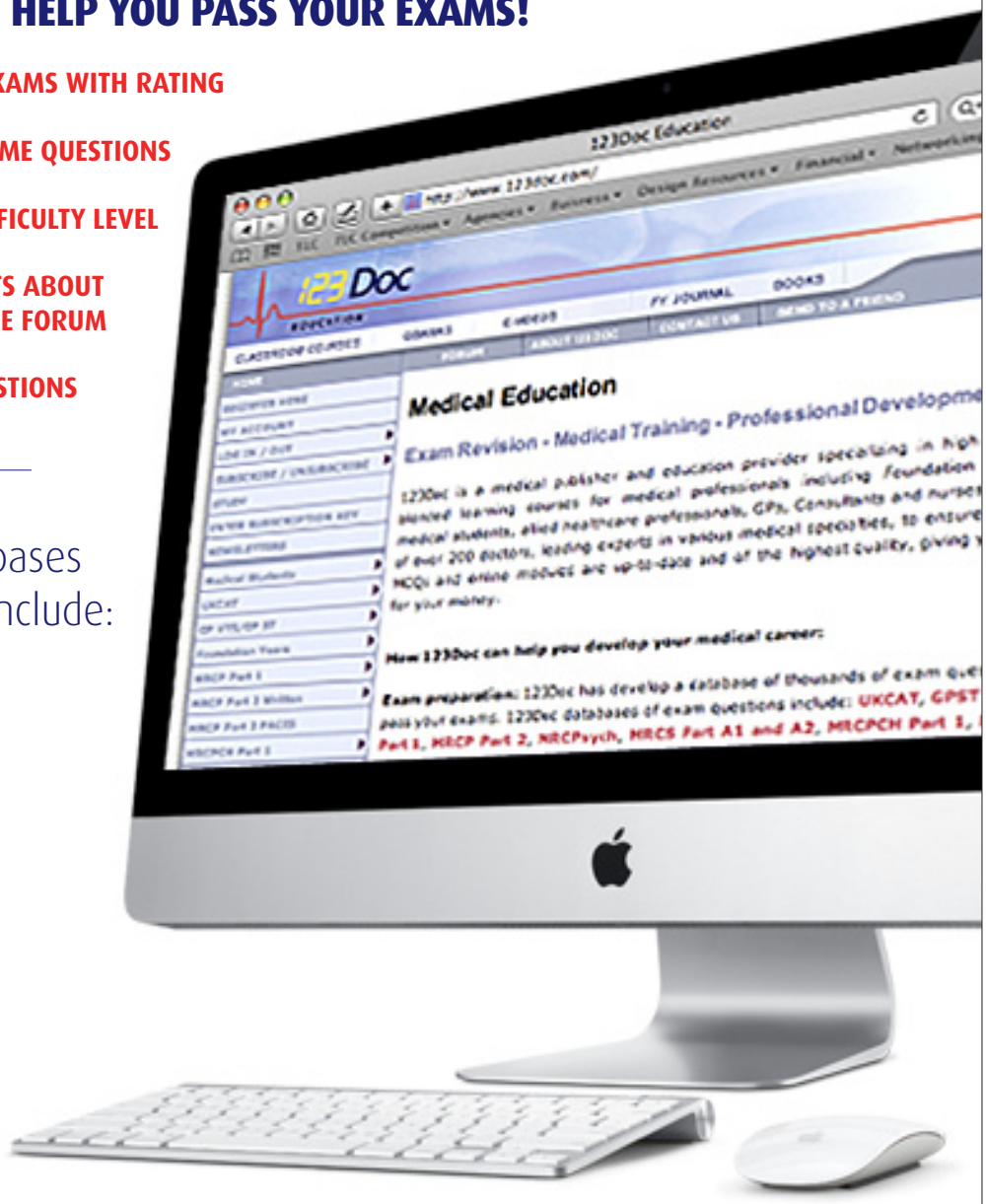

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Volume 11

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FOUNDATION YEARS JOURNAL 2017

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Foundation years journal

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AN UNUSUAL CAUSE OF BACK-PAIN PRESENTING AS RENAL COLIC: RADIOLOGY CASE BASED DISCUSSION

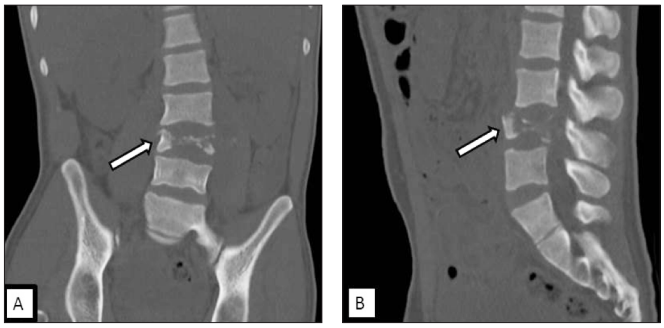
A Chattopadhyay, N Spencer

Abstract

Radiology is increasingly at the centre of immediate investigation and management of many diseases, and this case will demonstrate these uses. This case review highlights how unexpected radiological findings can dramatically change clinical thinking and likely diagnosis. Furthermore, the use of multiple, complimentary imaging modalities enhances evaluation of many pathologies, often guiding tissue sampling and intervention. Disease surveillance also utilises advanced imaging techniques, and this case demonstrates these uses as well.

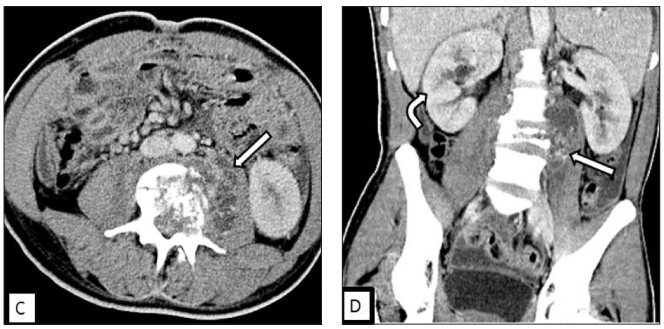
Case History

27 year old male presented to A&E with back-pain radiating into his left flank. Clinically thought to be renal colic, the patient was referred for non-contrast computerised tomography (CT) of the kidneys, ureters and bladder. The reporting radiologist found no renal calculus. Other abnormalities were identified on the scan, making the reporter suspect a para-vertebral mass with bone destruction (Figures A and B).



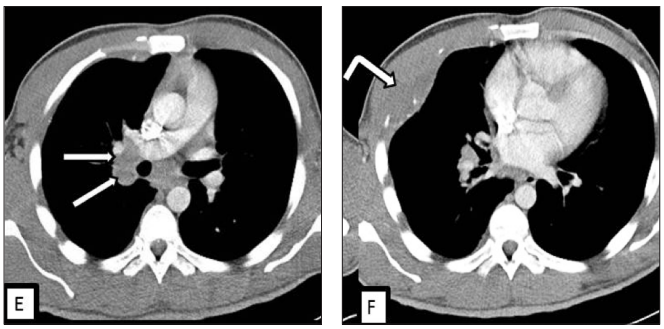
Figures A (coronal) and B (sagittal), are bony reformats of an unenhanced CT, which highlight the severe bony destruction at the L4 level (white arrow).

Further imaging evaluation with contrast-enhanced CT, revealed near-complete destruction of the L4 vertebral body, with multi-loculated paravertebral masses. These lesions had low-attenuation centres and rim enhancement, consistent with bilateral psoas abscesses (Figures C and D). There was extensive thickening and enhancement of the peritoneal reflections throughout the abdomen and pelvis, with prominent ascites. The remainder of the abdominal organs were normal in appearances, with no abdominal lymphadenopathy.



Figures C (axial) and D (coronal) are contrast-enhanced CT images through the abdomen. Both images show areas of low attenuation within the left psoas muscle, with peripheral edge-enhancement (straight white arrow). Appearances are consistent with multiloculated psoas abscesses. The coronal image also demonstrates normally enhancing kidneys (curved white arrow) with no evidence of hydronephrosis or renal calculi.

Due to the extensive pathology identified within the abdomen, the CT was extended to cover the patient's thorax. This demonstrated hilar and subcarinal lymphadenopathy (Figure E), and destruction of the right seventh rib, with an associated soft-tissue mass (Figures F and G). The lungs were clear, with no evidence of pulmonary infection (Figure H).



Figures E-H are axial, contrast-enhanced images through the chest. Figure E demonstrates right hilar lymph nodes (straight white arrows). Figure F shows destruction of the seventh rib on the right, with an associated soft-tissue component (curved white arrow).

AN UNUSUAL CAUSE OF BACK-PAIN PRESENTING AS RENAL COLIC: RADIOLOGY CASE BASED DISCUSSION

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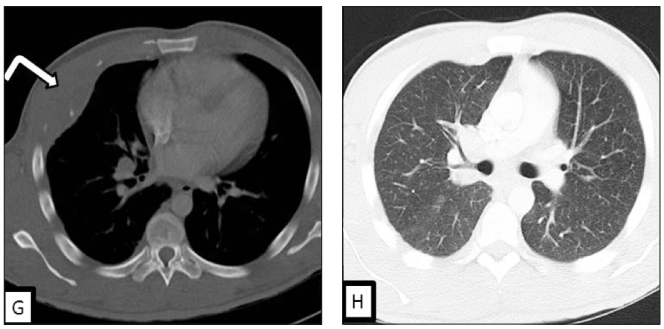
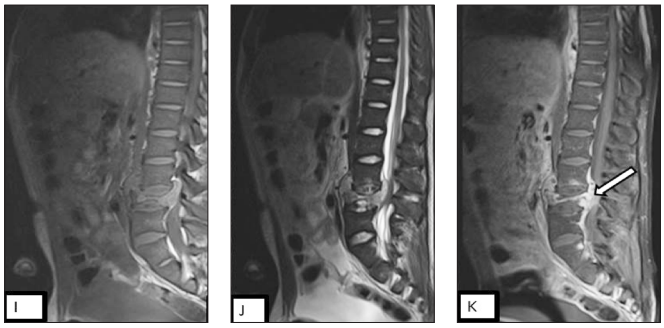


Figure G shows the same slice as figure F, but has been "windowed" to emphasise the bony destruction. Figure H an axial slice through the thorax showing normal appearances of the lungs, with no evidence of infection.

The working diagnosis was that of widespread atypical infection, likely tuberculous, due to the combination of multiple abscesses in the abdomen, vertebral body destruction, and the associated thoracic abnormalities. The differential diagnosis of disseminated malignancy was retained whilst further investigations took place.

The patient was admitted, and detailed clinical history revealed that the back-pain was chronic, and that the patient had also been suffering with lethargy and left-sided sciatica for several months. Magnetic resonance imaging (MRI) of the whole spine was performed to further assess possible neural compression. This confirmed collapse of the L4 vertebral body, with circumferential expansion and partial retropulsion into the central canal, with relative preservation of the intervertebral discs (Figures I and J).



Figures I-K are sagittal MRI images through the lumbar spine. Figure I is a T1 weighted image, Figure J is a T2 weighted image and Figure K is a T1 fat-saturated image, with contrast enhancement. All of the images re-demonstrate bony destruction at the L4 vertebral level, with an associated collection. This collection lies within the epidural space, and is avidly enhancing following contrast (white arrow). There is narrowing of the central spinal canal, with encroachment upon the cauda equina and exiting nerve roots.

Adjacent to the bony destruction, there was an avidly peripherally enhancing epidural collection, which communicated with the bilateral multiloculated psoas abscesses (Figure K). The collection caused significant central spinal canal narrowing and encroachment upon on the cauda equina and exiting nerve-roots. These appearances were consistent with a focal lumbar spondylitis, with mycobacterium tuberculosis (TB) as the most likely causative organism.

Ultrasound (US) guidance was used to collect a sample of ascitic fluid (Figure L). Blood-stained, turbid fluid was sent for biochemical analysis, as well as for microscopy, culture and sensitivity. This did not yield a microbiological diagnosis. Consequently, CT guidance was used to sample tissue from the right chest-wall lesion. Core biopsies were sent for histopathology and microbiology analysis.

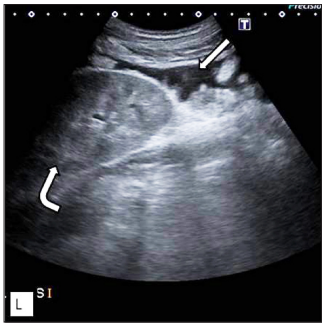


Figure L is an ultrasound image of the left upper quadrant. There is a trace of hypoechoic fluid, with low level of internal echoes (straight white arrow) located next to a normal left kidney (curved white arrow). This was targeted under ultrasound-guidance for the sample of ascitic fluid.

These confirmed acid and alcohol fast bacilli (AAFB), and necrotising granulomatous inflammation, clinching the diagnosis of disseminated TB.

Given the severity of the spinal involvement (Figure M), the most appropriate management for this patient was felt to be surgical fixation. The patient was transferred to the tertiary spinal centre, where he underwent L4 vertebrectomy, lumbar interbody fixation of L3-L5 and cage fixation under fluoroscopic guidance (Figures N and O). The patient made an uneventful recovery. He was discharged with full anti-tuberculous therapy, and remains under active care of thoracic physicians and spinal surgeons.

AN UNUSUAL CAUSE OF BACK-PAIN PRESENTING AS RENAL COLIC: RADIOLOGY CASE BASED DISCUSSION

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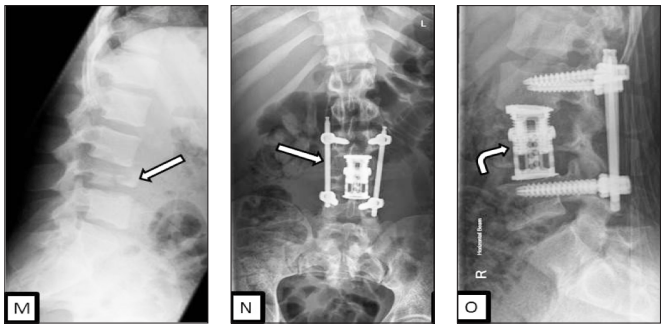

Figure M, a lateral lumbar spine radiograph, shows aggressive destruction of the L4 vertebral body, with cortical irregularity, loss of vertebral body height and anterior displacement of part of the vertebral body (white arrow). Figure N, an AP radiograph of the lumbar spine, and Figure O, a lateral radiograph, show post-operative appearances. There is evidence of a metallic cage device at the L4 level (curved white arrow), with spinal fixation at L3-L5 (straight white arrow)

Discussion

Learning to work with your local radiology service to get optimum access to essential tests like US, CT and MRI is a key to success as a Foundation Trainee. Understanding the technical factors and indications for these is also a challenge. Sometimes availability is limited particularly for MRI, and there are relative and absolute contraindications for some patients to undergo CT or MRI. The discussion below offers background information, plus advice on how to get requests for these tests accepted by your local radiology service, all framed in the context of this unusual and complex case.

Spinal TB, also known as Pott's disease or tuberculous spondylitis, is an important, yet often overlooked, differential to consider in the young patient presenting with back-pain. Characteristically, patients with spinal TB present acutely with severe focal back-pain, new lower-limb neurology or skeletal deformity, all on a background of chronic back-pain. Yet, some patients may only present with constitutional symptoms- an indicator of systemic TB infection, whilst others may be completely asymptomatic. (1, 2)

Occasionally, clinical suspicion for spinal TB is not raised, due to the misconception that patients must have either concomitant or a past history of pulmonary TB infection - this is only true for approximately 50% of spinal TB cases (3). Spinal involvement can occasionally be the initial presentation of TB (2, 4) with direct haematogenous spread of mycobacterium tuberculosis into the vertebral bodies via the venous plexus of Batson. (2) Left untreated, spinal TB can result in severe spinal deformities and spinal cord compression, and may eventually lead to Pott's paraplegia (5, 6).

As our case demonstrates, there are a number of radiological modalities which can be used to image the spine - each providing specific features to aid the diagnosis of spinal TB, and refute alternative diagnoses.

Conventional radiography is often the modality of choice at initial presentation with back-pain (2), as it is readily available, can be reviewed by non-radiologists, and gives a generalised overview of the spine.

Vertebral destruction on radiography is suspected when there is reduced bone density, or focal bone loss, with end-plate irregularity, loss of vertebral body height, and later, reduced disc space and sclerotic new bone formation (7). In the later stages of the disease, there may be complete flattening of the vertebral body, giving a vertebra plana appearances. Alternatively, uneven vertebral body collapse can cause kyphosis, and in the most severe cases, gibbus deformities - all well demonstrated on radiographic plain films, as well as on the advanced modalities (8).

Our case was unusual, in that the presenting history suggested renal colic, so CT was the primary imaging tool. Non-contrast CT provides a general overview of the whole abdomen, to rule out renal calculi, and as in this case to raise suspicion for an alternative disease process.

CT is excellent at demonstrating soft tissue, lung and bony pathologies. Following contrast enhancement, solid visceral organ diseases and lesions may be more conspicuous, and focal infection, in this case the multiloculated cystic psoas abscesses, clearly delineated. CT can also be used to guide intervention for tissue sampling. If necessary, CT guidance could have been used to target the deeper psoas abscesses.

CT requires significant ionising radiation, but is quick to acquire, and has a very wide range of applications throughout the body. It is well-tolerated by almost all patients. Use of intravenous (IV), oral or other cavity contrast agents can dramatically increase its diagnostic utility. However, the IV contrast agents may be contra-indicated in patients with impaired renal function, especially chronic kidney disease (CKD) stage 3 or more.

MRI is often considered the gold-standard when imaging the central nervous system and spine, due to the excellent multiplanar spatial resolution and native soft-tissue contrast. (8) As in this case, MRI is especially useful at evaluating paraspinal lesions, and spread of infection into the soft-tissue structures, and is clearly the best non-invasive test for imaging spinal cord and canal. (1)

Here, MRI clearly elegantly demonstrated a constellation of radiological features related to TB spondylitis. Unlike other forms of spondylitis, TB can involve multilevel contiguous vertebrae, as the infection spreads beneath the anterior longitudinal ligament. (7) As shown in this case, there is also relative preservation of the intervertebral discs, until the late stages of the disease (9).

Like CT, there are contra-indications to using MRI. The majority of these are related to known foreign bodies or medical implants (particularly cardiac pacemakers), though patient factors such as claustrophobia are also important.

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Conclusion

This case of unexpected disseminated tuberculosis with spondylitis highlights the importance of radiology in the multidisciplinary investigation and management of complicated patients. This includes several key modalities, and the ability to guide fluid and tissue sampling to facilitate diagnosis. The associated discussion has described the use of several of these imaging modalities, and emphasises the need for a complete clinicoradiological approach to managing spinal TB.

Test Yourself: MCQs

1) Which of the following symptoms could a patient with spinal TB present with?

a) Kyphotic spinal deformity
b) Weight loss and lethargy
c) No symptoms at all
d) Fevers and back-pain
e) All of the above

2) A patient presents to A&E with a 6 month history of back-pain. Over the last 2 weeks, the patient recalls that their pain has got more severe and today, is currently 9/10 in severity. This morning when he awoke, he was unable to move his left leg. On examination, there is objective left lower limb weakness. What is the imaging modality of choice in this scenario?

a) CT of the spine
b) MRI of the spine
c) Fluoroscopy of the spine
d) Conventional radiography of the spine
e) Ultrasound of the spine

3) Which of the following x-ray findings is NOT commonly associated with spinal TB?

a) Cortical irregularities of the vertebral body endplate
b) Vertebral plana
c) Posterior scalloping of the vertebral body
d) Anterior wedging of the vertebral body
e) Sclerotic new bone formation

4) Which of the following is NOT a relative contraindication for MRI scanning?

a) Previous intra-abdominal surgery within the last 6 weeks
b) Pregnancy in the second trimester
c) Clasutrophobia
d) Cardiac pacemaker
e) Joint prosthesis

5) In which of the following scenarios is contrast-enhanced CT absolutely contra-indicated?

a) Male patient aged 30
b) Patient with an eGFR of 59.
c) Previous anaphylactic reaction to iodinated contrast 20 years ago.
d) Elderly patient with a cardiac pacemaker
e) Previous spinal fixation

Answers

1. The correct answer is: e) All of the above

Spinal TB can present in a variety of ways, most of which are non-specific and can therefore mimic a range of alternative pathologies.

Most patients have chronic, indolent back-pain for a couple of months. Their visit to hospital is triggered by an acute feature- acutely worsening back-pain, altered neurology or a gross spinal deformity. Some patients may present with constitutional features, such as fevers, lethargy and weight loss. Occasionally, patients may be completely asymptomatic, and the diagnosis of spinal TB is completely incidental.

2. The correct answer is: b) MRI of the spine.

In this scenario, the most concerning symptom is the acute lower limb weakness, which would suggest that there has been acute encroachment and compromise of the spinal cord/cauda equina. MRI provides excellent, detailed imaging of the spine and spinal canal, and can determine any spinal cord or cauda equina compression as well as the extent of involvement.

CT of the spine can provide cross-sectional images showing the central spinal canal, but does not allow the same soft-tissue detail as MRI.

In the case of chronic back-pain (without acute features), conventional radiography would have been the modality of choice in the first instance. This would provide a general overview of the bony spine, and help determine if further imaging was necessary.

There is no role for ultrasound or fluoroscopy in the acute investigation of this patient.

AN UNUSUAL CAUSE OF BACK-PAIN PRESENTING AS RENAL COLIC: RADIOLOGY CASE BASED DISCUSSION

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3. The correct answer is: c) Posterior scalloping of the vertebral body.

The remaining options are all radiographic features of spinal TB. Further radiographic features include vertebral body lucencies, aggressive bony destruction, and spinal kyphotic and gibbus deformities.

Posterior scalloping of the vertebral body is not typically associated with spinal TB, and is a feature demonstrated in conditions such as neurofibromatosis type 1, achondroplasia and acromegaly. Anterior vertebral body scalloping can be associated with spinal TB when there is chronic abscess formation.

4. The correct answer is: d) Cardiac pacemaker

Having a cardiac pacemaker is an absolute contraindication to MRI. Newer pacemakers may be designed to be MRI-compatible, but caution is still taken if considering scanning a patient with these cardiac devices, due to concerns about the device malfunctioning.

The remaining options are all relative contra-indications to MRI scanning. Joint prostheses tend to be MRI-safe. If there is any concern, then operative notes should be referred to, and the manufacturer of the prostheses contacted.

If a patient thinks they may have a metallic foreign body (eg) metallic fragments within the eye, or gunshot pellets, conventional radiographs can be performed to confirm the presence of these foreign bodies pre-MRI scan.

5. The correct answer is: c) Previous anaphylactic reaction to iodinated contrast 20 years ago.

A previous anaphylactic reaction to iodinated contrast is an absolute contra-indication to a contrast-enhanced CT study. A non-contrast study can be performed, or alternative imaging such as MRI may be considered.

Patients with a slightly impaired renal function (ie eGFR 40-60 at our institution) can be scanned with IV contrast, but will need adequate hydration both before and after the scan, with close monitoring of renal function.

Implantable devices and joint prostheses are not contraindications for CT scans, but they may cause streak artefact, and consequently degrade the surrounding structures.

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BREAST CANCER SCREENING: A CASE-BASED DISCUSSION

A Redman, A Leaver, S Lowes, S Rizzo

Abstract

Breast cancer is the most common cancer affecting women both worldwide and in the UK, and is associated with significant mortality and morbidity. The introduction of the NHS Breast Screening Programme (NHSBSP) throughout the UK in 1988 has played a critical role in the detection of early and clinically occult cancers and has made a strong impact on the overall morbidity and mortality from this disease.

Radiology is central to the breast screening programme, not only for the detection of mammographic abnormalities but also for further assessment of women who are recalled to the "assessment clinics" and obtaining tissue for diagnosis. Radiologists also play a key role in the ongoing multidisciplinary management of breast cancer.

In this article we use a case example to illustrate the process of how women are screened within the NHSBSP, and what happens when women are recalled to assessment clinics for further evaluation. We will also briefly review the treatment options relevant to screen detected breast cancers, and we will discuss in greater depth the principal benefits and drawbacks of the current NHSBSP. We aim to provide a balanced view for non-specialist doctors who may be called upon to advise and educate women about breast screening.

Case History

A 52 year old woman attended for her screening mammogram. Review of the mammograms identified a poorly defined opacity in the upper outer quadrant of her right breast (Figure 1). The patient was therefore recalled to the radiologist-led breast assessment clinic for further investigation. This was a surprise to her as she had not felt any lumps despite regular self-examination.

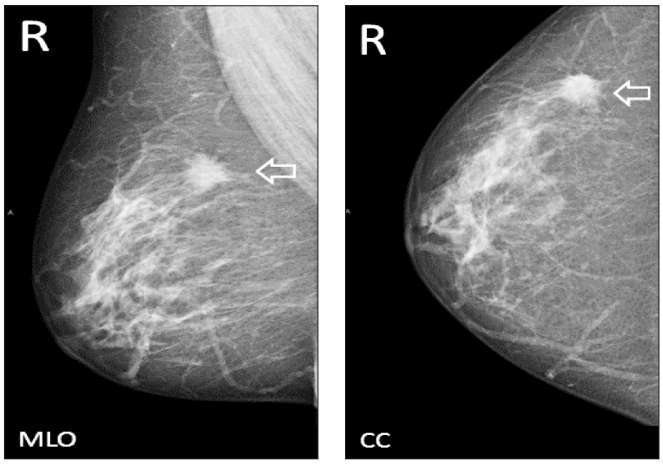

Figure 1: Two-view mammography of the right breast showing a poorly defined opacity in the upper outer quadrant (open arrow).

At the assessment clinic she had further mammograms of the right breast, clinical examination and an ultrasound. The ultrasound revealed a hypoechoic (low reflectivity) poorly defined mass corresponding to the mammographic finding (Figure 2). Ultrasound of the right axilla was also performed, showing morphologically normal lymph nodes (Figure 3).

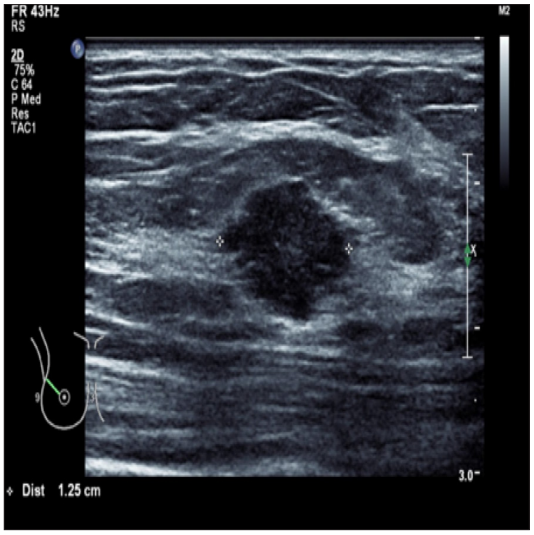

Figure 2: Ultrasound image of the abnormality in the right upper outer quadrant confirms a poorly defined hypoechoic mass. An ultrasound-guided needle biopsy confirmed this as an invasive ductal carcinoma, the most common type of invasive breast cancer.

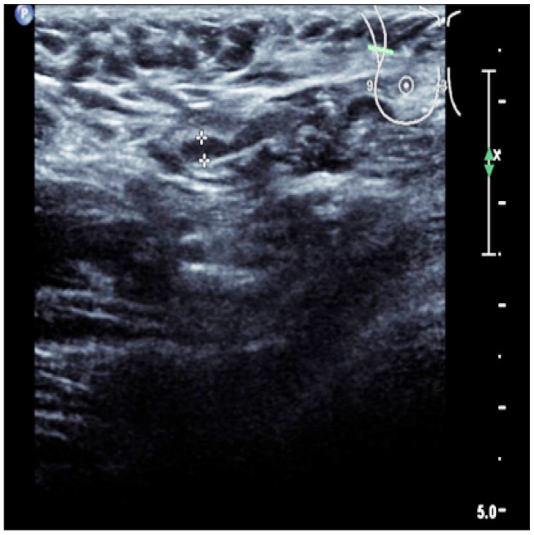

Figure 3: Ultrasound of the right axilla showed morphologically normal lymph node with a thin cortex (dark stripe indicated by the calipers).

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The radiologist then proceeded to an ultrasound-guided biopsy of the breast mass after administering local anaesthesia. Invasive ductal carcinoma was confirmed by histopathology.

After review at the local multidisciplinary breast meeting, treatment options were discussed with the patient. She opted for wide local excision (WLE) of the mass. The tumour was successfully removed with good margins, with conservation of the rest of that breast. At the same time she had a surgical sentinel lymph node biopsy (SLNB), which confirmed that there had been no metastatic spread of disease to the axilla. Following a short course of radiotherapy to the right breast, the patient was discharged and followed up annually for five years. There has been no evidence of recurrence.

Discussion

Breast cancer is the most common cancer affecting women both worldwide and in the UK (1). If left untreated, invasive breast cancers are associated with a poor outcome. Even at a relatively early stage they can spread systemically, metastasising to other parts of the body, with ipsilateral axillary lymph nodes recognised as the first site of metastatic spread beyond the breast. As they grow, breast cancers can invade local structures such as muscle, the chest wall, and may fungate through overlying skin.

Early treatment of breast cancer can be curative such as in the case we describe. Small cancers can usually be treated with breast conserving surgery such as a wide local excision (WLE) and radiotherapy to the ipsilateral breast. Women are then followed up for 5 years with annual mammography to monitor for recurrence. They are then discharged and, if eligible, undergo routine screening every three years as part of the NHS Breast Screening Programme.

If, however, a screen detected breast cancer is large, located in a difficult position and/or is multicentric a mastectomy may be advised for local disease control and/or optimal cosmetic outcome.

In respect of the axilla, if metastatic disease is identified pre-operatively by ultrasound guided biopsy, patients will often have an axillary node clearance procedure at the time of their breast operation. If preoperative ultrasound does not identify any axillary node metastases, the patient will have a surgical SLNB at the time of their breast operation as there may be metastases present which are too small to have been seen ultrasound.

If the SLNB does yield axillary nodal metastases the patient may then have a second operation to clear the axilla or may have axillary radiotherapy instead. There are two principal potential roles for chemotherapy in relation to screen detected breast malignancy.

In the small number of cases with tumours that are large at the time of diagnosis, chemotherapy may be given before surgery to reduce the size of the tumour prior to surgical excision (neo-adjuvant chemotherapy). The more common role for chemotherapy is after surgery, where it may be offered to cases with disease spread beyond the breast in which the oncology assessment suggests benefit may outweigh the risks.

A different form of systemic therapy which is often employed as part of the treatment package is endocrine therapy, delivered by agents such as tamoxifen or letrozole. Endocrine therapy is sometimes also utilised in the specific circumstance of patients who are unsuitable for surgery (for example, too frail) and have hormone-sensitive cancers; these cancers may be treated with primary endocrine therapy with careful radiological follow to check for tumour response.

The NHS Breast Screening Programme (NHSBSP) was set up to identify early-stage asymptomatic invasive breast cancers to allow effective early treatment, such as in the presented case. However, as well as identifying invasive cancers, mammographic screening is also very good at detecting pre-invasive disease, or ductal carcinoma in situ (DCIS).

There is still some uncertainty as to whether all forms of DCIS progress to invasive cancers, and at what rate, which has led to controversy and suggestions that diagnosing DCIS may result in overtreatment in some cases, including unnecessary surgery and the associated physical and psychological sequelae.

Having a basic understanding of the screening process and its advantages and disadvantages are important in providing a balanced view when counselling patients. Women should be advised to remain 'breast aware' and self-examine. If they discover a lump or other signs or symptoms such as bloody nipple discharge or skin changes they should be advised to contact their GP who can arrange referral to a breast assessment unit as appropriate.

The screening process

Until recently the NHSBSP offered screening mammography to all women aged between 50 and 70 years old who are registered with a GP. This has now been extended to some women between 47 and 73, on a trial basis. Women are invited by letter every 3 years. Those above 70 years of age can still undergo 3 yearly screening if they self-refer (2).

Mammograms consist of low dose X-rays taken of each breast in two different planes, craniocaudal (CC) and mediolateraloblique (MLO). Mammograms involve compressing the breast between two clear plastic plates in order to flatten and reduce the thickness of the breast, and as a result can be uncomfortable or even painful for some women, for just a few seconds.

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For convenience, women are invited to attend their closest screening centre; this could be their local hospital-based screening centre or one of the many mobile vans parked in accessible places (supermarket car parks, for example) within the community.

Each set of screening mammograms is independently interpreted by two trained film readers, and occasionally a third reader is called upon to "arbitrate" in the event of a disagreement between the first two readers.

Although mammograms provide a low false positive rate, possible abnormalities detected have low specificity for cancer. An abnormal finding results in the patient being recalled for further assessment. Signs of possible breast cancer on mammogram include poorly defined new densities, architectural distortion, spiculated/irregular densities, and microcalcifications.

Comparison of a lady's current mammograms with previous mammograms is important, identifying any new density that may need further investigation. The NHSBSP implements a low threshold for recalling patients to assessment. This is to maximise the opportunity to detect small cancers and thus reduce mortality in the population. Approximately 1 in 20 attendances for screening mammograms leads to a patient being invited to attend a specialist unit for further investigation (3).

Further evaluation after screening: recall for assessment

Patients recalled following a screening mammogram are sent a letter and undergo "triple" assessment in a radiologist-led clinic. Triple assessment consists of: clinical examination, further imaging and possible biopsy.

Additional imaging consists of further mammographic views and ultrasound. The further mammographic views help establish whether an abnormality is truly present, and can make a genuine abnormality more conspicuous for better evaluation of morphology.

Targeted ultrasound is then performed and, unless definitive benign features are demonstrated, a core biopsy and sometimes a fine needle aspiration (FNA) are performed. In some circumstances, particularly when assessing microcalcification, the patient will be offered stereotactic large bore core biopsy.

Biopsy results are discussed at a multi-disciplinary team meeting (MDT). Patient outcome and further management plans are formulated at the MDT, prior to further communication with the patient.

Benefits and drawbacks of screening

Since the implementation of the NHSBSP, numerous debates have taken place as to whether the programme is truly beneficial to the population, or whether it provides more harm than good.

The main parameter by which a screening programme is deemed to be beneficial is a reduction in mortality within the population. Breast cancer mortality has decreased by 35 % since 1971 despite an increase in breast cancer incidence (4).

This improvement is likely a reflection of several different factors including diagnosing disease at an earlier stage, both through the screening programme and through earlier symptomatic presentation (as a result of greater public awareness of breast cancer), together with improvements in treatment by specialist multidisciplinary teams and greater use of hormone therapy and chemotherapy (5).

An independent review performed jointly by Cancer Research UK and the Department of Health (England) in 2012 (6) concluded that for every ~250 women invited to screening, 1 breast cancer death is prevented, thus the NHSBSP delivers approximately a 20 % reduction in breast cancer mortality (6).

The main drawbacks to the NHSBSP are over-investigation and overdiagnosis. Overdiagnosis refers to cancers that are detected by screening but would not have otherwise come to attention in the woman's lifetime. Overdiagnosis subsequently leads to overtreatment, as well as unnecessary anxiety and investigations – thus increasing morbidity in the population. The breast screening review conducted by Cancer Research UK in 2012 demonstrated that screening leads to around 4000 women being overdiagnosed in the UK every year (7).

Screen-detected DCIS is thought to be particularly prone to overtreatment. It is generally acknowledged that high-grade DCIS, if left untreated, is more likely to progress to an invasive cancer, but there is less certainty around the significance of intermediate-grade or low-grade DCIS. This is currently the subject of the LORIS Trial, looking into patient outcomes when low-grade DCIS or intermediate-grade DCIS with low-grade features ("low-risk DCIS"), is not subjected to surgery (8).

Currently it is not possible for either patients or doctors to determine which screen-detected cancers represent overdiagnosed cancers. It is estimated that for every 180 women who attend screening, one death is prevented, and for each breast cancer death prevented, around three cancers are overdiagnosed and unnecessarily treated (6).

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Therefore, it can be argued that despite the definite drawback of overdiagnosis and its consequences, the NHSBSP bestows a significant benefit for the population. Clear communication with eligible women around the likely harms and benefits of breast screening should take place, however, in order to maximise patient choice and informed consent.

MCQs

1. DCIS stands for which of the following:

a. Ductal calcification in situ

b. Ductal carcinoma in situ

c. Ductal carcinoma invading stroma

d. Ductal calcification involving stroma

e. Ductal carcinoma involving sidewall

2. The term 'triple assessment' applies to:

a. CC, MLO and lateral mammograms

b. Clinical examination, further imaging and possible biopsy.

c. Examination of breasts, axillae and supraclavicular fossae

d. Appointment with breast surgeon, radiologist and breast care nurse

e. MDT discussion involving pathologist, surgeon and radiologist

3. The independent review performed jointly by Cancer Research UK and the Department of Health (England) in 2012(5) concluded that for every ~250 women invited to screening:

a. One breast cancer death is prevented, thus the NHSBSP delivers approximately a 20 % reduction in breast cancer mortality

b. Two breast cancer deaths are prevented, thus the NHSBSP delivers approximately a 20 % reduction in breast cancer mortality

c. One breast cancer death is prevented, thus the NHSBSP delivers approximately a 25 % reduction in breast cancer mortality

d. Five breast cancer deaths are prevented, thus the NHSBSP delivers approximately a 2 % reduction in breast cancer mortality

e. Four breast cancer deaths are prevented, thus the NHSBSP delivers approximately a 20 % reduction in breast cancer mortality

4. Which of the following is NOT a widely practiced treatment for breast cancer in the UK?

a. Surgical wide local excision

b. Surgical mastectomy

c. Primary endocrine treatment in surgically unfit patients with hormone receptor positive disease

d. Vacuum assisted large bore core biopsy excision of cancer under local anaesthetic

e. Neoadjuvant chemotherapy followed by breast surgery

5. When a patient has had their first normal routine NHSBSP screening mammogram which one of the following should happen:

a. The patient should be reassured that there is no cancer within the breast and therefore there is no need to continue with breast self-examination.

b. The patient should be sent a letter informing them of their result and advising them that they will next be called for screening in 2 years' time.

c. The patient should be sent a letter informing them of their result and advising them that they will next be called for screening in 3 years' time.

d. The patient should be recalled to a breast clinic for the routine adjunctive triple test examination.

e. The radiologists should congratulate themselves on another job well done, and return to their coffee.

Answers

1. b. Ductal carcinoma in situ.

This is the most common type of non-invasive breast cancer, which can be detected through the screening programme, and it is this sub-type of screen-detected breast cancer which is at the heart of debate in terms of possible overdiagnosis and overtreatment as a drawback of the NHSBP.

2. b. Clinical examination, further imaging and possible biopsy.

Triple assessment is the gold standard for evaluation of breast cancer in symptomatic and screening patients, and is the current practice in the NHS.

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3. a. One breast cancer death is prevented, thus the NHSBSP delivers approximately a 20 % reduction in breast cancer mortality.

This is a significant decrease in breast cancer mortality, and therefore although overdiagnosis and overtreatment represent definite drawbacks of the NHSBSP, this provides overall significant benefit to the population.

4. d. Vacuum assisted large bore core biopsy excision of cancer under local anaesthetic.

This technique is not currently recognised as a method of treatment for cancer within the NHS. Removal of breast cancer is surgical; the lesion is removed intact with a rim of normal tissue surrounding it ('margins') for pathological confirmation. Core biopsies, even large bore, perform piecemeal acquisition of pathology, making determination of complete lesion excision/ clear margins difficult.

5. c. The patient should be sent a letter informing them of their result and advising them that they will next be called for screening in 3 years' time.

Mammograms will only detect about 80% of breast cancers, and therefore patients are always advised to continue self-examination. The screening programme has a very robust 'right results' system for ensuring prompt and correct written communication with both the patient and their GP.

Around the world different screening programmes employ different intervals between screens, but in the UK the balance of cost versus effectiveness is considered optimum at 3 years. The radiologists probably won't return to their coffee until they have read at least 2 mammograms.

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CHRONIC MESENTERIC ISCHAEMIA - A HIDDEN EPIDEMIC

H Joshi, D Ettles

Abstract

Mesenteric ischaemia is a complex disorder in which presentations can range from non-specific symptoms to the acute surgical abdomen. It is a condition that can pose diagnostic challenges, both clinically and radiologically and where delayed diagnosis can lead to significant morbidity and even death.

The incidence of mesenteric ischaemia increases as the population age rises with most cases seen in patients over the age of 60. It is multifactorial in aetiology with atherosclerosis being the most common cause. If a diagnosis of mesenteric ischaemia is considered, then appropriate investigations should take place as soon as possible to obtain prompt confirmation of the diagnosis and planning of treatment.

In this article we mainly discuss chronic mesenteric ischaemia with a focus on the important role of role of interventional radiology in the management of this challenging condition.

Case History

A 74 year old woman with a background of ischaemic heart disease and diabetes presented with a 6 month history of vague abdominal pain and bloating which always began approximately one hour following eating. There was associated significant weight loss but no diarrhea or constipation. She underwent OGD which was normal.

A CT scan of her abdomen showed no abnormal masses or gallbladder disease but identified occlusion of the coelic trunk and severe stenosis of the superior mesenteric artery. Further assessment by duplex ultrasonography confirmed functionally severe superior mesenteric artery stenosis. The patient underwent successful stenting of the superior mesenteric artery with complete resolution of her symptoms and steady gain in weight.

Discussion

Mesenteric ischaemia is an under-recognised condition that if undiagnosed leads to high morbidity and mortality. Increasing awareness of the condition, aided by improved diagnostic imaging and the availability in minimally invasive interventional treatments, means that the outlook for many of these patients can be improved (1).

In terms of clinical presentation it can be subdivided into acute and chronic types. Acute mesenteric ischaemia (AMI) has a high mortality if not treated promptly. Patients present with signs and symptoms of an acute abdomen along with acute biochemical derangement. The causes of AMI include arterial occlusion due to thrombosis or emboli, venous outflow obstruction and bowel obstruction.

The clinical presentation is usually dramatic with pathological events taking a predictable course of bowel wall ischaemia, wall necrosis, release of gas within the bowel wall from bacterial proliferation (pneumatosis intestinalis), entry of gas into the mesenteric vessels and portal vein (pneumatosis portalis), bowel perforation, sepsis and ultimately death (2).

It is often stated that chronic mesenteric ischaemia (CMI) or abdominal angina, is relatively rare but evolving clinical experience suggests that it has, in the past, been under-diagnosed. The majority of patients are over the age of 60 with an approximately an equal sex distribution. However, CMI can present in patients from the third decade onwards, particularly where there is history of peripheral arterial disease and heavy smoking.

Mesenteric ischaemia occurs when the blood supply to the postprandial bowel does not meet its metabolic demands, leading to a state of intestinal hypoperfusion. Atherosclerosis of mesenteric vessels is the most common cause and probably accounts for about 95% of cases. Risk factors include smoking, hypertension, hypercholesterolaemia and diabetes mellitus. Other rarer causes of CMI include:

- **Takayasu arteritis**
- **Thromoboangiitis obliterans**
- **Dysplastic lesions**
- **Radiation induced vascular disease**
- **Aortic dissection with extension into the visceral arteries**

CMI most often manifests with nonspecific symptoms which leads to delayed diagnosis (Table 1).

Post-prandial pain
Weight loss
Diarrhoea
Constipation
Post-exercise pain

Table 1 - Symptoms of chronic mesenteric ischaemia.

Patients usually present when symptoms begin to affect their functional ability and they experience significant weight loss. In severe cases, patients may develop fear of eating and experience prolonged bouts of abdominal pain with associated weight loss and hypoalbuminaemia (Figure1).

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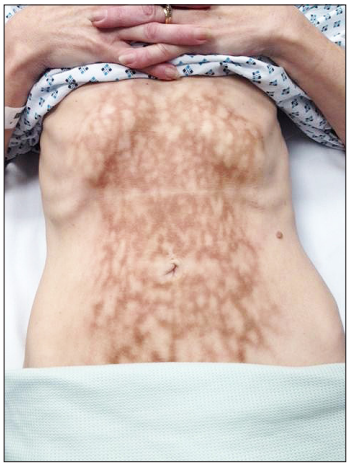

Figure 1 – Because of severe recurrent abdominal pain, this patient with chronic mesenteric ischaemia has used hot water bottles to gain relief. This has resulted in skin discolouration known as erythema ab igne. Note the features of significant weight loss.

A combination of increased age and presence of vague symptoms often prompts an initial diagnosis of suspected malignancy which is later retracted following multiple investigations. Similar to AMI, if left untreated CMI patients can suffer from profound malnutrition, bowel infarction/perforation, sepsis and death. Patients can also present in the acutely setting as described earlier with an acute on chronic episode (3).

The major abdominal visceral arteries are the coeliac axis, superior mesenteric artery (SMA) and inferior mesenteric artery (IMA). Although it is widely accepted that the involvement of at least two of these major vessels is required for the diagnosis of CMI, in the authors' experience this is not necessarily the case. We shall briefly discuss the anatomy of the major visceral arteries.

The coeliac artery is the first major visceral branch of the abdominal aorta arising anteriorly at the level of approximately T12. It typically has three branches; left gastric artery, splenic artery and common hepatic artery. It is the artery to the foregut supplying the gut from the distal oesophagus to the 2nd part of the duodenum, liver, gallbladder, pancreas and spleen.

The SMA is the second unpaired anterior branch of the abdominal aorta arising at the level of L1. The majority of the SMA course is to travel within the small bowel mesentery giving off jejunal and ileal branches on the left and branches to the proximal and mid colon on the right. The SMA supplies the gut from the 2nd part of the duodenum to the splenic flexure of the colon.

The IMA is the third unpaired anterior branch of the abdominal aorta arising at the level of L3. The IMA is the smallest of the three major visceral arteries and supplies the hindgut from the splenic flexure to the proximal rectum (4).

Investigation

Once a diagnosis of chronic mesenteric ischaemia is suspected, investigations should be carried out urgently for confirmation and planning of subsequent treatment.

In CMI, imaging can be broadly divided into abdominal imaging and visceral artery imaging. As presentations are typically vague, patients are often initially suspected to have other abdominal pathology such as an underlying malignancy. Due to this, common initial investigations will include a CT scan of the abdomen with intravenous and oral contrast.

Biochemical testing may reveal deranged liver function tests (LFTs) and further assessment by ultrasound (USS) or magnetic resonance cholangiopancreatography (MRCP) will have often been performed for the assessment of the biliary system and pancreas. Upper and lower gastrointestinal tract endoscopy is commonly performed if a primary gut pathology is suspected.

The above investigations will rule out the majority of the nonvascular causes of abdominal pain. Assessment of the bowel vasculature should be the next step. Abdominal CT scans, as discussed earlier, can demonstrate vascular disease in the form of vessel wall calcification. They may also demonstrate occlusions or stenoses of the major vessels and these are best assessed in the sagittal plane of an arterial phase contrast enhanced study (Figure 2).

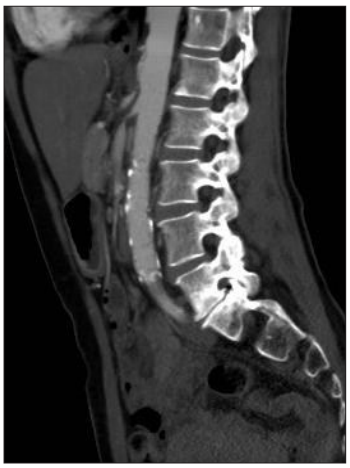

Figure 2 – Contrast enhanced abdominal CT scan showing in the sagittal plane demonstrates a severe stenosis at the origin of the coeliac axis and a severe stenosis in the proximal superior mesenteric artery.

Although the CT scan can potentially identify a vascular abnormality, it may not give a reliable indication of the severity of the disease. A further assessment to assess degree of stenosis can be carried out using duplex ultrasound scanning. Duplex USS is a low cost and noninvasive method of assessing the central abdominal arteries and can reveal the extent of mesenteric vessel disease with high sensitivity and specificity in trained hands.

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Both the coeliac axis and SMA can be readily assessed using initially B-mode USS imaging followed by duplex USS with measurements of blood flow velocity. Measurements of peak systolic flow velocity (PSV) are made and compared to flow velocity within the proximal abdominal aorta. The PSV is considered to be the single best parameter for grading stenosis of the mesenteric vessels.

As the severity of stenosis increases the arterial waveform on duplex USS broadens with an increase in PSV. If flow velocity more than doubles, then the degree of stenosis is considered to be significant. In some cases, velocities in excess of 6m/s may be recorded – normal flow velocity would be expected to be around 1.2 m/s (Figure 3).

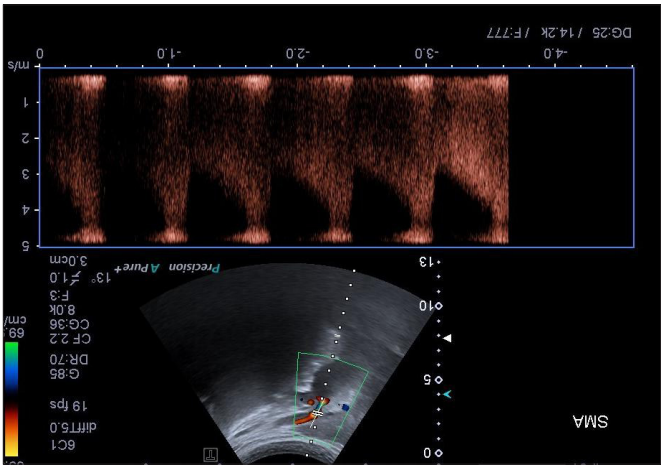

Figure 3 – Duplex ultrasound examination of the superior mesenteric artery showing broadening of the arterial waveform with a peak systolic velocity in excess of 4m/s. There is aliasing artifact indicating that the true peak velocity may be even higher. These findings are consistent with critical vessel stenosis

Duplex USS can be used for serial monitoring of the mesenteric vessels if patients are initially managed conservatively and also following any intervention that has taken place.

The gold standard for the assessment of the mesenteric vessels remains that of digital subtraction catheter angiography. This gives detailed anatomical information of the vessels including variant anatomy along with the extent of any disease present. Often patients will develop collateral vascular supply, a sign of chronic disease, and this is usually easily identifiable.

Mesenteric catheter angiography is commonly performed as a daycase procedure via a single femoral artery access route. Findings may then be discussed at the vascular multidisciplinary team (MDT) meeting before any further intervention is carried out although in many cases this will be combined with endovascular treatment on the same attendance (Figure 4).

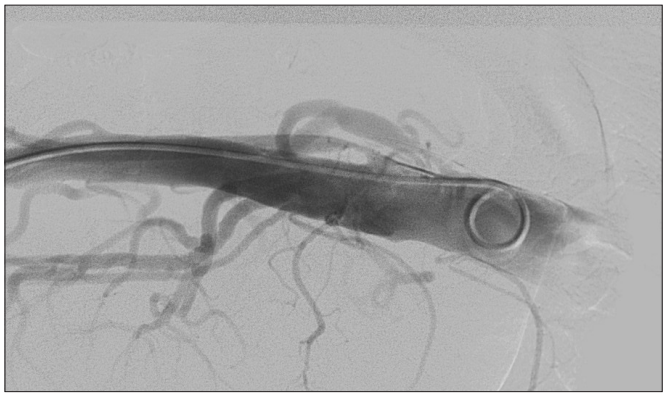

Figure 4 – Lateral digital subtraction catheter angiogram is showing a significant stenosis of the coeliac trunk and a severe stenosis in the proximal superior mesenteric artery.

Magnetic resonance angiography can also be used in the assessment of CMI but is more susceptible to artifact and less commonly used as the investigation of choice in these patients.

In the setting of acute mesenteric ischaemia, patients are usually critically unwell with signs of sepsis. The principle investigation here is abdominal CT with intravenous contrast. Oral contrast should not be administered as this hinders the assessment of bowel. The CT scan can demonstrate multiple findings to support the diagnosis including bowel obstruction, perforation, lack of bowel wall enhancement, pneumatointestinalis, pneumatoportalis and occlusion of major abdominal visceral arteries (Figure 5a-b). A normal CT scan does not exclude acute mesenteric ischaemia.

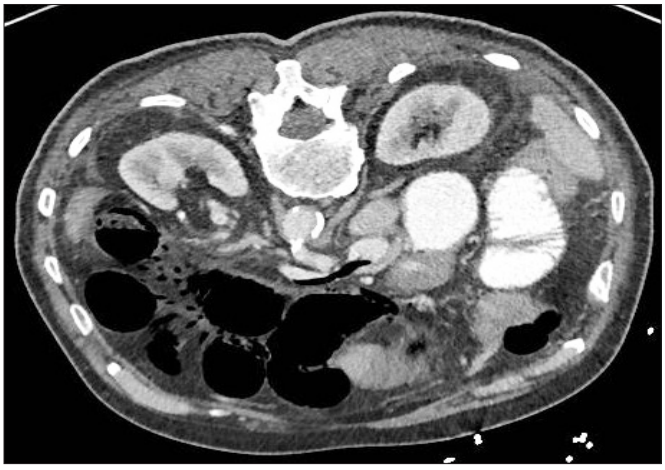

Figure 5a – Transaxial contrast enhanced CT scan is showing gas within the portal vein and small bowel intramural gas (pneumatosis intestinalis).

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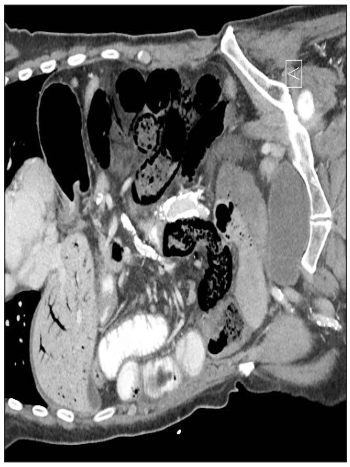

Figure 5b – Coronal reformat of the same CT scan is showing gas within the intrahepatic portal venous system along with pneumatosis intestinalis, and gas within the portal vein.

Management

Treatment of CMI has evolved over the last 20 years with options broadly consisting of medical, surgical or endovascular management. Intervention is generally offered to the symptomatic patient with medical treatment reserved for a small number of patients considered to be at too high a risk. Radiologically guided intervention has now all but replaced traditional surgical treatment s it offers significant reductions in morbidity and mortality as well as shorter hospital stay and greater patient acceptability.

Surgical revascularization

There are principally two methods of surgical vascularization. Endarterectomy of the vessel walls can be performed to increase vessel caliber and is usually performed when stenosis of the vessel is >70%. All three major visceral vessels can be treated with reported symptom improvement in up to 90% of patients. The second option consists of surgical bypass and this can either be antegrade (supracoeliac aorta to visceral vessel) or retrograde (distal aorta or iliac artery to visceral vessel). Both procedures carry significant risks and symptoms can reoccur in approximately 10% of patients.

Endovascular revascularisation

Endovascular revascularization has increased in popularity and taken over open surgical procedures in the last two decades (5,6). These are minimally invasive procedures performed by interventional radiologists under X-ray fluoroscopic guidance to identify the extent of disease and perform intervention. Endovascular treatment principally can be categorized into two forms; balloon angioplasty and stent insertion. In some cases a combination of both will be necessary.

Arterial access for these procedures is typically acquired through a femoral or brachial arteriotomy. With the use of specific shaped catheters and guidewires, access into the target vessel is gained and the planned intervention performed. Nowadays, the majority of patients will undergo preliminary balloon angioplasty followed by insertion of a metallic stent. The superior mesenteric artery is the most commonly treated vessel followed by the coeliac artery with only a few cases involving the inferior mesenteric artery.

During the procedure the patient is given intra-arterial heparin and often commenced on dual platelet therapy following the procedure - commonly 3-6 months of clopidogrel and life-long aspirin. These procedures are generally well tolerated and can be performed either as a day case or single overnight admission. Although endovascular revascularization carries some risks such as access site complications, distal embolisation and stent dislodgement, these are rare in practice (Figure 6a-c). Follow-up is by clinical review and annual duplex ultrasound to monitor stent patency and detect restenosis.

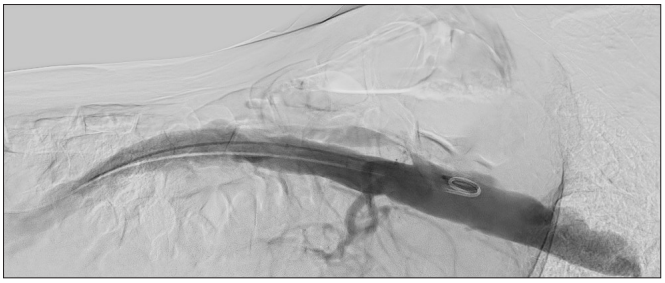

Figure 6a – Initial catheter aortogram demonstrates a critical stenosis of the superior mesenteric artery.

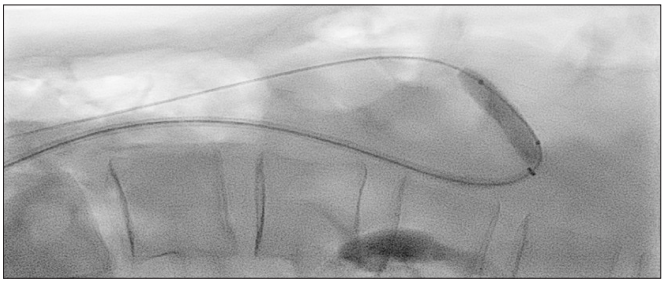

Figure 6b – During the procedure, the collapsed stent is passed through the SMA stenosis, deployed using a balloon and moulded into position.

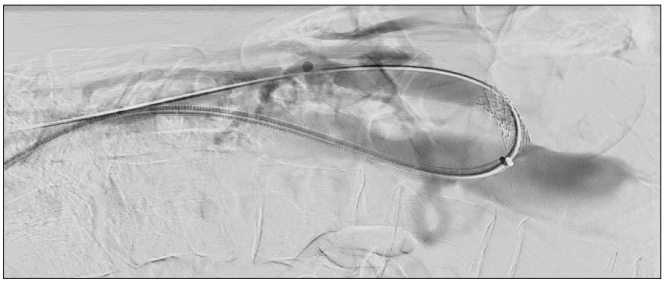

Figure 6c – Repeat angiogram after at the end of the procedure demonstrates an excellent angiographic result with a patent SMA.

CHRONIC MESENTERIC ISCHAEMIA - A HIDDEN EPIDEMIC

H Joshi, D Ettles

Conclusions

Mesenteric ischaemia is a multifactorial condition that is often recognised late. The delayed presentation is due to non-specific symptoms and diagnosis is often made only after multiple investigations have been performed. Radiological intervention with balloon angioplasty and stent placement can transform a patient's quality of life and avoid progression to sever acute mesenteric ischaemia. CMI is a diagnosis that should be considered in all patients with vague abdominal symptoms and who are at increased risk of vascular disease.

MCQ s – Best of 5

1. The findings of acute mesenteric ischaemia on an abdominal CT scan include:

a. Normal appearing bowel

b. Pneumatointestinalis

c. Pneumatoportalis

d. Thrombus within mesenteric vessels

e. All of the above

2. Which of the following statements is correct:

a. The coeliac axis supplies blood to the liver, pancreas, spleen, stomach and small bowel

b. The superior mesenteric artery is the arterial supply to the foregut

c. The superior mesenteric artery supplies the gut from the second part of the duodenum to the splenic flexure of the colon

d. The inferior mesenteric artery supplies the entire colon

e. The inferior mesenteric is the arterial supply to the midgut

3. A 45 year old female with a history of post-prandial pain and weight loss was suspected to have mesenteric ischaemia. The patient is also known to suffer from cold hands and feet.

They underwent a mesenteric catheter angiogram, which demonstrated multiple irregular narrowing's of the superior mesenteric artery with aneurysm formation. The most likely diagnosis is:

a. Atherosclerosis

b. Chronic arterial dissection

c. Takayasu arteritis

d. Thromboangiitis obliterans

e. Rheumatoid vasculitis

4. A 74 year old female with a history of coronary heart disease and diabetes, presents to her GP with an 8 month history of post-prandial pain and weight loss of 13kg. She has lost interest in eating. An abdominal CT scan is performed which showed significant atherosclerosis of the visceral vessels and no other abnormality.

Chronic mesenteric ischaemia is suspected. Which low cost investigation will provide a functional assessment of the visceral vessels and aid in diagnosis quickly?

a. Abdominal ultrasound

b. MRI scan of mesenteric vessels

c. Catheter angiography of the mesenteric vessels

d. Duplex ultrasonography of the coeliac trunk and superior mesenteric artery

e. CT angiogram of the abdominal aorta

5. A 77 year old male with post-prandial abdominal pain and weight loss is suspected to have chronic mesenteric ischaemia. He has a past medical history of hypertension only.

Duplex ultrasonography is performed and identifies a significant stenosis of the superior mesenteric artery. What is the next best management option?

a. Conservative management

b. Medical management with anticoagulant therapy

c. Open surgical endarterectomy

d. Endovascular revascularisation

e. Bypass surgery

CHRONIC MESENTERIC ISCHAEMIA - A HIDDEN EPIDEMIC

H Joshi, D Ettles

MCQ Answers

Answer 1: e

Any of the above findings can be present in acute mesenteric ischaemia with the more concerning signs (e.g. pneumatointestinalis and portal venous system gas) being present as the severity of the condition increases.

Answer 2: c

The superior mesenteric artery is the blood supply to the midgut and supplies bowel from the second part of the duodenum to the splenic flexure of the colon.

Answer 3: e

All of the options are causes of mesenteric ischaemia but the clue to the answer is the history of cold hands and feet and the angiographic findings. Takayasu arteritis is a granulomatous large vessel vasculitis with a strong female predominance. Angiographic findings include areas of vessel stenosis, pseudoaneurysm formation as well as occlusion.

Answer 4: d

Duplex ultrasonography is a low cost procedure that can be carried out quickly and provide a assessment on the degree of stenosis of a vessel and this can ultimately help guide further management.

Answer 5: d

Endovascular revascularisation is the next best management option. This carries less risk compared to open surgery and patients can notice an improvement in their symptoms within hours of the procedure. In cases of severe mesenteric stenosis, medical management is unlikely to provide a significant benefit.

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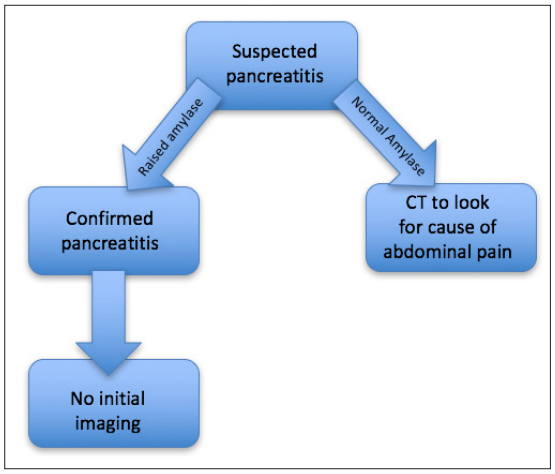
IMAGING OF ACUTE PANCREATITIS

AE Helmy, AS Shaw

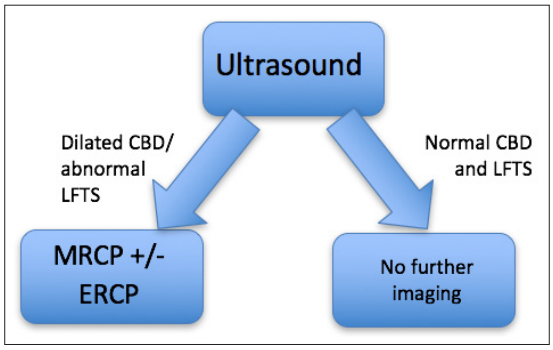
Abstract

Pancreatitis is a well-recognised cause of acute abdominal pain. Patients may be very sick, with non-specific clinical findings on initial presentation, later on in the disease's course multi-organ failure is common. Imaging in pancreatitis can seem confusing. In this article we present a case of acute pancreatitis and present a pictorial review of imaging findings and complications. Finally we will review the rationale for imaging patients with pancreatitis at various stages of the illness.

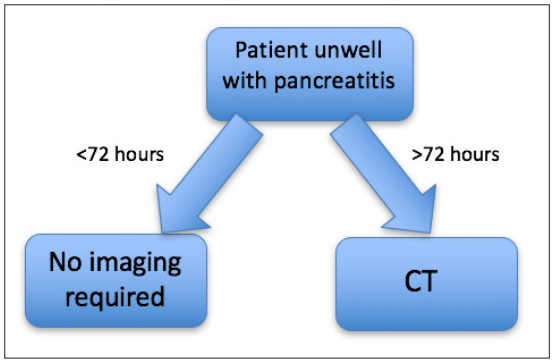
Diagnosis



Establishing Cause Of Parcreatitis



Looking For Complications Of Pancreatitis



Case History

A 45 year old female presented to the Emergency Department with a 12 hour history of severe upper abdominal pain, vomiting and pyrexia. Observations at presentation: temperature 38.2°C; P 100 bpm; BP 100/80 mmHg; O_2 saturation 85%.

Selected initial investigations (normal ranges in brackets) revealed a serum amylase of 2000 u/l (25-140 u/l); bilirubin 120 µmol/l (<17 µmol/l), Urea 22 mmmol/l (3-6.5 mmmol/l) ; WCC 21 x 10^9/l (4.5-11 x10^9/l); CRP 220mg/l (<5/l) PO_2 7 kPa (>10.5 kPA) PH of 7.1 (7.35-7.45) ;lactate of 5 mEq/l (<2 mEq/l) . Urine output was recorded at 10 ml/hr (>30 ml/hr).

In the light of the clinical features and elevated amylase, the admitting surgical team made the diagnosis of acute pancreatitis (AP), with multi-organ failure, and the patient was admitted to intensive care for supportive management.

An ultrasound scan was requested (Figure 1A and 1B). This revealed numerous gallstones within a thin walled gallbladder and a dilated common bile duct measuring 15mm.

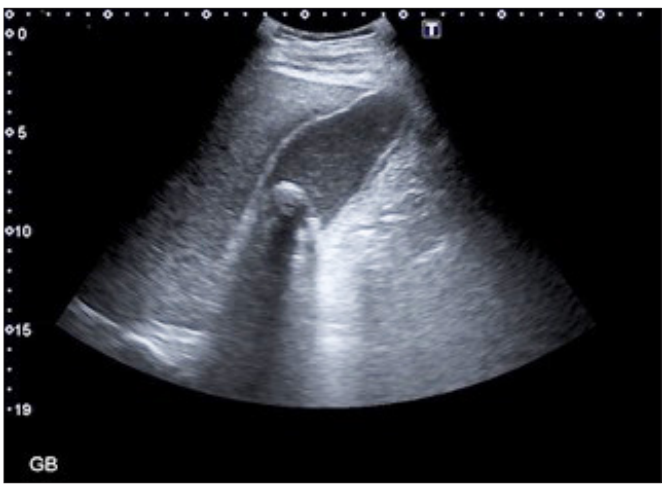


Figure 1A: Multiple hyperechoic structures in the gallbladder which produce an acoustic shadow consistent with gallstones.

IMAGING OF ACUTE PANCREATITIS

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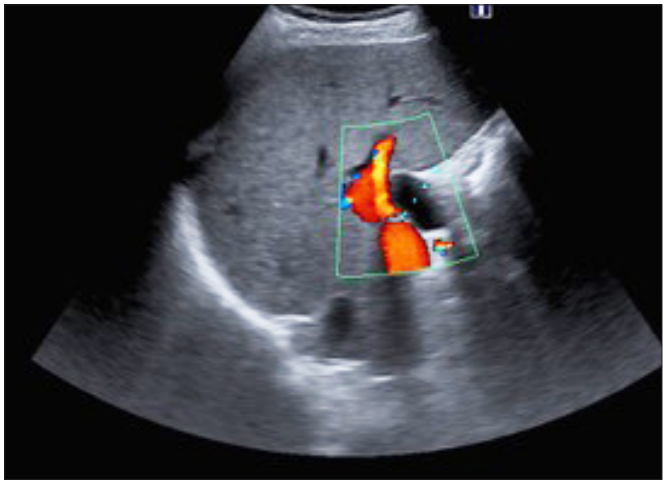

Figure 1B: Dilated CBD measuring 1.5cm, CBD should normally measure up to 7mm.

To further evaluate the bile duct, an MRCP study was performed (Figure 2), which confirmed obstructing calculi.

Figure 2: MRCP coronal fluid sensitive sequence showing CBD dilatation with gallbladder and CBD stones.

The patient proceeded to ERCP, where several obstructing calculi were removed (Figure 3).

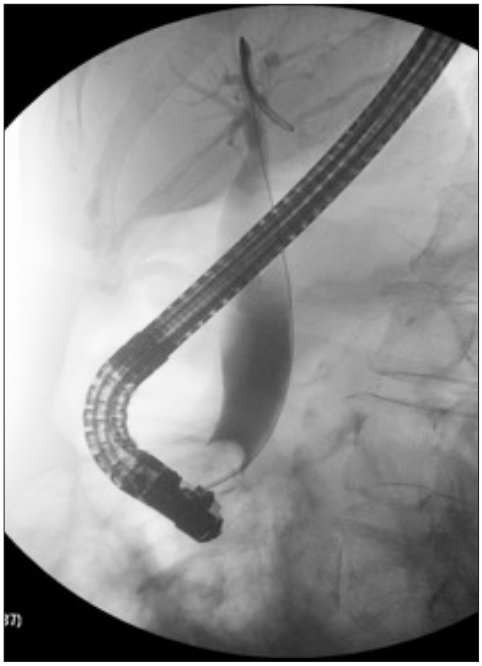

Figure 3: ERCP, with a large filling defect in the distal CBD and biliary dilatation.

Over the next week the patient remained unwell, with features of ongoing sepsis. A CT of the pancreas showed extensive pancreatic necrosis and a fluid collection anterior to the pancreas (Figure 4).

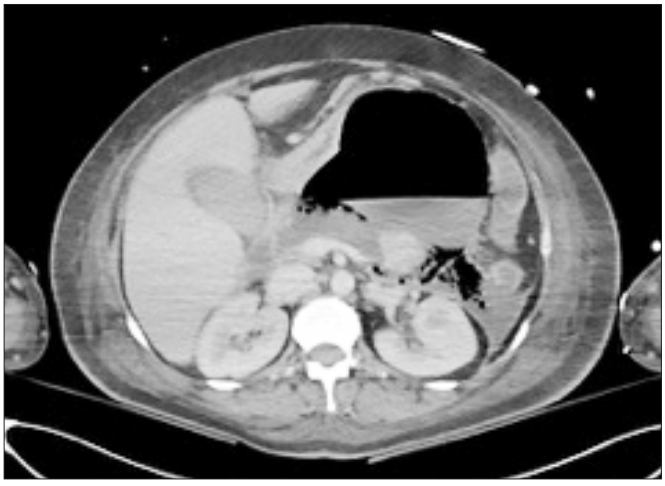

Figure 4: CT showing pancreatic necrosis with poorly enhancing head and tail of pancreas containing air. Body of pancreas enhances normally. Large air-containing collection anterior to the pancreas.

IMAGING OF ACUTE PANCREATITIS

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In an attempt to treat these collections, several CT guided peripancreatic drains were inserted (Figure 5).

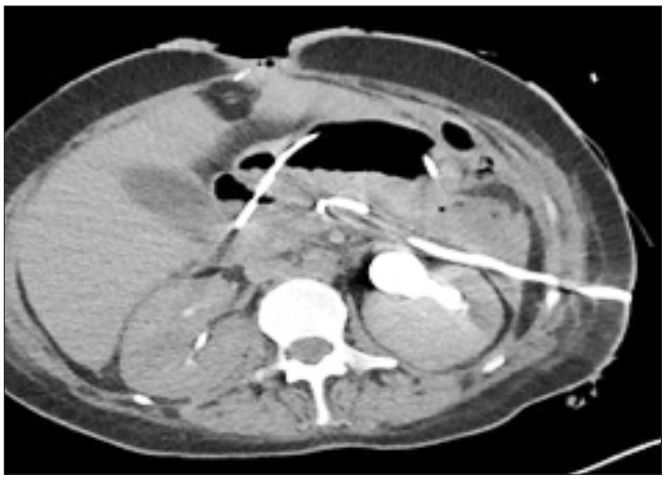

Figure 5: Left flank approach CT-guided drain.

Despite best supportive treatment and multiple drains, the patient did not improve and a percutaneous necrosectomy was performed by the hepatobiliary surgeons. Following necrosectomy the sepsis gradually resolved. However, two weeks after initial presentation, the patient became hypotensive. In view of the clinical concern of haemorrhage, a triple phase CT scan of the abdomen was performed, which showed a bleeding pseudoaneurysm adjacent to the pancreas.

The patient was transferred to the interventional radiology suite where this was successfully embolised. The patient had a prolonged convalescence, developing both endocrine and exocrine pancreatic failure requiring insulin and pancreatic enzyme replacement, but was eventually discharged home.

Discussion

Pancreatitis is a common condition, and the mnemonic 'GETSMASHED' 2 lists the causes, (Gall stones, Ethanol, Trauma, Steroids, Mumps, Autoimmune, Scorpion bites, Hypercalcaemia, ERCP and Drugs). Approximately 50% of pancreatitis cases are caused by gallstones and 20% by alcohol excess 3 (these proportions depend on the population being examined and their drinking habits). Consequently, a careful alcohol history should be taken for patients presenting with pancreatitis and an ultrasound performed to exclude gallstones. The rarer causes of pancreatitis are usually easy to identify, (e,g, the patient who has just had an ERCP).

Regarding imaging in acute pancreatitis, it is best to consider the following stages:

1. Diagnosis

Acute pancreatitis (AP) is a clinical and biochemical diagnosis. If there is clinical uncertainty, CT may be used to exclude other causes of an acute abdomen. However, imaging within the first 48-72 hours may be normal or underestimate the severity of AP.

2. Establishing causation

Ultrasound +/- MRCP imaging to look for gallstones or bile duct calculi may be helpful, but a careful history including alcohol consumption should be sought. Ultrasound is a quick, non-invasive test that is superior to CT in identifying gallstones. ERCP is reserved for therapeutic intervention given its attendant risks.

3. Disease severity

CT imaging of the abdomen 48 hours after the onset of symptoms is the best time to assess disease severity radiologically. This should be used judiciously in combination with other clinical scoring systems (e.g. Ranson's Criteria, Modified Glasgow score).

4. Identifying complications

CT is the best modality for identifying complications of AP. Focal fluid collections may require image-guided drainage. If there are suspected vascular complications (e.g. pseudoaneurysm), arterial phase imaging should also be performed.

Pancreatitis, particularly necrotising pancreatitis, can be a very severe disease with significant mortality and morbidity (1). Treatment has traditionally been supportive. Many treatments have been attempted, including peritoneal lavage and open surgical necrosectomy, with poor results. More recently, percutaneous necrosectomy has been shown to reduce mortality in necrotising pancreatitis (4).

Initially, pancreatic drains are inserted (usually under CT guidance), then these are serially dilated under fluoroscopic (video x-ray) guidance. Pancreatic surgeons then perform surgery through these tubes in a procedure similar to laparoscopy to remove foci of necrotic tissue. This differs from laparoscopy in that necrosectomy is often retroperitoneal and does not require a pneumoperitoneum.

Test yourself

1. What are the two most common causes of pancreatitis in the UK?

Gallstones, Scorpion bites, Autoimmune pancreatitis, Alcohol excess, Mumps, ERCP.

2. What is the first line imaging to establish causation in pancreatitis?

CT, MRCP, ERCP, HIDA scan, Ultrasound.

3. Which of these are complications of pancreatitis?

Pancreatic pseudocyst, Pseudoaneurysm, ARDS, duodenal perforation, All of the above.

IMAGING OF ACUTE PANCREATITIS

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4. How is pancreatitis usually diagnosed?

Ultrasound, CT, clinical diagnosis, Serum biochemistry - (Amylase and Lipase), none of the above.

5. Which of these is not a cause of pancreatitis?

ERCP, Gallstones, Trauma, Mumps, hypokalaemia.

Answers

Answer 1

Gallstones account for around 50% of pancreatitis, alcohol excess 20% other causes account for the remaining 30%.

Answer 2

Ultrasound is the first line investigation, as it is readily accessible, good at identifying gallstones and does not involve ionising radiation. CT may be used to evaluate the cause of pancreatitis when this is in doubt and later in the course of the disease to evaluate complications of pancreatitis.

MRCP is time consuming and difficult to perform on ill patients; certain patients such as those with pacemakers may not be able to have an MRI scan. ERCP is an invasive procedure that is reserved for patients who require treatment for biliary obstruction. HIDA scan is a nuclear medicine study that can be used to diagnose cholecystitis, It is not routinely used in imaging pancreatitis.

Answer 3

All of the above. ARDS can develop 12-24 hours after initial presentation with pancreatitis. Direct complications of pancreatitis generally develop after 5 days of initial presentation.

Answer 4

Serum biochemistry. Pancreatitis is generally diagnosed with an amylase 3 x the upper limit of normal i.e. 300-400 u/l (normal range 25-140 u/l), serum amylase can be mildly elevated when patient is vomiting for another reason such as bowel obstruction. In cases of chronic pancreatitis or delayed presentation when the amylase may not be raised, then CT may have a role in diagnosing pancreatitis.

Answer 5

Hypokaleamia. All the others are causes of pancreatitis. Don't get confused with hypo and hypercalcaemia, which are causes of pancreatitis. Pancreatitis can also cause hypocalcaemia.

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IMAGING OF ACUTE PULMONARY EMBOLISM: CT PULMONARY ANGIOGRAPHY & OTHER IMAGING TECHNIQUES

J Coates, J Martin, M Kon

Abstract

Acute pulmonary embolism is a serious and potentially fatal condition that can present non-specifically and be challenging to diagnose clinically. It is a diagnosis that many clinicians fear missing. Recent increasing awareness has led to further demand for accurate diagnosis. Clinical assessment should determine risk, and in selected patients radiological investigation is required. Computed tomography pulmonary angiogram is the current investigation of choice allowing diagnosis or exclusion of pulmonary embolism, as well as diagnosing alternative causes for a patient's symptoms. The purpose of this review is to provide an overview of the background, clinical presentation and investigation of pulmonary embolism.

Introduction

Acute pulmonary embolism (PE) is a serious condition and a diagnosis that can be challenging for even the most experienced physician and one that many fear missing. In recent decades there has been increasing awareness among clinicians and patients about deep vein thrombosis (DVT) and PE which are manifestations of venous thromboembolism (VTE). There is an increasing demand for accurate and safe diagnosis and as clinical diagnosis is difficult, imaging lies at the heart of this process. Currently the most commonly used imaging modality is computed tomography pulmonary angiography (CTPA). Imaging may also aid in the diagnosis of a causative factor, such as occult malignancy.

This article reviews the clinical aspects of PE and radiological investigations that are used to refute or confirm its diagnosis. The roles and limitations of common imaging modalities will be discussed as well as the use of imaging for prognosis and treatment planning.

Epidemiology

Determining the true incidence of PE is difficult because of the challenges surrounding clinical diagnosis. The incidence of asymptomatic PE is uncertain and the diagnosis may be an incidental one. Previous large population based studies have shown the incidence to be 60-70 cases per 100000 (1, 2). More recently the figure has been estimated to be closer to 110 cases per 100000 (3), although it has been postulated that this apparent increased incidence is actually due to the increased detection ability of CTPA. The overall mortality of PE at 3 months is around 15% (4, 5).

Risk Factors for Pulmonary Embolism

Risk factors for VTE are well established, including inherited thombophilias, acquired medical conditions, undergoing certain surgical procedures, medications and the peripartum state. Between 25 and 50% of pulmonary emboli are idiopathic, without any recognised risk factor present. The British Thoracic Society has classified risk factors into major and minor depending on their relative contribution to the risk of VTE (6) (table 1).

Pathophysiology

The pathological basis of VTE is Virchow's Triad: thrombosis occurs in the presence of venous stasis, a hypercoaguable state and where vessel wall damage has occurred. PE can be considered a complication of a DVT. A DVT will normally start in the calf veins, proliferating proximally and then may break free to cause PE (7). Less commonly a PE will originate from a thrombus in the pelvic, renal or upper limb veins or the right heart chamber. Larger PE lodge at the bifurcation of the pulmonary trunk or lobar branches and cause consequent haemodynamic compromise. Smaller thrombi travel distally and are more likely to cause pain as the emboli produce an inflammatory response and irritate the parietal pleura. The lower lobes are more commonly affected due to the preferential blood flow to these areas.

Major Risk Factors (relative risk 5-20)	
Surgery	Major/abdominal/pelvic surgery, hip/knee replacement, postoperative intensive care
Obstetrics	Late pregnancy, caesarean section, puerperium
Lower limb problems	Fracture, varicose veins
Malignancy	Abdominal/pelvic, advanced/metastatic
Reduced mobility	Hospitalisation, institutional care
Miscellaneous	Previous proven VTE
Minor Risk Factors (relative risk 2-4)	
Cardiovascular	Congenital heart disease, congestive cardiac failure, hypertension, superficial venous thrombosis, indwelling central venous catheter
Oestrogens	Oral contraceptive, hormone replacement therapy
Miscellaneous	COPD, neurological disability, occult malignancy, thrombotic disorders, long distance sedentary travel, obesity

Table 1. Risk factors associated with venous thromboembolism. Adapted from BTS guidance on PE12.

Classification of Pulmonary Embolism

PE may be classified according whether it is acute or chronic, or according to the severity of clinical presentation. PE may be acute with an abrupt onset in symptoms or chronic where the patient develops symptoms more insidiously. In the latter cases these patients will tend to present with features of pulmonary hypertension, primarily shortness of breath.

Further classification may be made according the patient's haemodynamic state. The 2014 European Society of Cardiology (ESC) guidelines on PE divide patients into high risk and not high risk (8). A high risk patient will have haemodynamic compromise whereas not high risk patients have a normal BP. Haemodynamic compromise is used because it is associated with a poorer outcome (8, 9). The American Heart Association refers to these patients as having a massive PE.

IMAGING OF ACUTE PULMONARY EMBOLISM: CT PULMONARY ANGIOGRAPHY & OTHER IMAGING TECHNIQUES

J Coates, J Martin, M Kon

Patients who are normotensive but have evidence of right heart dysfunction associated with acute pulmonary embolism are classified as having submassive PE. This may be demonstrated at echocardiography, CTPA or by elevated biomarkers. These patients also have worse short term outcomes than those with uncomplicated PE (10).

Clinical Features of Pulmonary Embolism

The symptoms and signs associated with pulmonary embolism are often non-specific, contributing to the difficulty of clinical diagnosis. The single most common symptom in patients is dyspnoea, likely to be abrupt in onset (11, 12). Other symptoms include haemoptysis, pleuritic chest pain, cough, fever or symptoms of a DVT. Syncope is a less common presentation and may be associated with larger PE. The classic triad of dyspnoea, haemoptysis and pleuritic chest pain occurs relatively uncommonly.

Signs that may be present on examination include tachypnoea, tachycardia and hypoxia. On examination of the chest there may be reduced breath sounds or crackles. The patient may have features of right ventricular dysfunction such as right ventricular lift or jugular venous distension. Cardiogenic shock occurs in just 5-8% of cases but is associated with a worse outcome (13).

D-dimer and Risk Scoring

D-dimer is an enzymatic degradation product that is produced as clots are broken down. The value of the d-dimer rises with increasing turnover of clot within the body as occurs with DVT or PE. D-dimer is non-specific and increases in response to a range of different conditions including pregnancy, malignancy and trauma. It is a sensitive test and when used in the correct clinical situations it is effective at ruling out DVT or PE in low risk patients. Indiscriminate use of d-dimer assay may lead to inappropriate investigation for PE.

The sensitive but non-specific nature of the d-dimer led to the development of clinical risk scores allowing accurate use of the test. The most commonly accepted is the Wells score, originally published in 2000 (13). The original score used a combination of risk factors and clinical parameters to derive a score out of 12.5 (table 2). Patients were then placed into low, intermediate or high risk groups depending on their score; this determined their onward investigation, reflecting the probability that these patients would have a PE. D-dimer would only be used to rule out VTE in low risk patients. Patients in the intermediate risk group could be investigated with d-dimer or imaging and patients in the high risk group would always undergo imaging.

A simplified 2-level version using the same scoring criteria is employed as part of the national institute of health and clinical excellence (NICE) guidance on the diagnosis and management of VTE (14). The diagnostic pathway is demonstrated in figure 1.

Clinical Feature	Score
Clinical signs and symptoms of deep vein thrombosis	3
Alternative diagnosis is less likely than PE	3
Heart rate > 100	1.5
Immobilisation for at least 3 days or surgery in the previous 4 weeks	1.5
Previous objectively diagnosed PE or DVT	1.5
Haemoptysis	1
Malignancy with treatment within 6 months or palliative	1

Table 2. Wells score.

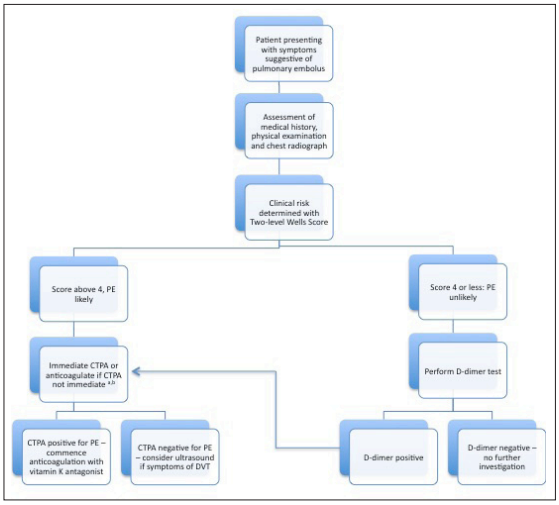

Figure 1. Diagnostic pathway for acute PE. Adapted from NICE guidance CG144 (13).

a) If CTPA not immediately available commence parenteral anticoagulation with low-molecular weight heparin.

b) Consider planar or SPECT V/Q if the patient has a severe contrast allergy or severe renal impairment.

Radiological Investigation of Pulmonary Embolism

Chest Radiograph

All patients who are suspected of having a PE should have a chest radiograph. But, as there are no specific findings on the radiograph for PE, its main benefit is to rule out an alternative cause for the patient's symptoms, such as infection or pneumothorax. The majority of patients with PE will have an abnormal radiograph (11, 15).

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The commonest abnormalities are atelectasis or parenchymal abnormalities such as consolidation. Other less common radiographic abnormalities include pleural effusion, elevated hemidiaphragm, reduced vascular markings and cardiomegaly. Several eponymous radiographic signs have been described in connection with PE:

- *Westermark sign - focal segmental oligaemia in the area affected by the PE*

- *Hamptons hump - a pleural based, dome-shaped hump due to pulmonary infarction*

- *Fleischner sign - a prominent central pulmonary artery expanded by PE*

These radiographic signs have subsequently found not to be specific to pulmonary embolism and occur infrequently (15).

Computed Tomography Pulmonary Angiography (CTPA)

In recent times CTPA has become widely accepted as the first line imaging modality in the diagnosis of PE.

Two major technological advances in computed tomography have pushed it to the forefront - these are the development of the spiral or helical CT scanner and the development of the multi-detector receptor. These allow the scan to be acquired much quicker reducing the likelihood of respiratory motion artefact. Additionally there is better spatial resolution and PEs in smaller vessels can be more confidently diagnosed. The PIOPED II study showed that a good diagnostic quality CTPA was highly specific and moderately sensitive (16). Subsequently it has been shown that CTPA is sensitive enough to exclude PE even in patients with a high clinical probability (17).

A standard CTPA requires the patient to have an 18 or 20-gauge venous cannula, ideally in the antecubital fossa, allowing rapid delivery of the contrast bolus. For the scan to be diagnostic the pulmonary arteries need to be adequately opacified with contrast to allow detection of an embolus and avoid false positive diagnosis due to flow artefacts. Additionally, depending on the protocol, a CT venogram of the lower limbs may be included.

After acquisition the images are interrogated for pulmonary emboli, which appear as filling defects in the contrast-opacified vessels. If no PE is demonstrated an alternative cause for the patient's symptoms may be identified, such as infective consolidation, malignancy or pulmonary oedema due to heart failure.

Diagnostic criteria for PE include (18):

- *Arterial occlusion with failure to enhance the entire lumen due to a large filling defect; the artery may be enlarged compared to adjacent patent vessels (figure 2)*

- *Partial filling defect surrounded by contrast material producing a polo mint sign on images perpendicular to the vessel long axis (figure 3) and a railway track sign on longitudinal images of the vessel (figure 4)*

- *Peripheral intraluminal filling defect that forms acute angles with the arterial wall (figure 5).*

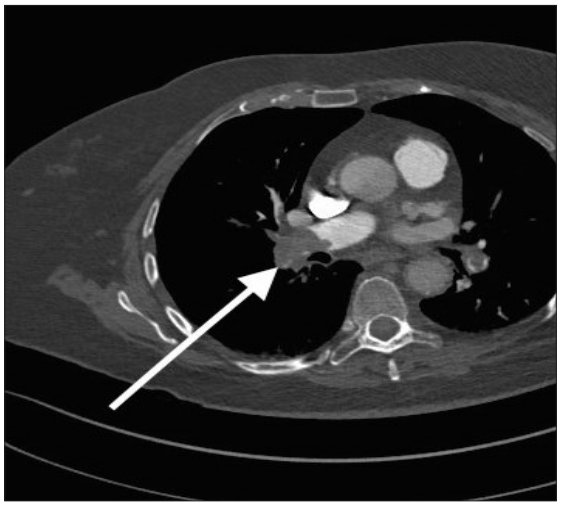

Figure 2. Right main pulmonary artery completely occluded by embolus.

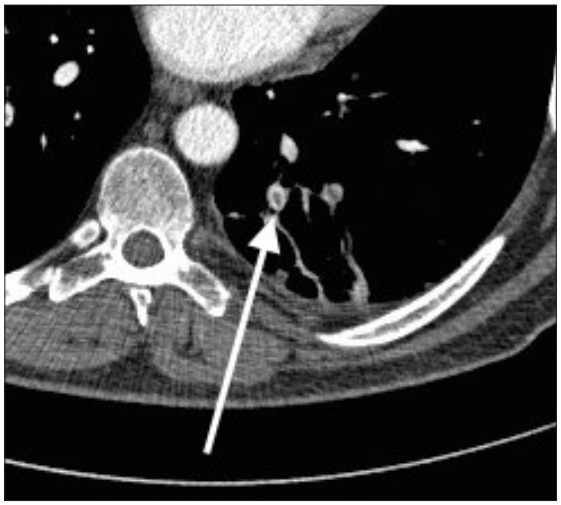

Figure 3. The polo mint sign – an embolus appearing as filling defect within a pulmonary artery entirely surrounded by contrast. Note the adjacent atelectasis that is likely the result of the PE.

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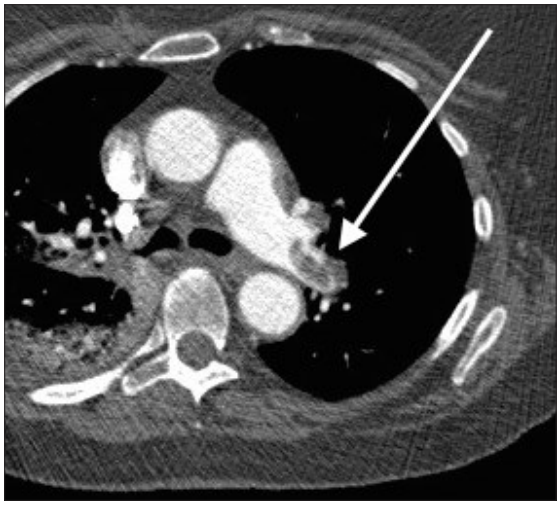

Figure 4. The railway track sign – embolus centrally in the left main pulmonary.

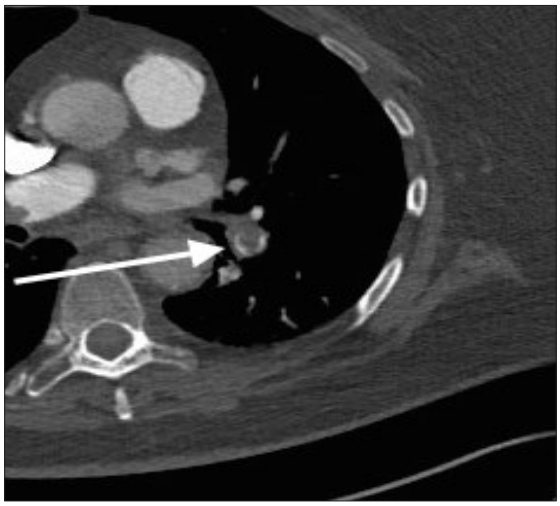

Figure 5. Filling defect in the left lower lobe segmental pulmonary artery forming an acute angle with the vessel wall.

Occasionally the embolus is large enough to lodge and straddle the pulmonary artery bifurcation, giving rise to a saddle embolism (figure 6). A DVT on the venogram would appear as a filling defect in one of the lower limb veins (figure 7).

The CTPA may also show the subsequent lung injury caused by the pulmonary embolism in the form of infarction, appearing as consolidation, or there may be areas of atelectasis.

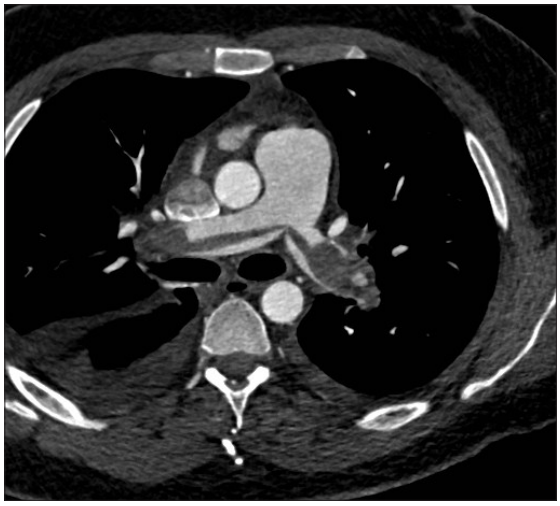

Figure 6. CT showing saddle pulmonary embolism extending into the main right and left pulmonary artery.

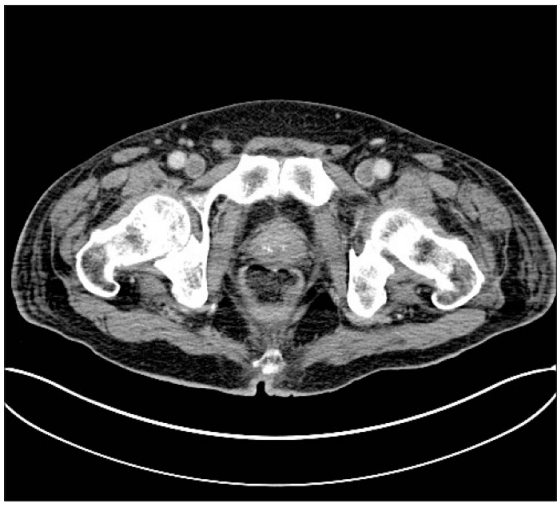

Figure 7. Venogram showing filling defects in expanded femoral veins in keeping with bilateral DVT.

CT can provide information that may be of prognostic use for clinicians. If the PE is large enough or the clot burden of many small PEs is high enough they may cause right ventricular (RV) strain shown by:

- *RV dilatation – the right ventricle is larger than the left ventricle. The ventricular diameters should be measured on a 4-chamber view via multi-planar reformats (figure 8) or as a ratio of ventricular volumes.*
- *Abnormal position of the interventricular septum – normally its bowed towards the RV, straightening or bowing towards the LV indicates raised RV pressure (figure 8).*
- *Reflux of contrast material into the inferior vena cava (figure 9).*
- *Pulmonary trunk dilatation such that it is larger than the aorta.*

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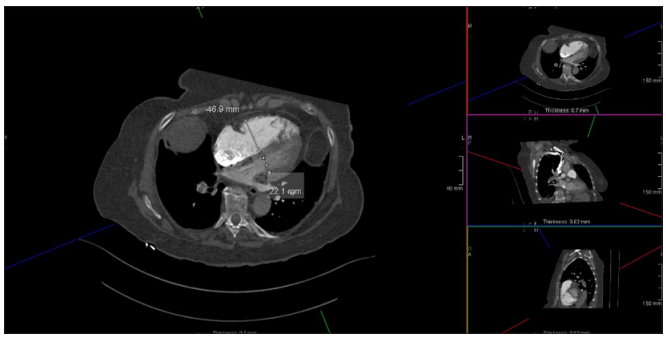

Figure 8. Multi-planar reformat of CTPA. Submassive PE with RV dilatation and straightening of the interventricular septum.

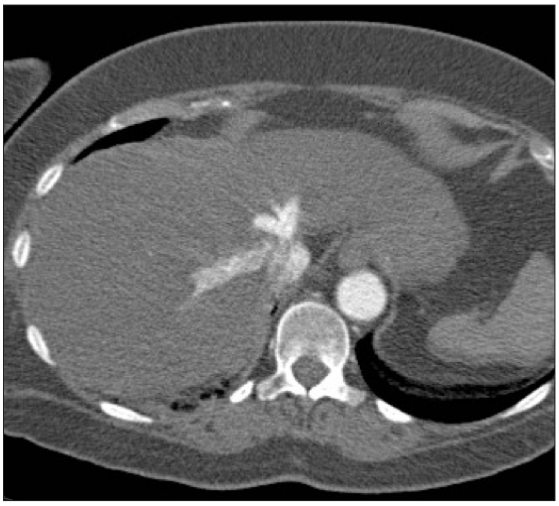

Figure 9. CTPA showing opacification of the IVC and the hepatic veins due to reflux of contrast out of the right ventricle as a consequence of a large PE.

As well as its diagnostic ability, CTPA has become the primary imaging modality for PE due to its relative availability and the speed of acquisition. Downsides to CTPA are few and mainly relate to radiation dose and contrast. The long-term risk associated with the radiation can only be estimated and the decision to go ahead with the CT should be made on a case-by-case basis, weighing up the risk benefit ratio.

CTPA requires intravenous iodinated contrast be given which may be contraindicated in the case of severe allergy or renal disease. In these circumstances another modality should be considered.

Ventilation Perfusion Scanning

Alongside catheter angiography ventilation perfusion (V/Q) scanning had been the main investigation for diagnosing PE until CTPA became widely available. The first PIOPED study showed that when V/Q scans were used in the correct patient groups it was highly effective at ruling pulmonary embolism out and in high-risk groups you could rule-in PE. Due to its lack of specificity there were many indeterminate results (19). This is part of the reason why the patients must be carefully selected for V/Q scanning; ideally the patient should have a normal chest radiograph and no history of significant lung disease.

A V/Q scan is performed in two stages; the patient inhales a radioactive aerosol before being imaged by a gamma camera. This is followed by an injection of radioactive albumin (e.g. macroaggregated albumin spheres, which are of an appropriate size to lodge in the pulmonary vessels) and further imaging. This gives images of the ventilation and perfusion of the lungs which are compared. Normally they match i.e. radiotracer has perfused via the blood vessels throughout the lungs in an identical way to the aerosol moving through the airways (figure 10). A PE creates a V/Q mismatch, a perfusion defect seen where there is normal ventilation (figure 11). What is actually being demonstrated is the PE causing a lack of blood flow rather than the embolism itself.

VQ scans are used less commonly with the advent of CTPA, mainly due to the fact that they are less readily available, take longer to acquire and can provide indeterminate results if used in the wrong patient group. Despite these factors V/Q scans still have a role to play, particularly in patients in whom iodinated contrast is contraindicated.

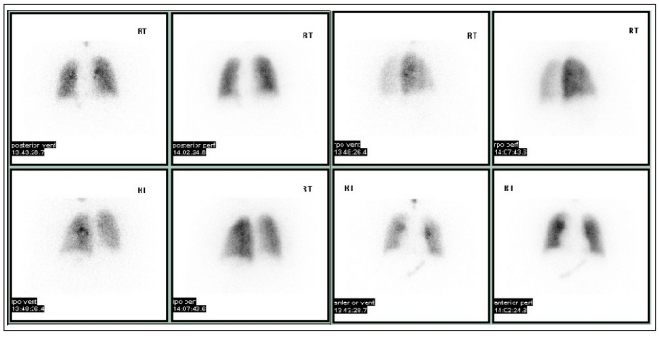

Figure 10. A normal V/Q scan showing perfusion and ventilation images alongside each other for a range of projections. There are no perfusion ventilation mismatches. A chest radiograph may be used as a surrogate for the ventilation phase.

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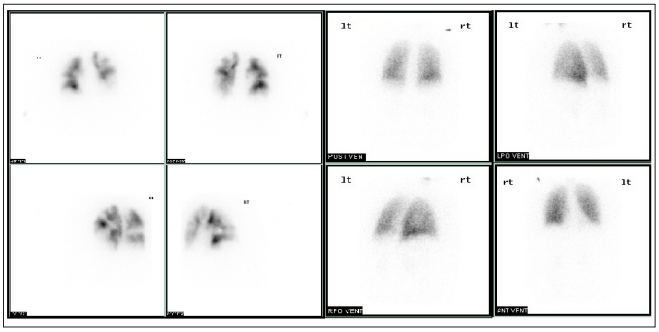

Figure 11. Abnormal V/Q scan. The perfusion scan shows multiple wedge-shaped mismatched defects indicating a high probability of pulmonary embolism.

Catheter Angiography

Once considered to be the gold standard in the diagnosis of PE, catheter pulmonary angiography is now essentially reserved for therapeutic interventions. The main reason for the declining use is the availability of alternative, non-invasive diagnostic imaging. The reported rate of major complication with conventional angiography is 0.5-1% (20), such as death, arrythmia, respiratory failure, renal failure or haematoma. Pulmonary emboli are seen as filling defects within the pulmonary arteries (figure 12).

The technique involves gaining venous access either via the internal jugular or the common femoral vein and then guiding a catheter through the right heart and into the pulmonary trunk. Injections of iodinated contrast are used to form the pulmonary angiogram and look for PEs that show as filling defects. To increase the diagnostic accuracy, subtraction angiography is used; an image of the lungs without contrast is taken and then this is subtracted from the angiogram image and this leaves just the vessels filled with contrast.

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) of the pulmonary vessels had promise as a radiation and iodinated-contrast free alternative to other imaging. Early studies had found that it was equivalent in sensitivity and specificity to both CTPA and conventional angiography (21). The PIOPED III study showed that the rate of technically inadequate scans was 25% and it concluded that the investigation should only be performed in centers that do it routinely (22).

Echocardiography

Although unable to make a primary diagnosis of pulmonary embolism, transthoracic echocardiography (echo), can still play a role in its management. In the patient with a known PE it can be used to risk-stratify patients by determining right heart dysfunction and assessing right ventricular pressures, right ventricular dysfunction or tricuspid incompetence (23).

In less than 10% of patients it can demonstrate free floating thrombus in the right ventricle. Echo may be used in the peri-arrest patient with a known DVT that is too unwell for transfer to CT. One may make a presumptive diagnosis of massive PE if there are features of right heart dysfunction and then guide systemic therapy. Rarely, trans-oesophageal echo can be used to diagnose a proximal pulmonary embolus (24).

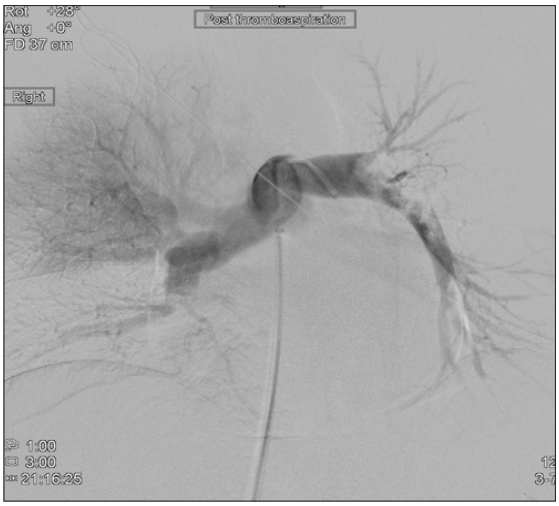

Figure 12. Catheter angiography showing a filling defect in the left main pulmonary artery. Angiography was performed in a patient with ongoing haemodynamic instability despite systemic thrombolysis. They underwent catheter directed thrombolysis and thromboaspiration.

Treatment of PE

For the majority, PE treatment is aimed at preventing further formation and propagation of new thrombus. Initially patients are started on either low-molecular weight or unfractionated heparin whilst waiting for confirmation of the diagnosis. Subsequently they are commenced on a vitamin K antagonist, such as warfarin, for a time period determined by the patient's risk factors.

Although not first-line, a new class of treatments, the direct Xa inhibitors, such as rivaroxaban may be used instead of warfarin. The advantage of these newer therapies is that they have a simplified dosing regimen and require no monitoring of clotting profile. Patients who have pulmonary embolism with haemodynamic instability should be considered for systemic thrombolysis (14). If patients with PE have right ventricular dysfunction without haemodynamic compromise thrombolysis is not indicated.

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Alternative treatment options include catheter directed therapy or surgical embolectomy. Catheter based therapies may include ultrasound fragmentation or mechanical disruption of the clot or catheter-directed thrombolysis.

Figure 13 shows the CTPA of a patient with large bilateral PE that caused a cardiac arrest and the subsequent pulmonary angiography with catheter thromboaspiration. Surgical embolectomy is very rarely used. It is performed only in specialist centers, requires cardiorespiratory bypass and is reserved for selected high risk patients.

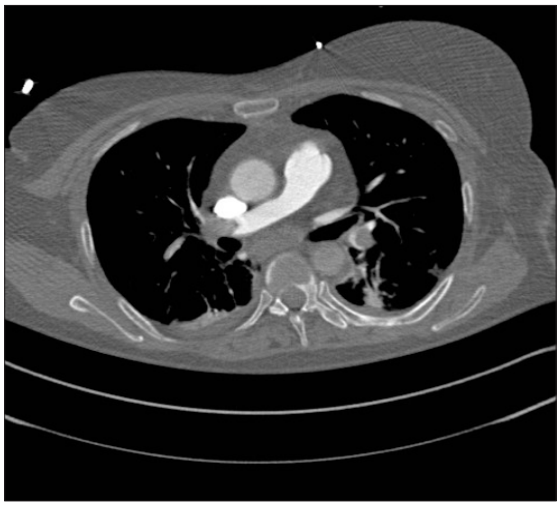

Figure 13a. CTPA showing in the bilateral PEs in a patient after cardiac arrest.

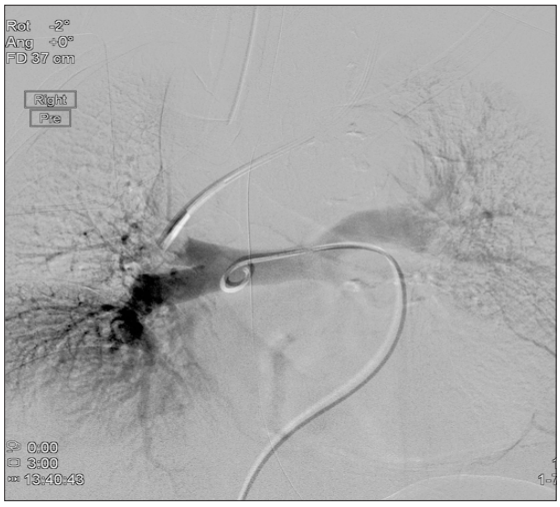

Figure 13b. Catheter Angiography showing near total occlusion of the right upper lobe pulmonary artery due to thrombus.

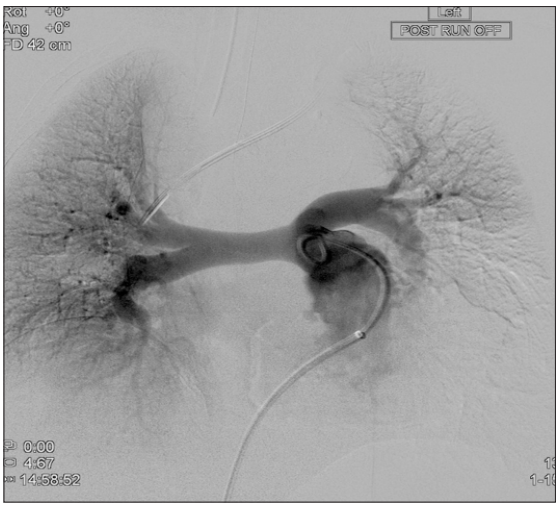

Figure 13c. Post thromboaspiration angiogram showing non-occluded right upper lobe PA. Despite therapy the left lower lobe PA remained occluded.

Patients with contraindications to anticoagulation and an objectively proven proximal DVT or PE may have an inferior vena cava filter as a preventative measure. IVC filters are also indicated if a patient has recurrent DVT/PE whilst on adequate anticoagulation. Figure 14 shows the insertion and removal of an IVC filter. In general retrievable IVC filters are used that can be removed at a later date or left in situ if clinically indicated.

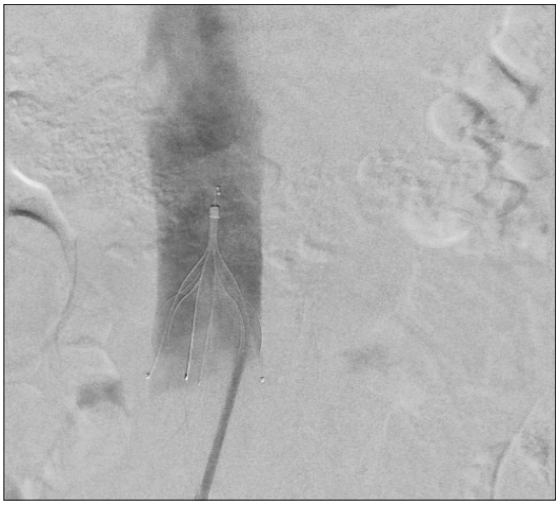

Figure 14a. Venography showing IVC filter and catheter in the inferior vena cava, which is opacified with contrast.

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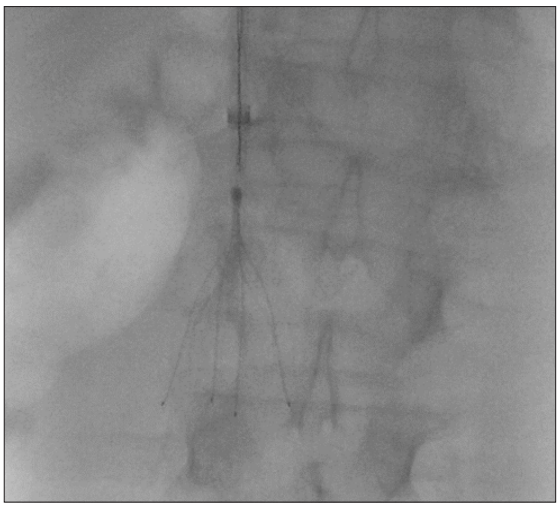

Figure 14b. Removal of IVC stent under fluoroscopic guidance using internal jugular approach.

Conclusion

Acute PE is serious and sometime life-threatening condition that can present in a non-specific way making clinical diagnosis troublesome. Use of clinical risk scores allows risk stratification of patients and determination of an investigative pathway, either use of d-dimer or imaging. Radiology plays a major role in diagnosis of PE, with CTPA the most commonly used investigation. Radiology also plays a role in therapy for PE with radiologically guided catheter-based treatments and deployment of IVC filters.

Questions

1) Which of these patients has only a minor risk factor for pulmonary embolism?

a) A 67 year old female who is undergoing a laparotomy for small bowel obstruction

b) A 54 year old man who has pancreatic cancer with metastatic spread to the liver

c) A 48 year old man who has previously been diagnosed with a deep vein thrombosis

d) A 32 year old woman who has just been prescribed an oral contraceptive pill

e) A 78 year old man who is undergoing an elective total hip replacement

2) Which of these is the commonest presenting symptom for pulmonary embolism?

a) Pleuritic chest pain

b) Shortness of breath

c) Haemoptysis

d) Collapse

e) Cough

3) Which of these investigations cannot be used to diagnose a PE?

a) CT pulmonary angiogram

b) Chest radiograph

c) MR pulmonary angiogram

d) Conventional angiogram

e) V/Q SPECT scan

Answers

1) Answer d)

The risk factors for venous thromboembolism have been well defined into major and minor groups in the British Thoracic Society guidelines on diagnosis of PE, depending on their relative contribution. Use of the oral contraceptive pill falls into the minor risk group. The remaining patients all have major risk factors for PE.

2) Answer b)

By far the commonest presenting feature of PE is shortness of breath and this tends to be abrupt in onset. The classic triad of haemoptysis, pleuritic chest pain and shortness of breath actually occurs relatively infrequently.

3) Answer b)

Signs of a PE on a chest radiograph are non-specific and therefore cannot be used for a confident diagnosis. The main reason for performing a chest radiograph is to exclude other diagnoses such a pneumothorax. The remaining options are all modalities that can be used to diagnose PE but CTPA is used most commonly and NICE recommend it as the first-line investigation.

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MANAGEMENT OF REFRACTORY VARICEAL BLEEDING WITH TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

N Heptonstall, T Ali, T See

Abstract

Upper Gastrointestinal bleeding (UGIB) is a common presentation in the emergency department. Understanding how to appropriately manage these patients is essential. Varices are a common cause of Upper GI bleeding UGIB and carry a high mortality rate. Endoscopy is the first line investigation and provides the opportunity for treatment with Terlipressin vasoactive drugs and band ligation. For those patients in whomIn refractory variceal bleeding, a Transjugular Intrahepatic Portosystemic Shunt (TIPSS) can be inserted. We will discuss key facts to recognition, management and treatment options.

Case History

A 58-year-old frequent attender presented to the emergency department with haematemasis and several episodes of malaena. He was a known alcoholic consuming approximately 20 units of lager per day. His previous admissions included alcohol withdrawal syndrome requiring medical treatment. He recently had a liver and doppler ultrasound examination, which revealed a heterogeneous liver with an irregular surface and increased reflectivity in keeping with cirrhosis. There was evidence of portal hypertension with retrograde, high velocity flow demonstrated in the portal vein and recannalised paraumbilical veins. He was a known hypertensive, although he had not been taking his medication recently.

At presentation he continued to have haematemasis and was haemodynamically unstable with a blood pressure of 84/53 mmHg, heart rate of 123bpm and reduced Glasgow Coma Scale (GCS). Despite resuscitation, following the local massive transfusion protocol and intubation to secure his airway, his observations did not respond.

He was taken for an urgent endoscopy and was commenced on IV antibiotics. A variceal bleed was diagnosed and multiple attempts at band ligation to control bleeding were unsuccessful.

The patient was subsequently taken to the interventional radiology suite for management with a Transjugular Intrahepatic Portosystemic Shunt (TIPSS).

Discussion

This case is a classic presentation of an acute UGIB. It is a common medical emergency with an incidence of 50-150 per 100,000 (1) and a mortality rate of up to 10% (2). By far the most common cause is due to gastric ulcer disease occurring in up to 60% of cases (3). Oesophageal varices occur in approximately 11% of cases (4). Other causes include oesophageal or gastric malignancy, Mallory Weiss tear, gastritis or oesophagitis and vascular abnormalities.

Oesophageal varices have a significantly higher mortality of up to 50 % for the initial bleed and an inpatient mortality of 30 % for subsequent bleeds, when compared with the other causes of UGIB bleeding (5, 6, 7, 8, 9). They form as a consequence of liver cirrhosis and portal hypertension. Blood is shunted away from the liver via porto-systemic collaterals causing varices at anastomoses of the portal and systemic venous systems.

90 % of varices are in the oesophagus while 10% are in the stomach or more rarely small bowel (10). They are particularly prone to bleeding due to local luminal invasion. There is a risk of re-bleeding following treatment of up to 40% within 6 weeks (11). Patients who present with a variceal bleed may also present with evidence of liver decompensation including ascites, encephalopathy or anaemia (10).

Picture Of Oesophageal Varices

Endoscopy

Endoscopy is currently considered the first line diagnostic and therapeutic procedure for the management of UGIB (12). Patients who are haemodynamically unstable despite resuscitation should be offered an immediate endoscopy within 2 hours (2). All other patients are offered endoscopy within 24 hours. Patients are given intravenous antibiotics to reduce the high risk of infection following a variceal bleed. Terlipressin, a synthetic analogue to vasopressin, is also used. It triggers vasoconstriction to reduce portal venous flow and intrahepatic resistance, therefore reducing the variceal pressure and variceal bleeding.

Occasionally variceal bleeding may continue despite endoscopic therapy and drug therapy. In patients with refractory bleeding, a TIPSS can be inserted by the interventional radiologist (2). There are other surgical options available, such as surgical portosystemic shunts with or without splenectomy. These are invasive procedures and carry a higher mortality; therefore TIPSS is the favored flow diversion treatment (11, 13, 14).

TIPSS

A TIPSS is positioned within the liver parenchyma between the portal vein and a hepatic vein. The TIPSS diverges blood arriving to the liver via the portal vein directly into the hepatic vein and then the IVC, bypassing the liver altogether. This reduces the pressure within the varices and reduces the risk of bleeding.

There are a number of contraindications to TIPSS insertion including uncontrolled sepsis, liver abscess, biliary obstruction, right heart failure and severe polycystic liver disease (12). TIPSS can also be used for the treatment of refractory ascites, Budd-Chiari syndrome or hepatic veno-occlusive disease and hepatic hydrothorax (11).

TIPSS insertion by an interventional radiologist is performed in a theatre designed specifically for interventional procedures. This is a fluoroscopy unit with Digital Subtraction Angiography (DSA) capabilities, allowing better visualisation of vessels.

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As the TIPSS name suggests, intravenous access is obtained with a large cannula usually via the right internal jugular vein in the neck (11). This provides a straight course down the brachiocephalic vein, SVC, IVC and then a hepatic vein. Other options include other internal or external jugular veins.

Access is gained under ultrasound guidance, after checking vessels patency, with an 18-G needle. Guidewires, placed with a Seldinger technique, and dilators are used to exchange the cannula to a 10-Fr sheath. The sheath remains in place throughout the procedure. A catheter is then advanced into the preferred right or middle hepatic vein, although the left can also be used. This is confirmed with hepatic venography.

At this stage, connecting the catheter to a transducer allows measurements of intravascular pressure. The pressure recorded is called the free hepatic vein pressure (FHVP). An indirect measurement of the portal pressure can be obtained by advancing the catheter until it wedges at the distal hepatic vein, also known as the wedged hepatic vein pressure (WHVP) and corresponds to the portal vein pressure. The difference between the FHVP and WHVP is normally less than 6mmHg. A gradient of ≥10mmHg defines clinically significant portal hypertension and at ≥12mmHg, variceal haemorrhage may occur for which TIPSS is usually recommended. A balloon occlusion catheter can also be used to measure wedged pressures.

Wedged hepatic venography can be done by injecting a small amount of iodinated contrast medium (or CO2) via the catheter, forcing contrast medium into the liver parenchyma and subsequently into a branch of the portal vein (Fig.1).

Lateral views are obtained to demonstrate the anatomical relationship between the hepatic and portal veins. Once the anatomy is defined; a tract is formed by a puncture, between the hepatic and portal veins, using a special TIPSS instrument (containing a long needle inside a catheter).

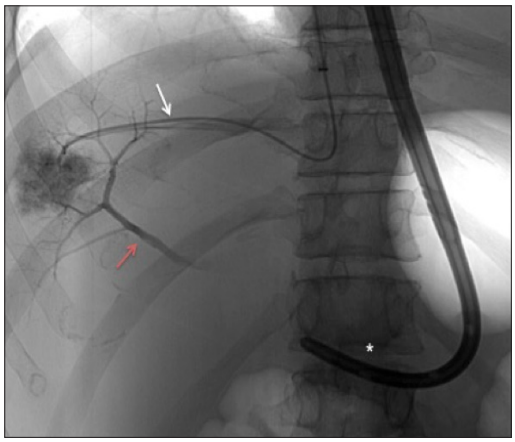

Figure 1: Wedged hepatic venography. Catheter in right hepatic vein (white arrow) with its tip wedged distally. Contrast medium injection results in parenchymal staining and subsequent retrograde opacification of a branch of right portal vein (red arrow). Note the presence of a Sengstaken tube to control haemorrhage from the varices (asterisk).

In patients with severe liver cirrhosis this can be difficult as the liver is firm and atrophied. High resistance is often felt directly prior to puncturing the portal vein. Confirmation of entering the portal vein is made with contrast medium injection via the TIPSS catheter (Fig.2).

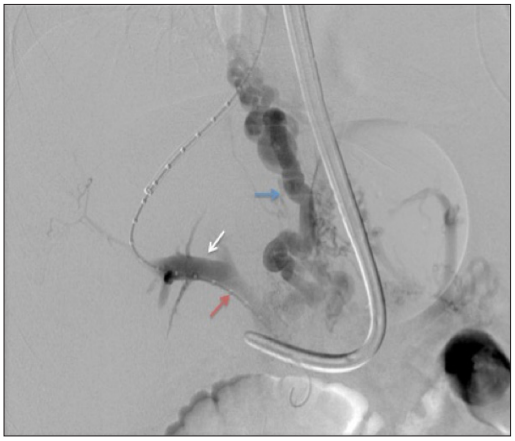

Figure 2: Portal venography. The portal vein (white arrow) has successfully been cannulated and a measuring pig-tail catheter is in-situ (red arrow). This facilitates accurate selection of an appropriately sized stent-graft for the shunt. Note the presence of large oesophageal varices (blue arrow).

The tract between the hepatic vein and main portal vein is then dilated using a balloon catheter (Fig.3). The size of the balloon used usually ranges from 8 mm to 10 mm in diameter and is followed by the deployment of a stent across the tract (Fig.4). Nowadays a stent graft is used instead of a bare metal stent due to better patency. Depending on the degree of expansion of the stent-graft, the TIPSS can be dilated with a balloon catheter if required.

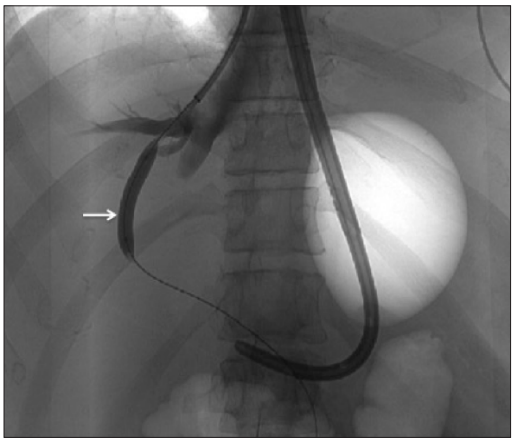

Figure 3: Dilatation of the tract between the hepatic vein and portal vein using an inflatable balloon (white arrow).

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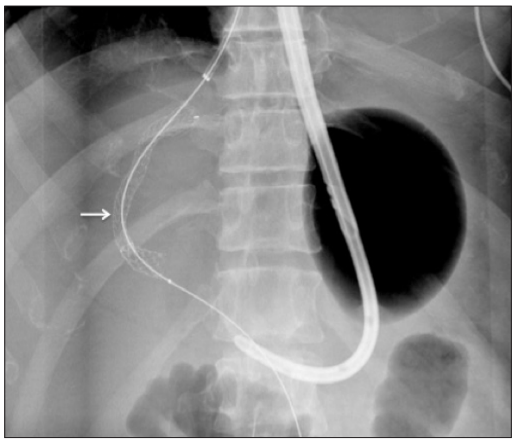

Figure 4: Stent-graft deployed, bridging the hepatic vein and the portal vein (white arrow)

Pressure measurements can now be obtained in the portal vein, TIPSS, hepatic vein, right atrium and inferior vena cava. A gradient of less than 12mmHg is desired to reduce risk of variceal bleeding (11). IV contrast is injected to ensure patency of the TIPSS. Minimal to no flow in the varices is often seen.

Additional procedures can be carried out following the insertion of the TIPSS. If there remains a gradient of greater than 12mmHg and persistent opacification of the varices, embolisation may be carried out using coils or plugs (Fig. 5-6).

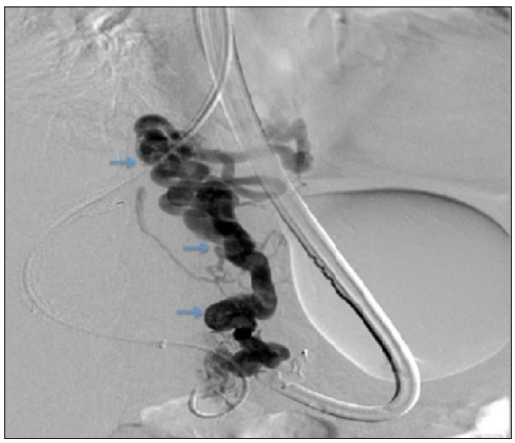

Figure 5: Large oesophageal varices still demonstrated post stent-graft deployment (blue arrows).

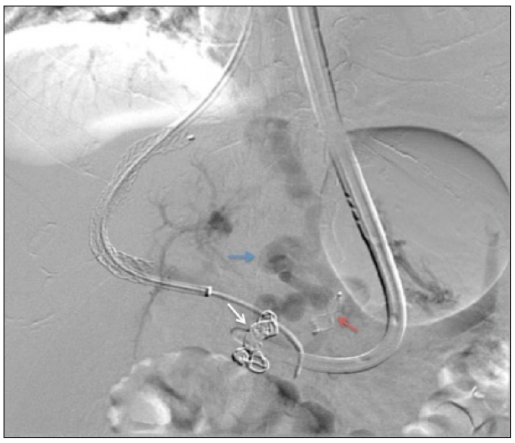

Figure 6: Embolisation. Coils (white arrow) and an Amplatzer plug (red arrow) has been deployed in the varices to reduce flow. As a result, there is less filling of the oesophageal varices (blue arrow).

Complication of TIPSS

TIPSS complication rate is less that 5 % (15, 16). TIPSS related complications include difficulty with venous access such as haematoma, infection, carotid artery injury or pneumothorax. As the guide wires and catheters pass from the SVC to the IVC via the right atrium, cardiac arrhythmias may occur. Wedged hepatic pressure may cause hepatic laceration and subcapsular haematoma.

Passing the needle through the hepatic vein may result in perforation of the liver capsule causing intraperitoneal haemorrhage. Damage to the biliary tree can cause biliary fistula formation. Hepatic arteries can also be punctured, although this is rare (17). Non-target organs at risk of needle puncture include the gallbladder, right kidney, duodenum and the colonic hepatic flexure.

By far the most common long-term complications are stent stenosis and occlusion (17). Therefore, surveillance with Doppler ultrasound is required.

Other complications include stent migration and although rare may result in significant morbidity due to cardiac injury. Encephalopathy has also been seen (18). Radiation injuries can occur especially in lengthy procedures. Steps are taken to reduce radiation risk intraoperatively.

Conclusion

TIPSS is an interventional radiology procedure that can be successfully used in refractory variceal bleeding.

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MCQs

1. A patient attends the emergency department with profuse haematemsis and is found to have a Hb of 56. She is started on the massive transfusion protocol. What forms part of the massive transfusion protocol?

a) IV Fluids, Red Blood Cells, Fresh Frozen Plasma consider platelets and cryoprecipitate. Transexamic acid if trauma within 3 hours.

b) IV Fluids, Red Blood Cells, Transexamic acid, Fresh Frozen Plasma and platelets.

c) Red Blood Cells, Fresh Frozen Plasma and platelets and cryoprecipitate. Transexamic acid if trauma within 3 hours.

d) Transexamic Acid, Red Blood Cells, Fresh Frozen Plasma consider platelets.

e) Red Blood Cells, Fresh Frozen Plasma and platelets and cryoprecipitate. Transexamic acid if trauma within 3 hours.

2. What is a contraindication to TIPSS insertion?

a) Refractory ascites

b) Hepatorenal Syndrome

c) Hydrothorax

d) Polycystic Liver Disease

e) Budd-Chiari Syndrome

3. Causes of Liver cirrhosis include?

a) Viral Hepatitis

b) Primary Sclerosing Cholangitis

c) Cystic Fibrosis

d) Nonalcoholic Steatohepatitis

e) all of the above

4. What are the sonographic features of cirrhosis?

a) Homogenous reflectivity of the liver with antegrade portal venous flow.

b) Heterogeneous reflectivity of the liver with surface irregularity and antegrade portal venous flow.

c) Homogenous reflectivity of the liver with retrograde portal venous flow and recannalised para-umbilical collaterals.

d) Heterogenous reflectivity of the liver with surface irregularity, retrograde portal venous flow and recannalised para-umbilical collaterals.

e) None of the above.

5. Regarding risk assessment for upper GI bleeding, which of the following is not true?

a) The Rockall score uses clinical criteria as well as endoscopic findings to identify patients at risk of adverse outcomes following an acute upper GI bleed.

b) A total Rockall score of < 3 carries a good prognosis

c) A Glasgow-Blatchford score requires endoscopy to complete the risk assessment score.

d) A Glasgow-Blatchford score of '0' identifies low risk patients who may be suitable for outpatient management

e) The clinical variables used in the Rockall risk assessment include; increasing age, co-morbidity and shock.

Answers

1. Answer 'a'

A massive haemorrhage is defined as loss of one volume of blood (70ml/kg) within 24hours, 50% loss of total blood volume in less that 3 hours or bleeding excess in 150ml/min. When this is recognised baseline bloods must be taken including Full blood count, Group and Save, Clotting screen with fibrinogen and cross match. Massive haemorrahge may manifest as pulse >110bpm, RR >30, Hypotensive BP <90 systolic and urine output <20mls/hr.

Management includes IV Fluids, Red Blood Cells, Fresh Frozen Plasma consider platelets and cryoprecipitate. Transexamic acid may be considered if trauma is within 3 hours. Other things to consider include correcting hypothermia and hypocalcaemia. Ensure you monitor Full blood counts and coagulation after administration of blood products. Different regions of the country have different protocols. Make sure you familiarise yourself with them.

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2. Answer 'd'

Polycystic liver disease is an absolute contraindication to TIPSS insertion as a consequence of the hepatic architectural distortion due to the large cysts. This results in technical difficulties and reduced liver parenchyma surrounding the shunt. All other answers are indications for TIPSS insertion.

3. Answer 'e'

Liver cirrhosis is common. There are many causes for liver cirrhosis. By far the most common is alcohol (60-70%), followed by Non-alcoholic steatohepatitis (NASH) (10-15%), viral hepatitis (10%), Primary Biliary Cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC) (5-10%), metabolic diseases e.g. alpha-1-antitrypsin deficiency (5%), and cystic fibrosis. Liver hepatocellular necrosis is accompanied by three characteristics; fibrosis, nodular regeneration and hepatic architecture distortion. Patients with Liver cirrhosis are at increased risk of developing hepatocellular carcinoma and often have ultrasound follow-up.

4. Answer 'd'

Sonographic features of cirrhosis include: Heterogenous reflectivity of the liver with surface irregularity, retrograde portal venous flow and recannalised para-umbilical collaterals. Portal hypertension, a complication of cirrhosis, is defined as portal pressures > 12 mmHg with retrograde flow, (i.e. away from the liver), indicative of advanced portal hypertension. Other features which can be demonstrated on US include; splenic venous collaterals, splenomegaly and ascites.

5. Answer 'c'

The Glasgow-Blatchford score (GBS) is a screening tool at first assessment that uses clinical criteria to identify patients requiring an intervention such as blood transfusion or endoscopy. The advantage over the Rockall score is that endoscopy is NOT required to complete the score and therefore lacks subjectivity.

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PNEUMOCEPHALUS: A RARE COMPLICATION OF COLONIC CANCER

S Lowes, N Stock, D Bearn, J Latimer, G Wallace

Abstract

A 64 year old man with a known metastatic recto-sigmoid tumour was brought by ambulance to the emergency department with decreased consciousness following his first generalised tonic-clonic seizure at home. On arrival at hospital his GCS was 3 and he had signs of severe sepsis.

CT head showed extensive pneumocephalus but the cause of this could not be attributed to a cranial source. Subsequent CT chest, abdomen and pelvis showed extensive gas distributed throughout the entire spinal column (pneumorrhachis). It also demonstrated localised perforation of the known recto-sigmoid tumour into a gas-containing pelvic collection, which was contiguous with the prevertebral space. Moreover the collection had eroded into the sacral bone and CSF space confirming this as the source of the subarachnoid and subdural gas. Despite initial clinical improvement following broad spectrum intravenous antibiotics the patient died the following day.

Pneumorrhachis is an uncommon phenomenon, and causes such as the one we describe are exceptionally rare. The extensive pneumocephalus seen on the CT head examination represented tracking of the pneumorrhachis from the sacral region into the cranial vault. Neurological deficit resulting directly from the presence of intra- or extra-dural gas is uncommon and in this case the patient's clinical presentation was most likely due to widespread CNS sepsis rather than the extensive pneumocephalus.

This case highlights some of the diagnostic complexities that we are presented with throughout our career and presents some unusual radiological images that are worthy of discussion.

Case History

A 64 year old man was brought by ambulance to A&E with decreased consciousness after his wife was unable to rouse him in the morning. In the ambulance he went on to have three tonic-clonic seizures. His wife explained that he had been complaining of headache and lethargy for the preceding 24 hours.

On arrival at A&E his GCS was 3, with a fixed upward gaze and upgoing plantars, but no other localising neurological signs. He also had signs of sepsis with sinus tachycardia, pyrexia, and raised inflammatory markers; urgent admission bloods showed WCC 18.8 x 109/L (range 4 - 11) and CRP 201 mg/L (range 0-5).

He had no previous history of seizures or other neurological problems and no recent history of trauma. His known medical background included a T4N1M1 moderately differentiated rectal adenocarcinoma with liver metastases and small pulmonary metastases, which had been treated with palliative radiotherapy and chemotherapy.

An urgent non-contrast CT head examination showed extensive pneumocephalus (intracranial gas). Gas was distributed in the subarachnoid spaces surrounding the brain (following the contours of the sulci) and within the ventricles and basal cisterns (Figure 1).

It is also likely that there was gas within the subdural space, suggested by the pocket of gas overlying the left frontal convexity, which causes some displacement of the frontal lobe, but does not demonstrably follow the sulcal contours as it does elsewhere (Figure 1). Despite this widespread gas there were no findings to suggest that the source of the gas itself was intracranial; there was no evidence of intracranial collection or large cerebral abscess, the sinuses were normal, there were no skull metastases and, as expected, there was no fracture.

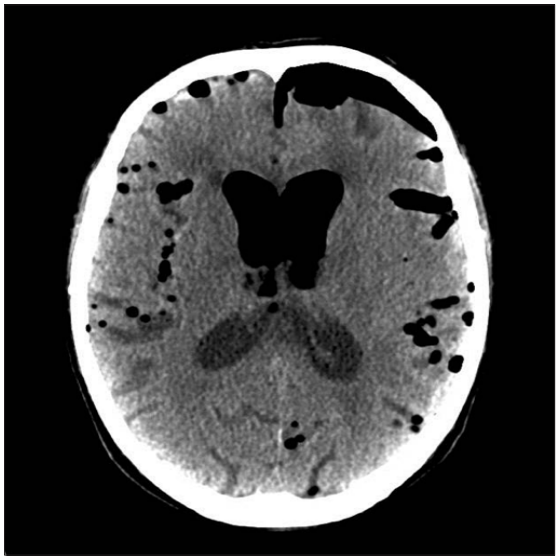

Figure 1: Axial CT head showing large amounts of subarachnoid gas within the sulci and ventricles.

A locule of gas was noted at the cisterna magna, suggesting that gas may also be distributed within the spinal canal (pneumorrhachis) and raising further suspicion that the actual source of gas may be extracranial. The source of sepsis also remained unexplained. A contrast-enhanced CT chest, abdomen and pelvis was therefore carried out to investigate the underlying cause.

This confirmed extensive pneumorrhachis distributed throughout the whole vertebral column (Figure 2).

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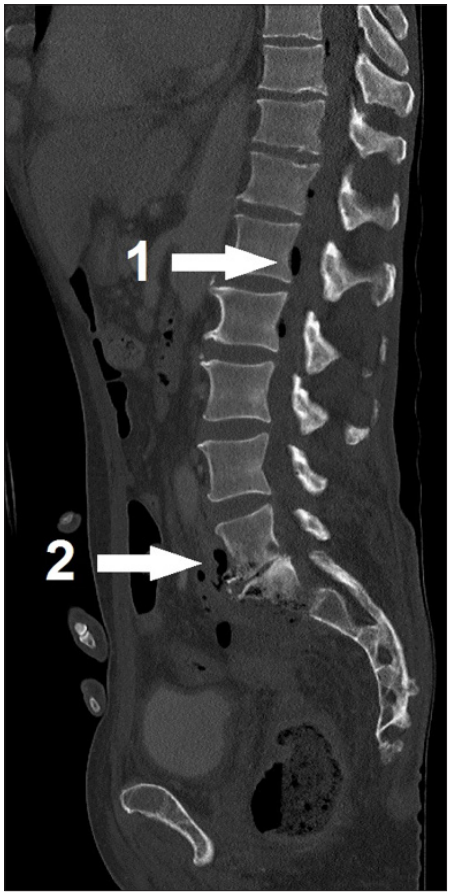

Figure 2: Sagittal CT image showing locules of gas within the spinal canal (arrow 1), which arose from a gas-containing pelvic collection eroding the sacrum and L5 vertebral body (arrow).

The most significant finding, however, was a localised perforation of the known recto-sigmoid tumour into a gas-containing pelvic collection, which was contiguous with the prevertebral space (Figure 2 and 3).

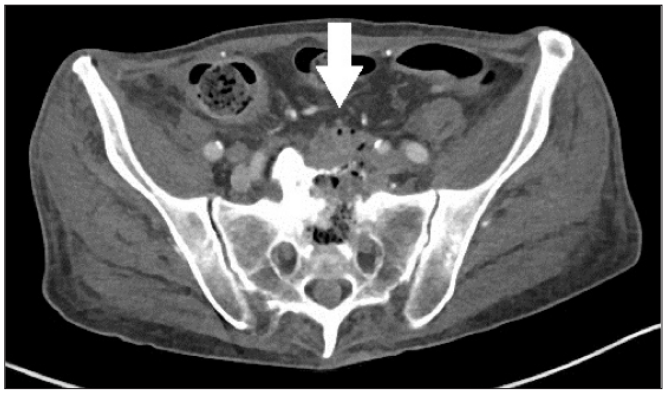

Figure 3: Axial CT image showing the gas-containing collection eroding into the sacrum (white arrow). This was the source of gas within the spinal canal.

There was associated bony erosion of the sacrum and L5 vertebral body with multiple locules of gas extending into the spinal canal. Therefore it seems most likely that the source of the pneumorrhachis and pneumocephalus originated from the erosion of the pre-sacral abscess through the dural coverings, ultimately communicating with the subarachnoid space of the spinal canal. The gas itself presumably arose from the gas-forming organisms associated with the abscess.

Another possibility to consider in this situation may have been direct fistulation of the recto-sigmoid tumour into the dura, introducing gas via direct communication between the bowel lumen and subdural/subarachnoid spaces. However, the CT appearances suggested that the only the abscess, and not the bowel, was in direct contact with the sacrum.

The patient was initially resuscitated and received broad spectrum intravenous antibiotics (meropenem, linezolid, and metronidazole). Given his in extremis clinical condition and background of palliative chemotherapy it was felt that his prognosis was too poor for immediate surgical intervention or escalation of care to the Intensive Care Unit. Overnight he initially showed clinical improvement, his GCS increasing to 11, but deteriorated again rapidly and died hours later.

Discussion

Complex cases such as this bring many challenges. The main diagnostic challenges were identifying the source of sepsis and identifying the cause of the seizures. Given that the patient had become acutely unwell over a short period it seemed more than likely the sepsis and seizures were linked. At the time of presentation the differential diagnosis for the seizures was broad. In view of the patient's known metastatic disease, cerebral metastases were possible but this would not have accounted for the signs of sepsis.

CNS infection therefore was also a possibility, though there were no obvious precipitating factors. Although the patient had previously received chemotherapy he was not neutropaenic or otherwise immunosuppressed. Sepsis from other sources can also on occasion be associated with seizures. Intracranial haemorrhage can also result in seizures, but this seemed less likely as there were no risk factors such as trauma, anticoagulation or hypertension, and no preceding history to suggest spontaneous subarachnoid haemorrhage (typically caused by a ruptured intracranial aneurysm). However, haemorrhage alone would not account for the sepsis.

If, as in this case, a patient presents with suspected acute intracranial pathology then a non-contrast CT head is a quick and accessible examination to investigate this.

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In the current case, the finding of extensive pneumocephalus was entirely unexpected. Pneumocephalus is actually a well-recognised phenomenon that usually results from direct communication of the extradural or intradural space with the atmosphere, typically following cranial surgery or fracture of the calvarium, skull base or sinuses. (1) Other established causes include tumour invasion of the sinuses, sinusitis, and mastoiditis. A few cases of spontaneous pneumocephalus have also been reported secondary to aerobic bacteraemia. (2)

But not all cases result from cranial causes. Pneumocephalus can also arise from intradural pneumorrhachis tracking superiorly into the cranium such as in the current case. This is however rarely seen, largely because pneumorrhachis itself is relatively rare. Like pneumocephalus, most causes of pneumorrhachis are traumatic or iatrogenic, however the precise mechanisms tend to differ. (3)

For example, whereas traumatic pneumocephalus results from a breach of the extra- or intradural space, most cases of traumatic pneumorrhachis arise from closed injuries, such as barotrauma to the lungs, which results in translocation of gas through the fascial planes of the mediastinum into the extradural space. (4, 5)

In the rare cases of traumatic pneumorrhachis where the gas is seen in the intradural space it implies severe injury. (5, 6) Other traumatic causes include fractures of the skull base, sinuses or open calvarial fractures. (4)

Iatrogenic cases of pneumorrhachis mainly result from direct contact with the spinal canal for example spinal surgery or anaesthetic procedures such as epidural anaesthesia and lumbar puncture. (3)

Much rarer still are cases of pneumorrhachis arising from causes such as the one we describe, in which a pre-sacral collection arising from a perforated recto-sigmoid tumour eroded into the sacrum and underlying CSF spaces. In fact, we have been unable to find an identical case within the literature, though there are a handful of other cases with some overlapping features.

The most similar case to ours we have found is a case of sigmoid diverticulitis fistulating via the sacrum causing pneumorrhachis and pneumocephalus. (7) The clinical presentation was very similar: pyrexia, reduced conscious level and a seizure-like episode. Lumbar puncture yielded frank pus harbouring a range of gas-forming organisms suggesting infection as the source of pneumorrhachis and pneumocephalus.

The patient recovered well following laparotomy and resection of the diseased segment of bowel, showing a mild residual left-sided hemiparesis at 2 year follow up. Shetty et al. (8) also documented a case of a diverticular pre-sacral abscess resulting in pneumocephalus but the patient presented more insidiously with a four week history of back pain, intermittent fever and rigors, and GCS 15/15. He underwent bowel resection, antibiotic treatment, and made a full recovery.

Another case (9) reported pneumocephalus in a 69 year old male with recurrent sigmoid tumour who developed tightness in his thighs and uncontrollable perineal pain four days after completing a palliative chemotherapy regimen, soon afterwards becoming unresponsive, requiring airway protection and respiratory support. CT findings suggested fistulation between the tumour and the sacral nerve root.

The patient died within a few days, an outcome unfortunately mirrored in our case. Had the risks of surgery not been too great, resection of the diseased bowel may have been a suitable course of management as was demonstrated in the prior two cases. (7,8)

So why was the patient in our case so unwell: was it sepsis or was it the presence of gas around the brain or spinal cord resulting in neurological deficit? Pneumocephalus for the most part tends to result from self-limiting causes and is not infrequently associated with mild symptoms, most commonly headache. Rarely however it can result in serious neurological deficit, notably in 'tension pneumocephalus', a life-threatening situation in which large volumes of gas under pressure create mass effect on the brain necessitating urgent surgical decompression. (1)

The high pressures of air generated in tension pneumocephalus are assumed to be due to a ball-valve mechanism caused by entry of air into the subdural space through a defect in the skull base or calvaria, with spontaneous egress of air subsequently blocked. Typical causes are neurosurgical procedures, most commonly evacuation of a subdural haematoma and trauma. (10)

Tension pneumocephalus has also rarely been shown to develop from fistulation into the dural sac; Patel et al. (11) describe an oesophageal–subarachnoid fistula at the cervical level caused by an oesophageal tumour, which following an episode of retching resulted in spontaneous tension pneumocephalus.

On imaging, tension pneumocephalus is classically associated with the 'Mount Fuji' sign in which bilateral subdural gas collections cause compression of the frontal lobes and widening of the interhemispheric space (10) (Figure 4).

PNEUMOCEPHALUS: A RARE COMPLICATION OF COLONIC CANCER

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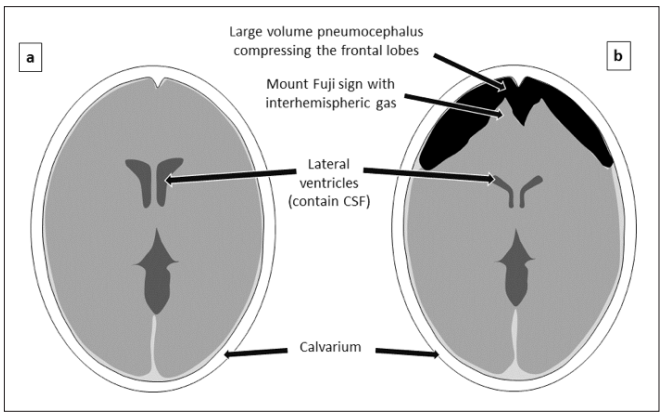

Figure 4: Schematic diagram illustrating the Mount Fuji sign seen in tension pneumocephalus.

In our case the imaging features were not entirely typical for this, although the fact that there was some mass effect on the left frontal lobe with some early separation of the interhemispheric fissure (Figure 1) does raise the possibility of early tension pneumocephalus. However the fact that the patient showed some improvement in GCS from 3 at the time of CT to 11 the following morning suggests that progressive tension pneumocephalus was less likely.

Pneumorrhachis on the other hand is typically asymptomatic and is usually discovered as a consequence of investigating the underlying cause; only a handful of cases have reported neurological symptoms attributed directly to the presence of intraspinal gas itself, and only in exceptionally rare cases has it necessitated decompressive surgery. (4)

It is likely therefore that the patient's condition in our case was contributed to more by the systemic/CNS sepsis rather than neurological deficit caused by the pneumocephalus/ pneumorrhachis.

Cases like this are a rarity, but they are a good example of how clinical medicine never fails to throw new challenges our way, no matter what our level of experience. Complex problems like this one require effective dialogue between specialities to allow a working diagnosis to be made. Unfortunately, despite our best efforts, the outcome is not always as we would have hoped, but as always this provides a good opportunity for learning and reflection.

It also demonstrates that the role of the radiologist often involves piecing together complex imaging findings in a coherent way to explain the clinical presentation of the patient and help guide the management plan of the referring clinicians. Adequate clinical information from the referring team together with good dialogue with the radiology team is therefore critical.

Multiple choice questions

1. The most commonly seen cause of pneumocephalus is:

a. Frontal craniotomy
b. Open calvarial fracture
c. Closed calvarial fracture
d. Sinusitis
e. Invasive tumour

2. A 82-year old man who takes warfarin for atrial fibrillation presents to A&E with new onset confusion following a minor fall two days earlier. A CT head examination is carried out, which shows intracranial haemorrhage. The most likely pattern of haemorrhage is:

a. Extradural haemorrhage
b. Subarachnoid haemorrhage
c. Subdural haemorrhage
d. Haemorrhagic contusions
e. Infarct with haemorrhagic transformation

3. Intravenous contrast agents used in CT are based around which element?

a. Barium
b. Iodine
c. Gadolinium
d. Fluorine
e. Thorium

4. A 25 year old male presents to the ED with a tonic clonic seizure. You apply oxygen, perform an ABC assessment, get IV access and place in the recovery position. After 5 minutes he is still seizing – what is the next appropriate management step:

a. Begin phenytoin (or fosphenytoin) infusion
b. General anaesthesia
c. PR paraldehyde
d. Lorazepam 4 mg
e. PR diazepam

5. A man presents to the emergency department having had a seizure at home. His wife called an ambulance. The paramedics report that en route he has been opening his eyes and moaning in response to verbal stimuli. He cannot obey commands to move his arms and legs but withdraws to painful stimuli. What is his GCS (Glasgow Coma Score)?

a. 11
b. 9
c. 5
d. 10
e. 8

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Answers

1. a. Frontal craniotomy

Pneumocephalus is an extremely common finding in the early postoperative periods following neurosurgical procedures involving the cranium. It is typically of small volume and resolves spontaneously over several days.

Open calvarial fractures or fractures involving the skull base, sinuses and mastoid air cells can also result in pneumocephalus though this is less commonly seen than following surgery. Closed fractures of the calvarium that do not involve the skull base, sinuses and mastoid air cells will not cause pneumocephalus. The presence of pneumocephalus in the presence of trauma should therefore prompt careful assessment of the images to identify the cause as this could influence patient management.

Tumour invasion of the sinuses and sinusitis/mastoiditis can cause pneumocephalus but much less commonly so than surgery or trauma.

2. c. Subdural haemorrhage

Subdural haemorrhage (SDH) is usually a venous bleed resulting from tearing of the subdural cortical bridging veins that extend to the dural sinuses. SDH is relatively common in the elderly and can present with a vague symptoms, often with no definite history of trauma, particularly chronic SDH. Cases of acute SDH usually present in the setting of trauma and if large can cause reduced conscious level. Anticoagulants are an additional risk factor.

Extradural haemorrhage (EDH) are mostly arterial bleeds that typically result from injury of the middle meningeal artery, whose anterior branch runs deep to the pterion, an H-shaped formation of sutures on the side of the calvarium representing the junction of the greater wing of the sphenoid, the squamous portion of the temporal bone, the frontal bone and the parietal bone.

The classical presentation of an EDH is of a young patient involved in a blow to the head who may or may not have a transient loss of consciousness. After a 'lucid interval' where they regain a normal level of consciousness (but often accompanied by a severe headache), they then gradually lose consciousness as the haematoma increases in size.

Subarachnoid haemorrhage (SAH) classically presents with a 'thunderclap headache', often described the patients' worst headache of their lives. It is often associated with photophobia and meningism, and in a large number of patients is associated with collapse and loss of consciousness.

The commonest cause of spontaneous SAH is a ruptured intracranial aneurysm. However, SAH does have other causes and it is not uncommon to see traumatic subarachnoid blood following significant head injury.

Cerebral haemorrhagic contusions are another type of intracranial haemorrhage. They are usually encountered in the setting of significant head injury, for example a road traffic collision. On CT they are typically seen as hyperdense (bright) foci within the brain parenchyma itself, often in the frontal lobes and in the temporal lobes.

Infarct with haemorrhagic transformation would tend to present with signs/symptoms more in keeping with a stroke.

3. a. Iodine

Intravenous (and oral) contrast agents used in CT are typically iodinated. The iodine attenuates the x-rays and causes the agents to be radio-opaque on CT. These agents are also used in many other radiological applications such as angiography and venography. Although these agents are safe and very widely used, they are in some patient groups associated with contrast-induced nephropathy and hypersensitivity reactions so an awareness of these risks is important.

Gadolinium-based IV contrast agents are used in MRI. Barium sulfate is an insoluble powder used mainly for gastrointestinal tract imaging such as barium swallow studies. Fluorine is used in some nuclear medicine studies in the form of fluorine-18 (18F). This is a positron-emitting radioisotope of fluorine and functions as a radiotracer in positron-emitting tomography (PET).

Thorotrast is an obsolete contrast agent based on thorium dioxide, which provided excellent contrast enhancement and was used in millions of patients before its cessation in the mid-20th century after it was found to be highly carcinogenic.

4. d. Lorazepam 4 mg

Most seizures terminate without treatment within 1-2 minutes. If a seizure lasts greater than 5 minutes they are unlikely to stop without treatment and develop Status Epilepticus. NICE guidelines recommend a dose of benzodiazepines after 5 minutes of seizure activity (usually 4 mg lorazepam if you have IV access, if no IV access buccal / intranasal midazolam and PR diazepam are alternatives).

If the patient continues to seize post benzodiazepines a repeat dose is indicated at 10 – 20 minutes post initial dose - at this stage you should be gaining senior anaesthetic help (if not done so already). Taken from NICE guidelines: (https://www.nice.org.uk/guidance/cg137/chapter/Appendix-F-Protocols-for-treating-convulsive-status-epilepticus-in-adults-and-children-adults-published-in-2004-and-children-published-in-2011)

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5. b. 9

GCS has 3 components – eyes, voice and motor. The best response to each of these is added together to give the overall score. GCS was initially created as an assessment of consciousness post head injury but is now widely used in other causes of reduced consciousness or for any acutely unwell patient. As well as overall score it is important to look for changes in score over time.

	1	2	3	4	5	6
Eye	Do not open	Open in response to pain	Open in response to voice	Open simultaneously		
Verbal	No sound	Incomprehensible sounds	Inappropriate words	Confused. disorientated	Orientated	
Motor	No movement	Extends to painful stimuli	Flexes to painful stimuli	Withdraws to painful stimuli	Localises to painful stimuli	Obeys commands

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RADIOLOGICAL EVALUATION OF PROSTATE CANCER

TJ Syer, K Godley, PN Malcolm

Abstract

Prostate cancer is the commonest malignancy in men with a growing incidence since the widespread use of prostate specific antigen (PSA) blood testing (1). The diagnosis of prostate cancer is usually made by trans-rectal ultrasound guided biopsy (TRUS). Accurate staging is required to determine the best treatment for the patient and staging is predominately determined by multi-parametric MRI (mpMRI) and sometimes isotope bone scans to detect bony metastases.

MRI uses multiple sequences both anatomical (T1 and T2) and functional (diffusion weighted imaging and dynamic contrast-enhanced imaging) to accurately diagnose and stage cancerous lesions. TRUS has limitations because of poor visualisation of malignancy and inability to biopsy the anterior gland effectively. This can result in missed cancers or under-grading of the disease, leading to delayed diagnosis or under-treatment (2, 3). For these reasons there has been increasing discussion of pre-biopsy MRI for the evaluation of suspected prostate cancer.

Introduction

Causing 26% of all male cancer diagnoses in the UK, Prostate cancer is the most common malignancy in men and second commonest cause of cancer mortality. There has been a rise in incidence in recent years with the introduction of Prostate Specific antigen (PSA) screening allowing earlier diagnosis (1). Management options are also expanding including; surgery, radiotherapy, brachytherapy, hormone treatment, high intensity focused ultrasound (HIFU), cryotherapy and active surveillance. Imaging is important for the diagnosis and staging of Prostate cancer and therefore informing treatment options. With developing technology, imaging is set to play an even larger role in prostate cancer assessment in the future.

Prostate Cancer

Prostate cancer is usually diagnosed in the 7th and 8th decades. However a quarter of cases occur in men under 60 years and is more common in Afro-Caribbean men or those with a family history (1). Over 95% of prostate malignancy is adenocarcinoma of the acinar or ductal epithelium, over 70% of which are located in the peripheral zone with the remaining in the transitional zone and around 85% being multifocal (2-4). Commonly men are asymptomatic at diagnosis after investigation of a high PSA.

Lower urinary tract symptoms can also occur in prostate cancer, more often because of benign prostatic hyperplasia with an associated finding of malignancy. These symptoms include; poor flow, hesitancy, increased frequency and the sensation of incomplete emptying. Locally invasive disease may present with incontinence, haematuria, haematospermia, perineal pain, obstructive uropathy or tenesmus. Metastatic disease can present with bone pain, spinal cord or cauda equine compression as well as systemic symptoms.

Imaging and staging

Patients with suspected prostate cancer will undergo a trans-rectal ultrasound guided biopsy for histopathological confirmation. If samples are positive for malignancy and the patient could be considered for radical treatment they will be offered multi-parametric magnetic resonance imaging (mpMRI) for localisation and staging of the tumour to decide their eligibility for prostatectomy or to plan radiotherapy.

If the biopsy is negative and there is still high clinical suspicion of prostate cancer, mpMRI can be done to determine if a template transperineal biopsy is necessary. This involves systematic sampling of the whole gland under general anaesthesia.

Isotope bone scanning may be recommended for individuals at risk of bones metastases based on grading, PSA and clinical findings.

mpMRI is also undertaken if active surveillance is being considered.

The most common reason for MRI is to stage the disease with particular attention to whether the cancer extends through the prostatic capsule, invades the seminal vesicles or if there is lymph node or pelvic involvement. These results form part of the TNM staging for adenocarcinoma in the prostate (5). (Table 1 a,b,c,d shows the TNM classification in full.)

T1a T1b T1c	Cancer non-palpable or visible by imaging	Incidental finding ≤ 5% of TURP specimen Incidental finding > 5% of TURP specimen Present in needle biopsy
T2a T2b T2c	Palpable Tumour, confined to prostate	≤ half of one lobe > half of one lobe In both lobes
T3a T3b	Spread outside the prostate	Through prostatic capsule into periprostatic fat Growing into seminal vesicle(s)
T4a	Spread into the adjacent tissues (other than seminal vesicles)	e.g. bladder sphincter, rectum, levator ani, or pelvic side wall

Table 1A: Primary Tumour Staging (T)

N0	No spread to lymph nodes
N1	One or more nearby lymph nodes involved

Table 1B: Nodal Staging (N)

M0	No spread beyond regional lymph nodes
M1a M1b M1c	Distant lymph nodes outside the pelvis Bony Metastasis Other organ involvement independent of bony involvement, e.g. lungs, liver, brain

Table 1C: Metastasis Staging (M)

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Stage	Tumour	Nodes	Metastasis	Grade
I	T1a	N0	M0	Gleason ≤6, PSA <10
	T2a	N0	M0	Gleason ≤6, PSA <10
IIa	T1	N0	M0	Gleason 7, PSA <20
	T1	N0	M0	Gleason ≤6 PSA 10 - <20
	T2a/b	N0	M0	Gleason ≤7 PSA <20
IIb	T2c	N0	M0	Any
	T1/2	N0	M0	PSA ≥20
	T1/2	N0	M0	Gleason ≥8
III	T3	N0	M0	Any
IV	T4	N0	M0	Any
	Any	N1	M0	Any
	Any	An	M1	Any

Table 1D: Final Stage

Imaging Modalities & Their Role

Trans-rectal ultrasound guided biopsy

The initial biopsy for prostate cancer is guided by ultrasound. A probe is inserted into the rectum to allow visualisation of the prostate and seminal vesicles in the transverse and sagittal planes. This allows a hand held biopsy gun to sample 10-12 cores from different areas of the prostate. Prostate cancer can sometimes appear as hypoechoic on ultrasound. If this is seen, the urologist may take an extra sample from this area. For the patient, haematuria and rectal bleeding are the more common complications, and fortunately more serious complications such as urosepsis and rectal bleeding requiring intervention, rarely occur.

The limitations of TRUS are that a majority of tumours cannot be visualized on ultrasound and although systematic in approach, biopsies may miss a cancer. Secondly the inability to sample the anterior gland which is furthest from the wall of the rectum in which the probe is sited, means many anterior gland cancers are missed. Thirdly prostate cancer is often multi-focal so TRUS can under grade the disease if there is more aggressive cancer elsewhere that was not sampled (3).

Magnetic Resonance Imaging

Multi-parametric MRI is a combination of anatomical T1 and T2 weighted sequences with the addition of functional sequences, particularly diffusion weighted imaging (DWI). Dynamic Contrast-Enhanced Imaging (DCE) is also frequently used. T2 weighted and DWI are the most important sequences for the assessment of prostate cancer and meta-analyses have shown sensitivities and specificities of 76% and 82% respectively with this combination (6, 7).

T2 weighted images are useful for examining the zonal anatomy of the prostate, differentiating peripheral and transitional zones. Prostate cancer is often apparent on T2 weighted images as a round or ill-defined low signal focus, but this appearance can overlap with the appearances of prostatitis, haemorrhage and benign hyperplasia and so requires correlation with functional imaging. It is also used to detect extra-glandular extension through the capsule or seminal vesicle invasion.

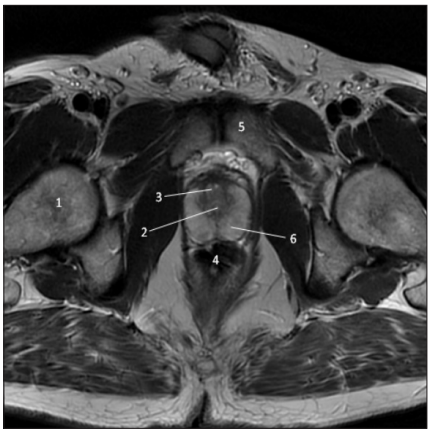

Fig 1A: Axial T2-weighted MRI - Normal

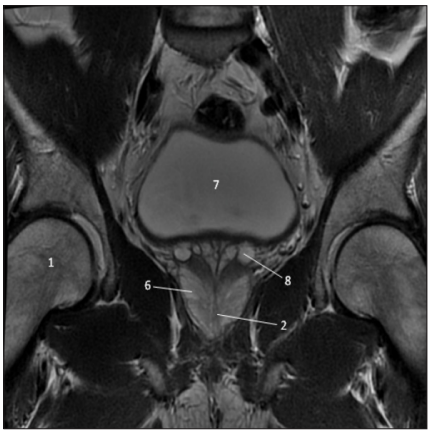

Fig 1B: Coronal T2-weighted MRI - Normal

1 – Head of Femur
2 – Prostatic Urethra
3 - Transitional Zone of Prostate
4 – Rectum
5 – Body of Pubis
6 – Peripheral Zone of Prostate
7 – Urinary Bladder
8 – Seminal Vesicle

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T1 weighted images are used predominantly to assess for post-biopsy haemorrhage which can limit diagnostic accuracy of Prostate MRI and is illustrated in Figure 2. Evidence of haemorrhage after a biopsy can be visible for several weeks afterwards and MRI is usually delayed to allow resolution of haemorrhage (8).

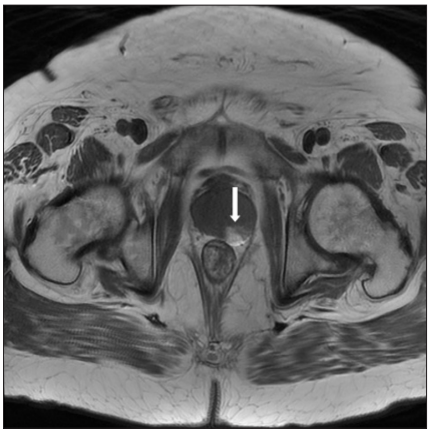

Fig 2: Axial T1-weighted MRI – A focal hyper-intense signal in the peripheral gland representing haemorrhage (arrow)

Diffusion weighted imaging reflects the movement of water within tissue. Prostate cancer creates a higher cell density which restricts diffusion of water. So using DWI and an image called the apparent diffusion coefficient (ADC) map, which is calculated from several diffusion measurements, we can see areas of restricted diffusion which are likely to be malignant. The numerical ADC value can be useful to determine the likelihood of lesions being malignant and have shown a potential to correlate with Gleason score (9). A patient with biopsy proven bilateral prostate cancer is illustrated in Figure 3.

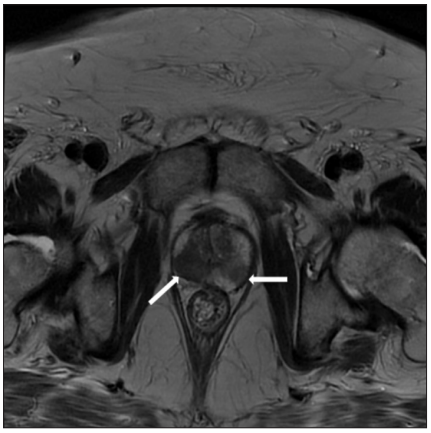

Fig 3A: Axial T2-weighted MRI – Showing ill-defined regions of low signal in both the right and left posterior gland (arrow)

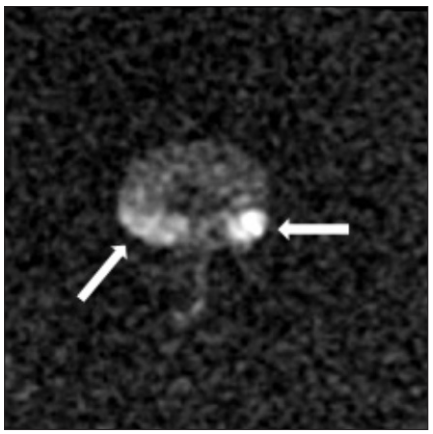

Fig 3B: DWI – Focal areas of hyper intensity in the posterior gland bilaterally (arrows)

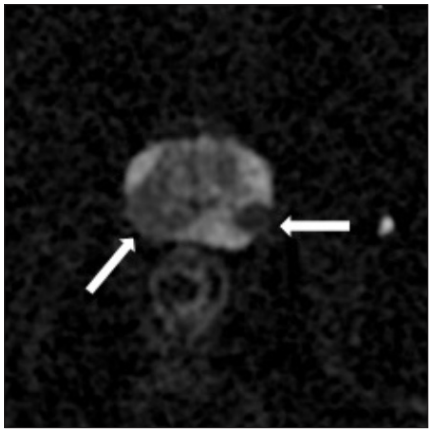

Fig 3C: ADC map – Showing corresponding areas of low signal intensity and hence restricted diffusion (arrows)

Dynamic Contrast-Enhanced Imaging takes images of the prostate before and in rapid succession after administering a gadolinium contrast agent. Prostate cancer often shows focal enhancement earlier than the rest of the gland but should be interpreted with other sequences.

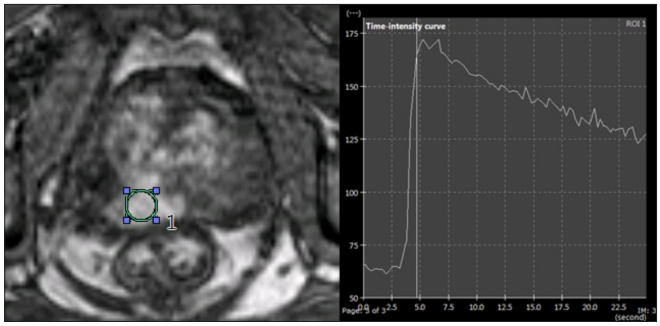

Fig 4A: DCE of cancerous lesion – The focal area of higher signal in the right posterior gland (circle) showing early enhancement and gradual washout on the time-intensity graph typical of a malignant tumour.

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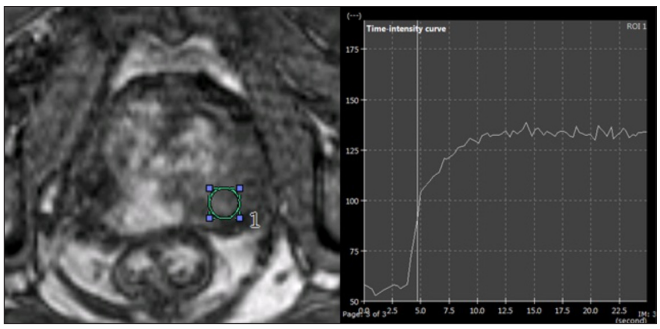

Fig 4B: DCE of normal prostate tissue – An area of normal prostate (circle) with less enhancement which enhances slightly later than that of the cancerous lesions (Fig 4A) without washout.

Magnetic resonance spectroscopic imaging is not routinely used to evaluate prostate cancer. It can assess the ratio between choline and creatinine to citrate within the tissue. Cancerous prostate often shows a higher ratio compared to normal tissue.

Metastases

The commonest site for metastasis is lymph nodes in the pelvis which are well demonstrated at MRI. Metastatic lymph nodes are often enlarged and abnormal in morphology, though it can be difficult to exclude metastatic disease in smaller lymph nodes. If the patient cannot undergo MRI, CT is a useful alternative to look for lymph node disease.

Another common sites for metastasis is the bony skeleton. Often prostatic bony metastases are sclerotic as opposed to lytic and can be visualised on a number of imaging modalities. They can be seen on MRI during the staging assessment of prostate. Sclerosis can be seen on plain film x-ray (Figure 5) which may be done if the presenting complaint is bony in nature.

However metastasis to the skeleton is usually assessed using Isotope bone scanning, which shows focal areas of increased uptake, usually in the axial skeleton (Figure5). Bone scanning is offered to newly diagnosed patients if there is a clinical indication, a Gleason score ≥ 7 or a PSA >10-20ng/mL for which the chance of detecting metastatic disease is over 5% (10). Positron emission tomography using fludeoxyglucose (FDG-PET) has not proved useful in the staging of prostate cancer, however there is ongoing research into new radiotracers that may be more accurate in staging prostate cancer.

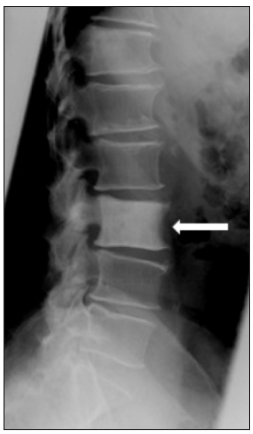

Fig 5: Plain film x-ray lateral lumbar spine – Increased density of L3 vertebra in keeping with sclerotic metastasis (arrow).

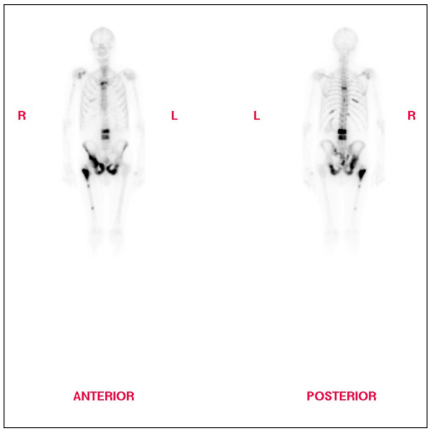

Fig 6A: Isotope Bone Scan: Foci of increased tracer uptake within T6, T9, L3, L4, the ribs, right ischium/acetabulum, sacrum, pubic rami and the right femur in keeping with skeletal metastases secondary to prostate cancer.

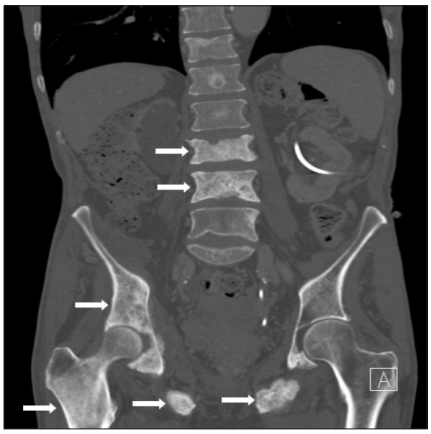

Fig 6B: Coronal CT: Corresponding regions of sclerotic bone in L3 and L4, right ischium, proximal femur and pubic rami bilaterally (arrows).

RADIOLOGICAL EVALUATION OF PROSTATE CANCER

TJ Syer, K Godley, PN Malcolm

Case

A 65 year old asymptomatic male presented to urology with a raised PSA of 9.2µg/L. He underwent TRUS biopsy which was negative, however his PSA continued to rise to 11.3µg/L. He underwent multi-parametric MRI (Figure 7) which showed a likely malignancy in the anterior gland. He proceeded to have a targeted biopsy that showed Gleason 7 adenocarcinoma within the anterior gland.

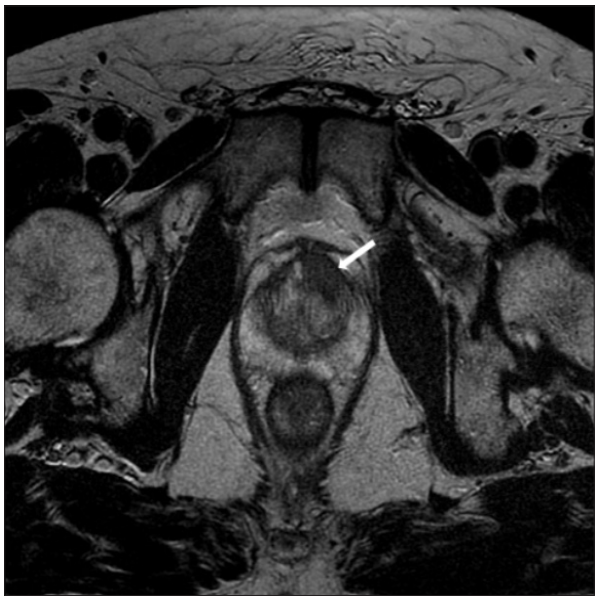

Fig 7A: T2-weighted MRI – Reduced signal in the anterior gland predominantly on the left involving the anterior capsule but no evidence of extracapsular disease (arrow).

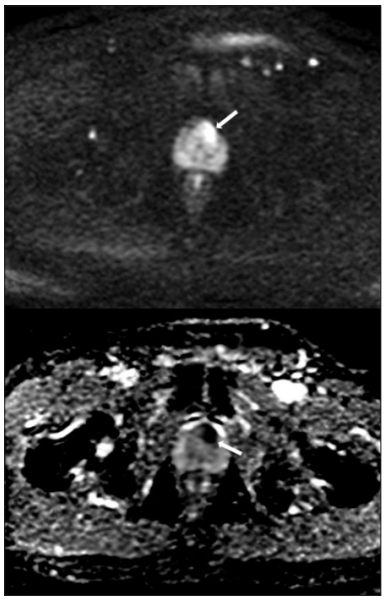

Fig 7B: DWI (top) and ADC map (bottom) – Focal area within the anterior gland on the left showing high signal on DWI and corresponding low signal on ADC.

Future Directions

Advances continue in the diagnosis of prostate cancer. Some centers are starting to use MRI before biopsy for a number of reasons. Firstly it avoids the problem of post biopsy haemorrhage, and reduces any delay in the cancer pathway. Secondly MRI visualises the entire gland including the anterior part which TRUS is poor at sampling. This may enable targeted biopsy and prevent a false negative diagnosis if histology from the posterior gland is normal. (Refer to Case and Figure 7)

One difficulty in the management of prostate cancer is we know many low grade tumours will not result in harm to the patient, and the risks of over-treatment are greater than those of the cancer. MRI does not demonstrate low grade tumours, therefore the use of MRI as a screening tool may prevent unnecessary biopsy of low grade tumours which do not require treatment. Reducing the number of unnecessary TRUS biopsies we carry out would in turn prevent the significant complications of such a procedure, notably false negatives and infection.

It is hoped that in the future, with improved diagnostic ability of MRI to reliably identify clinically significant cancers, pre-biopsy MRI will prevent cancers being missed at biopsy and avoid unnecessary biopsy and treatment for tumours that are not aggressive.

Questions

1. A majority of prostate tumours are?

a) Adenocarcinoma

b) Diagnosed in men under 60

c) Metastatic at presentation

d) Transitional zone tumours

e) Unifocal

RADIOLOGICAL EVALUATION OF PROSTATE CANCER

TJ Syer, K Godley, PN Malcolm

2. Multi-parametric MRI is NOT recommended in which of the following situations for prostate cancer assessment?

a) Men with a negative biopsy but with high

clinical suspicion of prostate cancer

b) Patients being considered for active surveillance

c) Post positive biopsy

d) Screening in asymptomatic men

e) To determine whether a patient may benefit from radical treatment

3. Which radiological finding would NOT affect the staging of prostate cancer?

a) Anteriorly located lesion

b) Extra-capsular extension

c) Invasion of the seminal vesicles

d) Involvement of an entire half of the gland

e) Involvement of one pelvic lymph node

4. Which is the commonest site for prostatic metastasis?

a) Axial skeleton

b) Liver

c) Lung

d) Para-aortic lymph nodes

e) Pelvic lymph nodes

5. Which of the following is not a routine part of multi-parametric MRI?

a) Diffusion Weighted Imaging (DWI)

b) Dynamic Contrast-Enhanced Imaging (DCE)

c) Magnetic Resonance Spectroscopy (MRS)

d) T1-Weighted MR Imaging

e) T2-Weighted MR Imaging

Answers

1. Answer: a

95% of prostate malignancies are adenocarcinoma. Only a quarter of cases are diagnosed under the age of 60 and is much more common in men between 60-80 years of age. Due to wide use of the PSA blood test a majority of men are asymptomatic and diagnosed at the stage where the disease is confined to the gland.

Only 30% of tumours arise from the transitional gland with 70% in the peripheral zone and 85% of cases are multifocal which can lead to under-grading from biopsy if only less aggressive foci are sampled.

2. Answer: d

Multi-parametric MRI is currently not used as a screening test but used solely for investigating patients with confirmed cancer or a clinical suspicion of cancer. Most commonly used in men with positive biopsies who are candidates for radical therapy and mpMRI is needed to stage the disease but it may also be done for patients with negative biopsy but with a high clinical suspicion of cancer as TRUS will sometimes give false negative results especially if there is cancer in the anterior zone.

If cancer is found on mpMRI the extent of it's size, position and spread will determine if the patient would benefit from radical treatment namely surgery or radiotherapy. If on active surveillance mpMRI is useful to track any change in the stage of the disease.

RADIOLOGICAL EVALUATION OF PROSTATE CANCER

TJ Syer, K Godley, PN Malcolm

3. Answer: a

Which part of the gland a lesion is located does not affect staging although anterior tumours are more likely to be missed at initial TRUS biopsy. The percentage of the gland affected by the tumour, any invasion outside the capsule, into the seminal vesicles or the involvement of any lymph nodes however, will alter the TNM staging.

4. Answer: e

These are all areas where prostate cancer can metastasise to, however local pelvic lymph nodes are the most common area of spread.

5. Answer: c

T1, T2 and Diffusion weighted Imaging are all considered essential for effective evaluation of prostate cancer. Dynamic contrast-enhanced (DCE) is a useful adjunct and is used widely in addition. MR spectroscopy however is not routinely recommended.

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SPINAL EMERGENCIES: A RADIOLOGICAL REVIEW

N Khan, R Bhatt

Abstract

"I'm suffering from the most awful back pain Doctor."
It remains one of the commonest complaints clinicians will be exposed to, whether it be in the Accident & Emergency (A&E) Department or in the General Practitioner (GP) setting. However, back pain as a presenting symptom can be easily misinterpreted or dismissed by even the most experienced of doctors. We put forward the case that you must ensure this group of patients are not overlooked.

Instead, thorough history taking and examination combined with an awareness of characteristic red flag symptoms may be what prevents these patients from suffering from potentially life threatening consequences.

In this article, we will focus on common acute spinal emergencies that every junior Doctor should be aware of. We will discuss the salient points including presentations, differential diagnosis and radiological findings associated with these through the use of clinical cases.

Case 1

A 71 year old diabetic was showing signs of improvement after having been treated with IV antibiotics for right leg cellulitis on the medical ward. However, the day prior to her anticipated discharge, she started spiking fevers. Bloods were taken by the junior Doctors.

These revealed a raised white cell count of 25.3, and a CRP of 305. Examination revealed an area of cellulitis over her lower back. She complained of pain at this site and stated she could feel pins and needles in both legs. Apart from tenderness in the upper lumbar spine, the rest of her neurological examination was normal. Post discussion with the Consultant, the junior Doctor decided to request an MRI Spine.

1. Study Figure (Fig.) 1. What does it show?

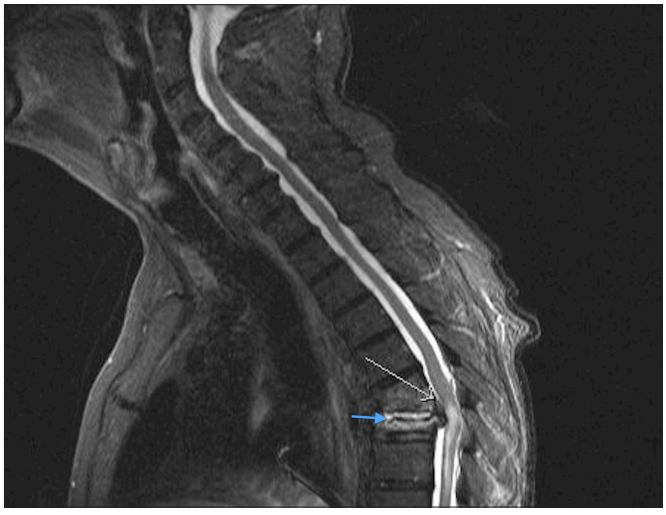

Fig. 1. MRI Spine: Sagittal T2 weighted fat-suppressed sequence

Blue arrow: High signal in the T6/T7 intervertebral disc, indicating fluid with collapse of the T6 vertebral body.

White arrow: Collapsed vertebra associated with posterior disc herniation into the spinal canal causing cord compression. Focus of high signal in the cord is indicative of cord injury.

2. What is Spondylodisciitis? Can you list routes by which a patient may become infected?

Spondylodisciitis is the infection of the vertebral endplates associated with spread to adjacent intervertebral disc spaces [1] (See Fig. 2 & Fig. 3). Dissemination routes can be haematogenous, lymphatic or by direct inoculation (such as through surgery/trauma) [2]. Staphyloccous aureus is the implicated organism in most cases [3].

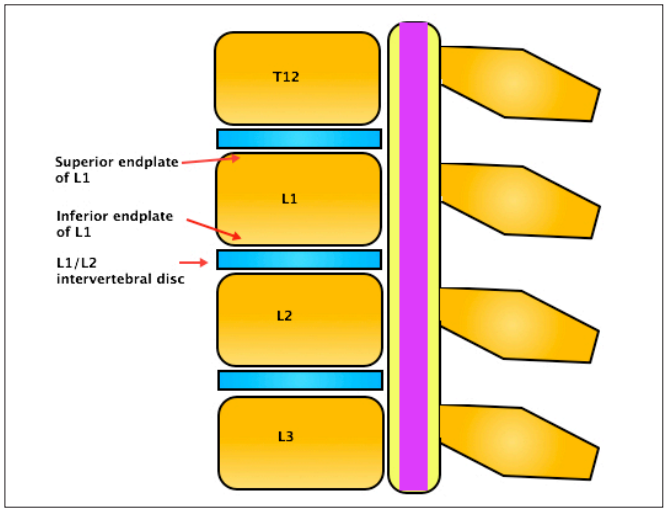

Fig. 2. Schematic representation: Normal appearances of the vertebral bodies and intervertebral discs

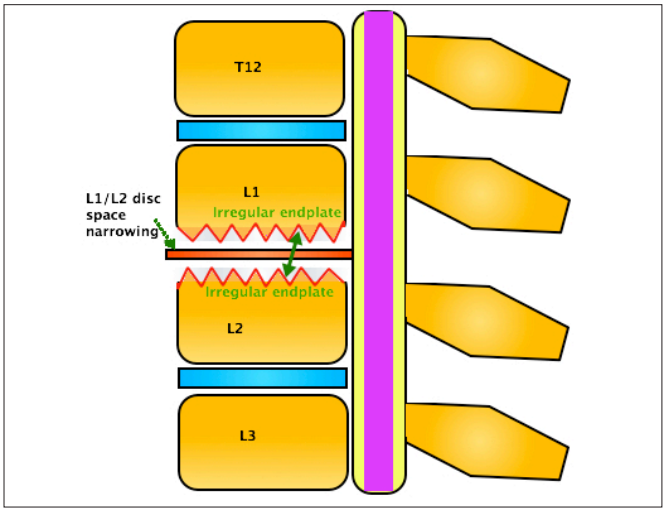

Fig. 3. Schematic representation: Spondylodisciitis: Note the irregularity of the inferior L1 vertebral endplate and the superior L2 vertebral endplate. There is associated L1/L2 disc narrowing secondary to destruction.

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3. Briefly describe the salient radiological findings associated with this disease (list 5):

- *Radiographs may be negative in early stages of the disease. MRI is the modality of choice.*
- *Disorganisation of the intervertebral disc (fragmentation/destruction).*
- *Low T1 signal/High T2 signal of the vertebral body/endplates with irregularity of the endplates on both sides of the affected disc.*
- *Segmental involvement (2 adjacent vertebrae)*
- *Presence of an epidural or paraspinal soft tissue mass.*

4. Fig. 4 is an MRI of a similar patient. Review the image.

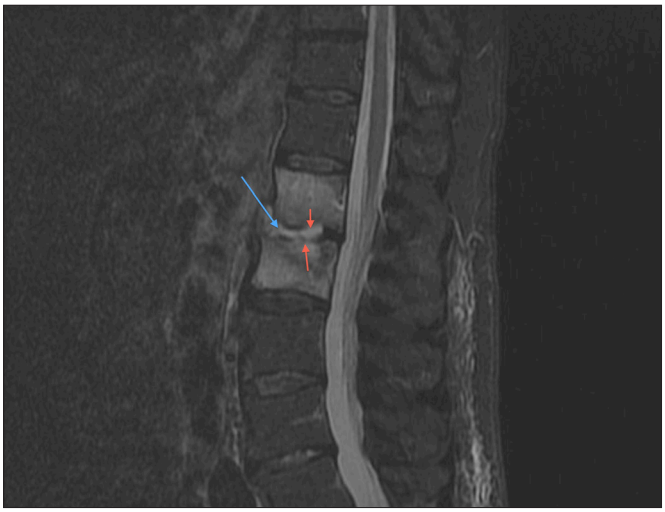

Fig. 4. MRI Spine: Sagittal T2 weighted fat-suppressed sequence

Red arrows: Irregularity of the L1 inferior endplate and the L2 superior endplate with high signal in L1/L2 vertebrae, indicating bone marrow oedema.

Blue arrow: High signal in the L1/L2 intervertebral disc

5. Study the images below [Fig. 5 & Fig. 6]. What infective disease process are these classical findings associated with?

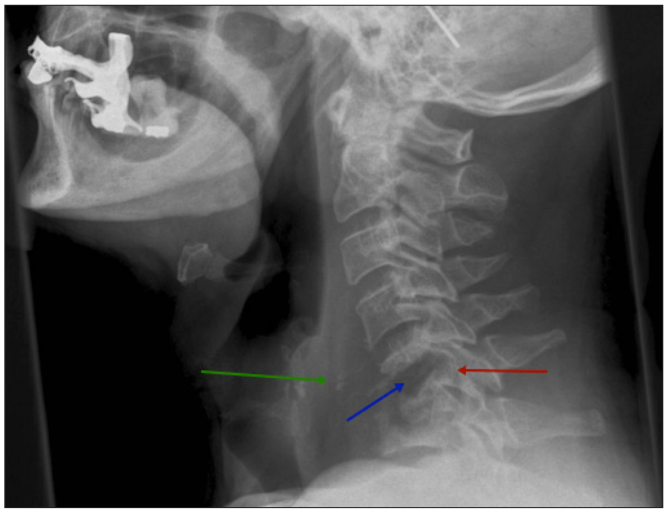

Fig 5. Cervical spine X-ray, lateral view.

There is destruction of the C5 -C7 vertebral bodies with widening of the C5/C6 disc space (blue arrow). Note the focal kyphosis at this level (red arrow) and the prevertebral soft tissue swelling (green arrow)

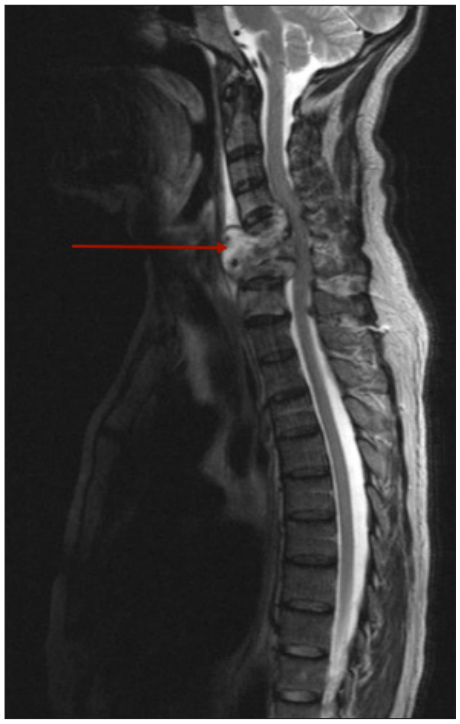

Fig 6. MRI Spine: Sagittal T2 weighted fat-suppressed sequence

Red arrow: Left prevertebral abscess which is invading into the C5/C6 disc space. This is causing significant spinal cord compression at this level. Appearances of Fig 5. And Fig. 6 are in keeping with TB of the spine (Pott's Disease).

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Case 2

A 45 year old man presented to the A&E Department with an acute history of low back pain associated with markedly reduced sensation in his legs. He had been helping move heavy boxes at work when he started suffering from these symptoms. On further interrogation, he revealed he was having trouble passing urine. Neurological examination elicited a positive straight leg raise, with reduced motor strength of the left leg. Furthermore, there was perineal hypoaesthesia and reduced anal tone. The Radiology Registrar was contacted who agreed to an urgent MRI of the spine.

1. What should be your most likely diagnosis for this case?

This patient is presenting with symptoms of cauda equina syndrome. This is compression of the cauda equina nerve roots (at the level of or below L1/L2) and is a neurosurgical emergency [4]. It requires prompt recognition and treatment.

2. What red flags should raise your suspicion of cauda equina syndrome?

Cauda equina syndrome is defined as a clinical diagnosis. It should be suspected in patients presenting with back pain with the following classically associated symptoms: urinary or faecal dysfunction, perianal paraesthesia, radiculopathy, neurological deficits in the lower limbs or reduced anal tone [5,6].

3. Look at Fig. 7 (MRI Spine of the patient in question). Can you briefly describe your findings and explain the cause of the patient's symptoms?

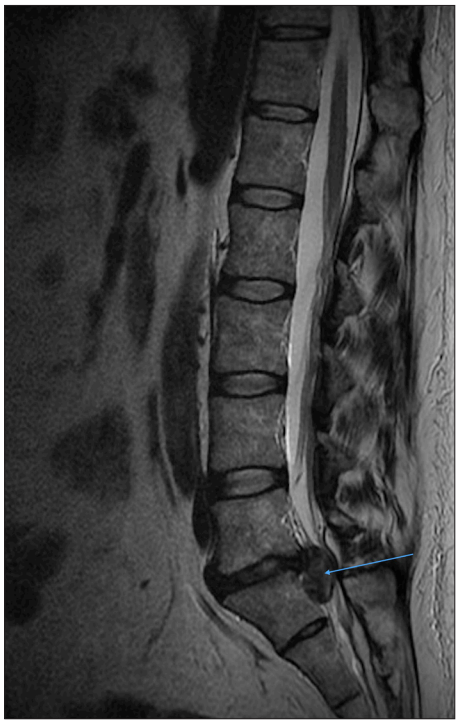

Fig 7. MRI Spine: Sagittal T2 weighted sequence.

Herniated and sequestered (fragmented) disc at the L5/S1 level causing compression of the cauda equina nerves with effacement of the CSF at this level.

4. What are the causes of cauda equina syndrome? (List 3):

- *Acute intervertebral disc herniation [4, 7]: The patient in this case has suffered from this secondary to recent heavy labour at his workplace.*

- *Trauma: retropulsion of fracture fragments into the spinal canal or malalignment of the vertebral column, epidural haematoma are all possible causes of cauda equina nerve root compression [7].*

- *Malignancy: Metastatic invasion of the vertebrae may cause encroachment of the spinal canal [7].*

Case 3

A 47 year old woman who was diagnosed with breast cancer 8 months prior to presentation was complaining of a month's history of bilateral leg pain, worse in the right. This was associated with a burning sensation, and numbness in the lower legs bilaterally. She had received chemotherapy for breast cancer but apart from this, had no other significant medical history. An MRI of the spine was requested.

1. Study Fig. 8. What does it show?

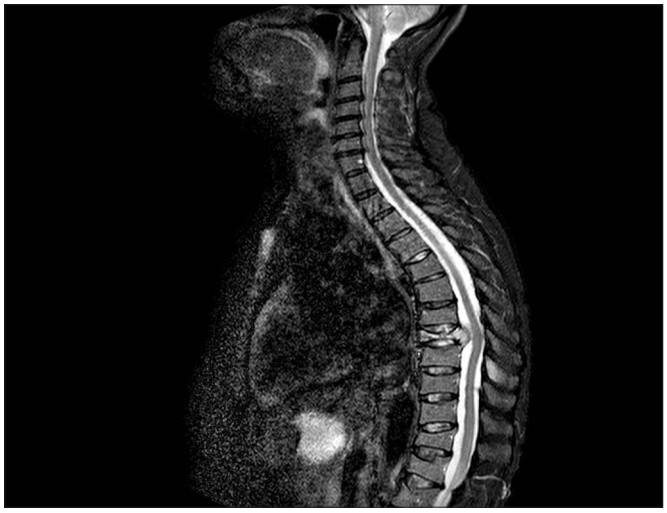

Fig 8. MRI Spine: Sagittal T2 weighted fat-suppressed sequence [no legend as this has been embedded into text as the answer to a question]

Answer

This MRI spine demonstrates collapse of T8 vertebra with associated high signal in keeping with metastatic infiltration of the vertebral body. The cortex is breached posteriorly, with encroachment of the spinal canal and compression of the spinal cord.

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2. How does spinal cord compression differ from cauda equina syndrome?

Cauda equina syndrome, as we have discussed, is a clinical diagnosis based on the patient's symptoms and the clinician's examination. It usually presents with an acute history. Patients with spinal cord compression present with motor weakness inferior to the affected level, with associated specific sensory nerve deficit. Expansion of vertebral bone marrow secondary to metastatic disease may be significant enough to encroach on the spinal canal and cause compression of the spinal cord, or soft tissue extension as in this case [7].

3. What are other common causes of spinal cord compression?

The same disease processes which cause cauda equina syndrome can cause acute spinal cord compression – malignancy, disc herniation and trauma [see Fig. 9 & Fig. 10 to understand how trauma may result in cord compression]. However, in cases of cord compression, the processes are anatomically located above the level of the cauda equine nerves. Remember the classical signs associated with cauda equina syndrome as well.

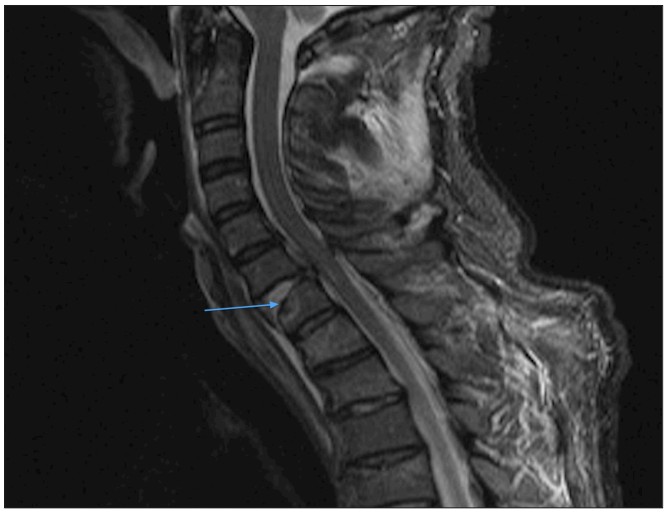

Fig 9. MRI Spine: Sagittal T2 weighted fat-suppressed sequence.

Traumatic oblique fracture of the C7 vertebral body with associated compression of the spinal cord.

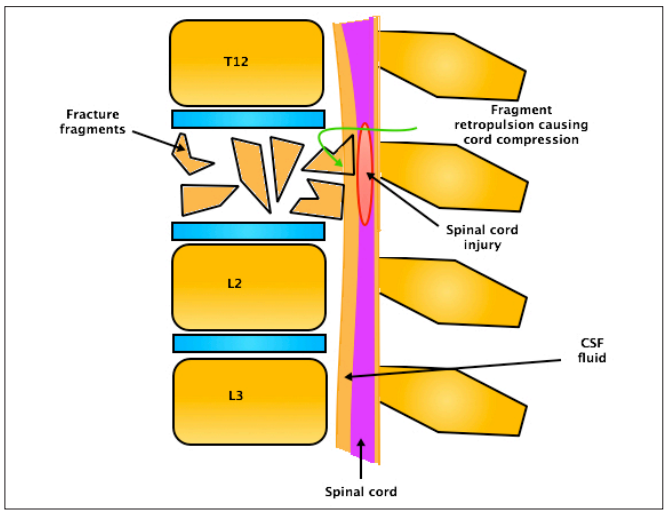

Fig 10. Schematic representation of traumatic spinal cord injury.

Comminuted fracture of the L1 vertebral body with retropulsion of the fragments into the spinal cord, resulting in significant spinal cord compression and high signal in the spinal cord; indicating spinal cord injury.

Case 4

A 64 year old man was recovering 1 day post spinal decompression surgery for a herniated disc. The team looking after him felt the surgery had been successful. However, late that evening the patient started to notice progressive weakness of his lower limbs. On examination, he was found to have reduced power in both legs and demonstrably associated reduced sensation in this region. An urgent MRI scan was performed.

1. Study Fig. 11 & Fig. 12. What do they show?

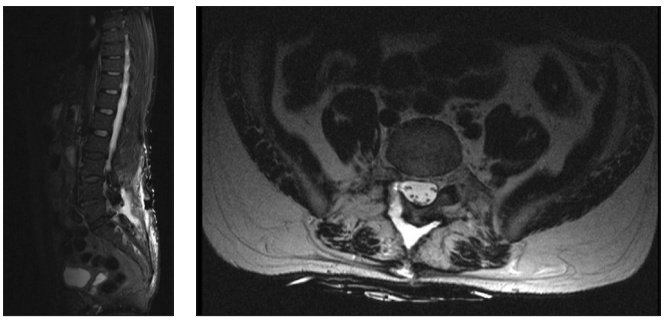

Fig. 11 & Fig 12. MRI Spine: Sagittal and axial T2 weighted sequences [no legend as this has been embedded into text as the answer to a question]

Answer

SPINAL EMERGENCIES: A RADIOLOGICAL REVIEW

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These demonstrate fluid signal similar to the cerebrospinal fluid (CSF) within the spinal canal extravasating into the soft tissues of the back. These appearances are occurring at the level of the lower lumbar spine. Appearances are in keeping with CSF fistula formation.

2. Why and how did this occur?

This complication has occurred in the patient secondary to the recent surgery he has had. Although uncommon, there are other case reports similar to this in the literature [8].

CSF fistulas occur secondary to tears of the dural matter during surgery. A connection between the CSF in the spinal canal and the wound site develops as a result. They require prompt surgery and careful re-closure of the dura.

3. What other post-operative complications should you be aware of in the context of spinal emergencies?

Study Fig. 13. This demonstrates a pseudomeningocele. It is another rare complication secondary to spinal surgery whereby a cerebrospinal fluid collection accumulates in the superficial tissues of the back, secondary to a dural tear [9]. Patients may complain of headache and may be suffering from nausea and vomiting [10].

Spinal epidural haematomas have been cited as another complication that patients may present with after undergoing spinal surgery [11]. As well as surgery, these are associated with a number of other risk factors, which include anticoagulation, coagulopathy disorders, spinal epidurals and vascular malformation [11, 12].

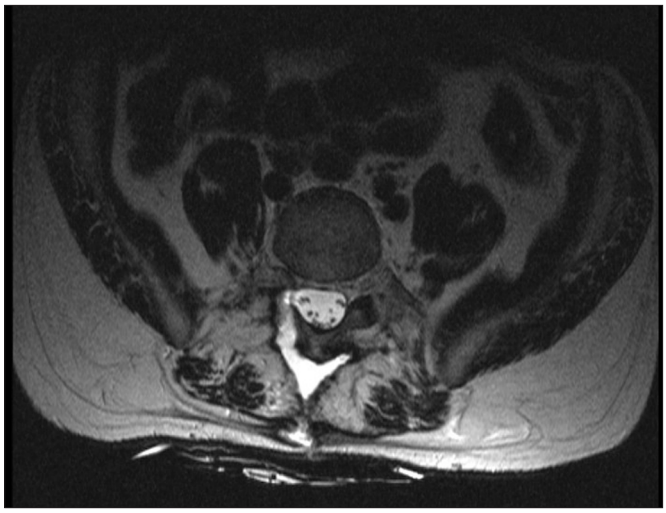

Fig. 13 MRI Spine: Sagittal T2 fat-suppressed weighted sequence.

This demonstrates a fluid collection with a signal intensity similar to the CSF posterior to the spinal canal, within the muscle and soft tissues of the back. Appearances are in keeping with a Pseudomeningocele.

Summary

We have discussed a wide range of spinal cord pathologies through the use of case studies including: infection, cauda equina syndrome, cord compression and post operative complications of the spine.

It should raise your awareness of the importance of a comprehensive history, a detailed examination and an understanding of relevant radiological investigations in the setting of back pain.

Keep in mind that early recognition and appropriate referral is imperative to the health of the next patient that presents with this apparently innocuous complaint.

EMQs

1. Spondylodisciitis is best described as:

a) Infection of the vertebral endplates associated with spread to adjacent prevertebral soft tissues

b) Infection of the vertebral endplates associated with spread to adjacent paravertebral soft tissues

c) Infection of the vertebral endplates associated with spread to adjacent intervertebral disc spaces

d) Infection of the vertebral bodies associated with spread to adjacent intervertebral disc spaces

e) None of the above

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2. Which one of the following radiological descriptions is typically associated with Spondylodisciitis?

a) Gibbus deformity of the affected vertebral body

b) Loss of pedicle in affected vertebral body

c) Fracture through the affected vertebral body

d) Low T1 signal/High T2 signal of the vertebral body/endplates with irregularity of the endplates on both sides of the affected disc

e) High T1 signal/Low T2 signal of the vertebral body/endplates with irregularity of the endplates on both sides of the affected disc

3. Which one of the following statement regarding cauda equina syndrome is correct?

a) It is defined as the compression of the cauda equina nerve roots at the level of or below L1/L2

b) It is defined as the compression of the cauda equina nerve roots at the level of S1

c) It is defined as the compression of the cauda equina nerve roots at or below the level of T12

d) It is defined as the compression of the spinal cord at or below C4

e) It is defined as the compression of the spinal cord at any point below C1

4. Which of the following features is not classically associated with cauda equina syndrome?

a) Urinary/faecal dysfunction

b) Perianal paraesthesia

c) Reduced anal tone

d) Neurological deficits in the lower limbs

e) Headache

5. A 48 year old woman was recovering from an elective laminectomy for a herniated disc. There was no other medical history. The day after surgery, a student nurse inadvertently restarted the patient on her Clopidogrel medication despite her already receiving thromboprophylaxis.

Soon after, she complained of leg weakness which progressed to complete paraplegia. This was associated with faecal incontinence. Neurological examination demonstrated paraplegia, absent reflexes in the lower limbs, associated with sensory deficit. Bloods revealed a drop in her Haemoglobin. Study Fig. 14. What are the arrows pointing to? Which of the following is the most likely cause?

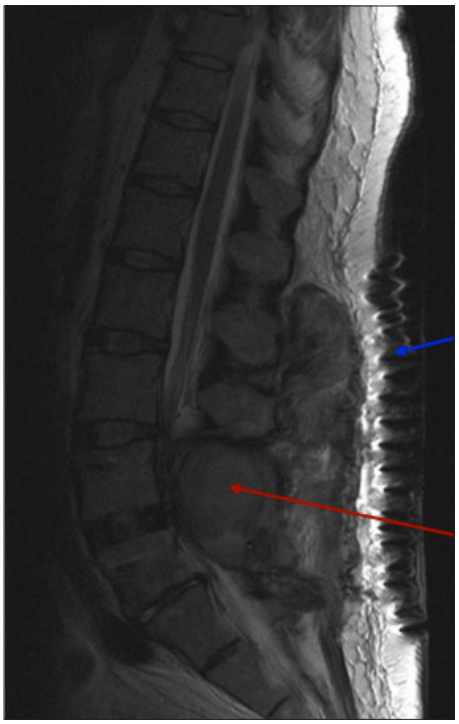

Fig 14. MRI Spine: Sagittal T2 weighted s equence [legend is included in answers]

a) Metastatic cord lesion

b) Epidural haematoma

c) Spondylodisciitis

d) CSF leak

e) pseudomeningocele.

SPINAL EMERGENCIES: A RADIOLOGICAL REVIEW

N Khan, R Bhatt

Answers

1. D

2. D

3. A

4. E

5. B

The red arrow demonstrates a large epidural haematoma causing compression of the cauda equina nerves at the level of L4/L5. The blue arrow shows the patient has had previous spinal surgery. Note the over anticoagulation the patient received, a risk factor for developing a haematoma. Haemoglobin drop also points to the correct answer.

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CASE REPORT: THE CURIOUS INCIDENT OF THE RUPTURE IN THE NIGHTTIME

M Dumba, R Kamanahalli, C Bicknell, N Qazi

Abstract

Penetrating aortic ulcers fall under the umbrella term 'acute aortic syndrome'. They usually present as an incidental finding following imaging for another pathology, however, they are susceptible to rupture and can present acutely. There are no clear guidelines on the best way to manage ruptured penetrating aortic ulcers. The subset of patients who tend to present acutely are older with multiple co-morbidities, so definitive and appropriate management is important to maximise successful outcomes.

We report the case of a 73 year old gentleman with multiple co-morbidities who presented following intra-scapular pain and collapse. He was subsequently found to have a ruptured penetrating descending thoracic aortic ulcer with an associated mediastinal haematoma. He underwent emergency endovascular aortic repair with stent insertion. Post-operative CT angiogram showed that the ulcer was not fully excluded, so thoracic endovascular aortic repair was performed with the insertion of a chimney stent, which successfully excluded the ulcer. No further intervention was required.

Although less common than the other acute aortic syndromes, ruptured penetrating aortic ulcer is a differential diagnosis that needs to be considered in the appropriate clinical context. Prompt and appropriate management is the key to maximise survival and reduce morbidity. Definitive guidelines are scarce, but endovascular management should be considered, particularly in the elderly patient with multiple co-morbidities.

Case History

A 73 year old gentleman presented to A&E following a collapse at home. Prior to the collapse he had reported intra-scapular back pain and left arm paresthesia. His past medical history included hypertension, hypercholesterolaemia, epilepsy and Parkinson's disease. On examination, he was haemodynamically stable, but note was made of differing BPs - left arm 135/87, right arm 160/100. His ECG showed poor R-wave progression, but otherwise had no acute changes. His chest x-ray (figure 1) had features suggestive of a widened mediastinum (white arrows) as well as a large left-sided effusion or area of collapse (yellow arrow). As is often the case with unwell patients, the chest x-ray was suboptimal due to rotation. This meant it was difficult to definitively attribute the widening to pathology. Given the clinical context, a contrast-enhanced CT aorta was recommended by the reporting radiologist.

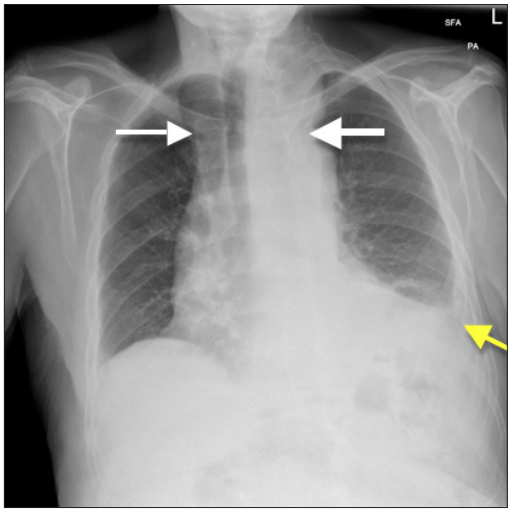


Figure 1: Admission chest x-ray

The contrast-enhanced CT aorta (figure 2) was performed immediately and revealed appearances consistent with a ruptured penetrating ulcer of the descending aorta. There was also a large haematoma that was dissecting mediastinal fat planes in direct continuity with the aortic arch, extending superiorly over the lung apex and displacing the adjacent mediastinal pleura. There was no evidence for active bleeding. No ascending aortic dissection was demonstrated. There was a dissection flap in the distal thoracic aorta extending to the origin of the coeliac artery, but the origin of the vessel itself was from the true lumen. Furthermore, there was a tri-lobed abdominal aortic aneurysm with mural thrombus. The superior mesenteric artery and bilateral renal artery origins were patent with no signs of rupture or impending rupture.

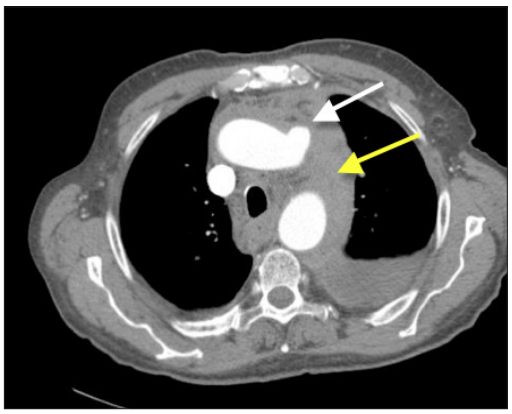


Figure 2: Contrast-enhanced CT aorta – penetrating aortic ulcer (white arrow) with surrounding haematoma (yellow arrow)

CASE REPORT: THE CURIOUS INCIDENT OF THE RUPTURE IN THE NIGHTTIME

M Dumba, R Kamanahalli, C Bicknell, N Qazi

The on-call interventional radiologist and vascular surgeon proceeded immediately to thoracic endovascular repair (TEVAR). It was decided to manage the abdominal aneurysm conservatively. Following a right to left carotid-carotid bypass, the stent was deployed via the right common femoral artery. Post procedure, stent position was satisfactory with good flow in the carotid arteries and crossover bypass (figure 3).

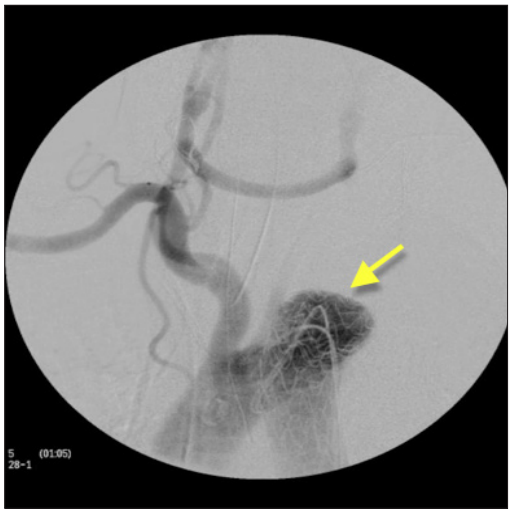
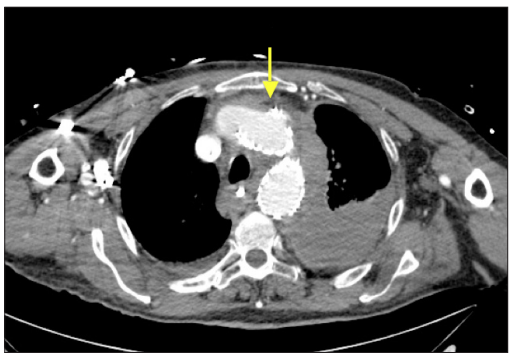


Figure 3: Angiogram during initial endovascular repair (stent graft in aorta – yellow arrow)

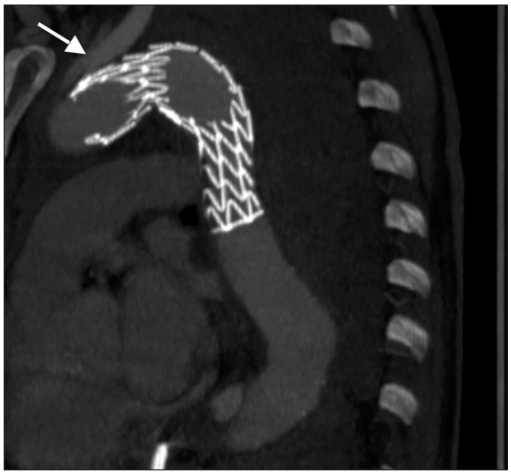
The contrast-enhanced CT aorta the following day however showed that the ruptured PAU had not been completely excluded (figure 4, yellow arrow).

Figure 4: Day 1 Contrast-enhanced CT aorta post-stent a) axial b) coronal

a)



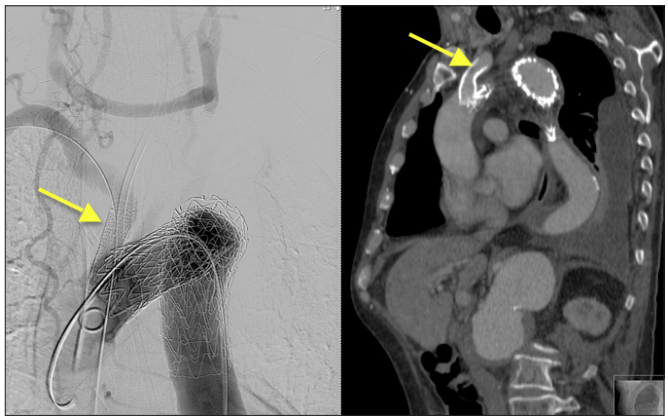
b)



At the proximal end of the stent, there was an uncovered loop that was opening into the ulcer and as a result it was still opacifying with contrast. This also meant the size of the haematoma was enlarging. The stent angle also meant that the brachiocephalic artery (figure 4b, white arrow) was aligned with the stent, so extension was not possible as this would have occluded the brachiocephalic artery. A chimney technique was recommended (figures 5 a & b, yellow arrows) with a view to exclude the ruptured ulcer without causing obstruction to the brachiocephalic artery.

Figure 5: a) Angiogram during 2nd TEVAR b) CT aorta post- 2nd-TEVAR

a)



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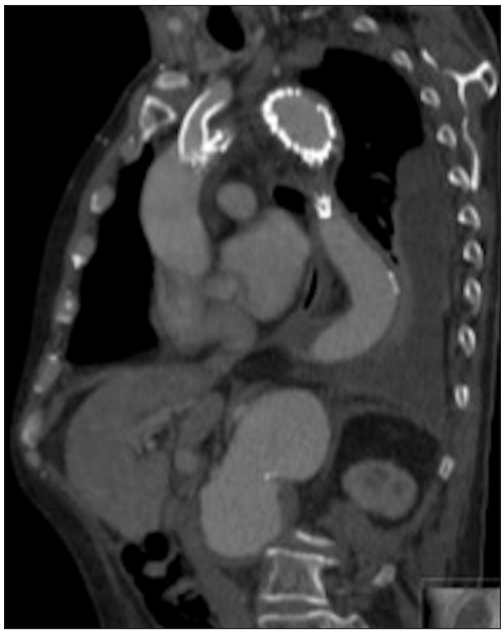
b)



The patient's post-operative course regarding his ruptured PAU required no further intervention. Regarding the patient's other co-morbidities, there were complications related to this including increased seizure activity, pneumonia, recurrent aspirations and poor feeding. The patient was discharged 41 days after admission, with an unsure prognosis due to these factors.

Discussion

Acute aortic syndrome (AAS) encompasses a group of conditions that includes aortic dissection, intramural haematoma (IMH) and penetrating atherosclerotic ulcer (PAU) [1]. The pathophysiology is well described in the literature, but was first described by Stanson et al. It involves ulceration of an atherosclerotic plaque through the elastic lamina layer of the aorta into the media [1].

Exposure of the media to pulsatile blood flow leads to haematoma formation within it that can be a) stable, b) lead to dissection or c) cause weakening of the peripheral adventitial layer of the aorta resulting in aneurysm or rupture [2,4,5]. The mid – descending aorta is most commonly affected [2, 4]. The appearances typically show aortic ulceration penetrating through the intima, with an out-pouching of the aortic contour [4].

The true incidence of PAU is unknown as they are often an incidental finding following CT imaging for other clinical indications [2,5,7]. Ruptured PAUs are not as common as some of the other AAS, accounting for 2-7% of presentations [2,7]. Patients tend to be advancing in age, typically in their 70's, with hypertension, atherosclerosis and cardiac disease, none of which is surprising given their presenting complaint [2,3]. It is important for clinicians to be aware of this as a possible diagnosis, otherwise appropriate management may be delayed.

There is still debate about how to manage PAU. Stable disease may be managed conservatively, but ruptured or symptomatic PAUs often present as an emergency, requiring surgical intervention [3]. This case illustrates how endovascular techniques can be harnessed in the acute situation to manage patients, particularly those with multiple co-morbidities. This patient had not only a ruptured PAU but also an abdominal aortic aneurysm and intramural haematoma. Open surgical management can be more problematic for these patients. Studies comparing open to endovascular techniques are limited, but a review by Cheng et al showed that an endovascular approach reduces early mortality when compared to open techniques for the management of descending thoracic aorta disease [6]. Using a less invasive technique is not the only issue.

A further complicating factor is the patency and success of the stent once deployed via this method. The initial EVAR had not adequately excluded the ruptured ulcer, but manipulation or extension was prohibited by the proximity of the brachiocephalic artery. This case demonstrates how a chimney technique was utilised to overcome this. This technique allows parallel insertion of a new stent adjacent to the original stent, which preserves the patency of the vulnerable vessel [8]. This technique avoids the need for a traditional stent-graft repair, which can be more problematic.

Clinical guidelines need to be in place to ensure the appropriate management of this vulnerable subset of patients. As interventional radiology techniques become more sophisticated and amenable, this may well be the most appropriate way to take care of these patients. For clinicians, considering this diagnosis in the differential is important to ensure they are taken down the most appropriate management pathway.

CASE REPORT: THE CURIOUS INCIDENT OF THE RUPTURE IN THE NIGHTTIME

M Dumba, R Kamanahalli, C Bicknell, N Qazi

MCQs - questions

1. Which ONE of the following is NOT encompassed in the acute aortic syndrome (AAS) spectrum:

a. penetrating ulcer

b. dissection

c. leaking aneurysm

d. intramural haematoma

e. arteritis

2. Which ONE of the following most correctly describes a type A Stanford dissection:

a. ALWAYS involves the aorta DISTAL to the left subclavian artery but NOT below the diaphragm

b. ALWAYS involves the aorta DISTAL to the left subclavian artery AND below the diaphragm

c. ALWAYS involves the aorta PROXIMAL to the left subclavian artery

d. ALWAYS involves the abdominal aorta ONLY

e. ALWAYS involves the left subclavian artery

3. Which of the following is NOT typically used in the investigation or management of a Stanford type B aortic dissection:

a. pain control with opiates

b. contrast-enhanced CT aorta

c. endovascular intervention

d. maintaining BP >120 systolic

e. invasive monitoring

4. Which of the following statements is FALSE regarding AAS:

a. PAU always rupture

b. IMH is caused by rupture of the vasa vasorum

c. dissection is the most common pathology within the AAS spectrum

d. hypertension is a significant risk factor for AAS

e. PAU are a cause of saccular aneurysms

5. Which if the following statements is TRUE regarding AAS:

a. medically managed Stanford type A dissections have a 40% mortality at 24 hours

b. genetic risk factors for dissection are usually autosomal recessive

c. a normal d-dimer and normal ECG are considered specific to exclude AAS

d. PAUs are most commonly found in the ascending aorta

e. all IMH should be medically managed

MCQs - answers

1. e

Arteritis – this is a condition caused by complex, granulomatous inflammatory changes to long segments of the vessel wall. AAS are caused by focal damage to the intimal layer of the vessel wall exposing the media to blood/ damage or rupture of the vasa vasorum.

2. c

Involves the aorta PROXIMAL to the left subclavian artery – Stanford type A ALWAYS involves the ASCENDING aorta (i.e. proximal to the left subclavian artery). The descending/abdominal aorta and great vessels may or may not be involved. Stanford type B does NOT involve the ascending aorta. Type A pathology is treated surgically/interventional radiology. Type B is managed medically.

CASE REPORT: THE CURIOUS INCIDENT OF THE RUPTURE IN THE NIGHTTIME

M Dumba, R Kamanahalli, C Bicknell, N Qazi

3. d

Maintaining BP >120 systolic - medical management consists of BP control using b-blockers or vasodilators to limit further extension of the dissection. Pain relief using opiates is useful to reduce sympathetic release of catecholamines that results in tachycardia and hypertension. If type B pathology is complicated by features such as end organ failure, limb ischaemia, dissection progression or uncontrolled pain then endovascular intervention should be considered.

4. d

PAU always rupture – PAUs rarely rupture, but when they do they have a worse prognosis.

5. c A normal d-dimer and normal ECG are considered specific to exclude AAS.

a. medically managed Stanford type A dissections have a 40% mortality at 24 hours - 20%

b. genetic risk factors for dissection are usually autosomal recessive – autosomal dominant

d. PAUs are most commonly found in the ascending aorta – descending

e. all IMH should be medically managed – they should be categorised and managed similarly to dissections: type A – surgically, type B medically

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CASE BASED DISCUSSION - ATYPICAL FRACTURE

A Mason, R Armstrong

Abstract

An atypical fracture refers to an insufficiency fracture occurring in the proximal third of the femur, usually in the subtrochanteric and diaphyseal regions; it may be unilateral or bilateral. It is distinct from 'typical' osteoporotic fractures which result from low energy trauma and would not usually occur in normal bone. It is a recognised, rare complication of prolonged bisphosphonate therapy. Atypical fracture is associated with significant morbidity and mortality (1). The aim of this article is to highlight the need to reassess patients taking long term bisphosphonate in order to make a clinical decision with regards to their continuation and to outline the medical and surgical management of these complex patients.

Case History

A 58 year lady presented to the emergency department with 3 weeks of left thigh pain. This had begun whilst walking on holiday and worsened following tripping down 2 steps on the day of presentation. She had a past medical history of brittle asthma and was on on treatment with long term oral steroid therapy. She had been taking Ibandronate 150mg once monthly for 7 years and alendronic acid 70mg once weekly for 5 years prior to this. X-rays of the left femur (Figure 1) revealed an angulated transverse fracture of the upper femur below the intertrochanteric line.

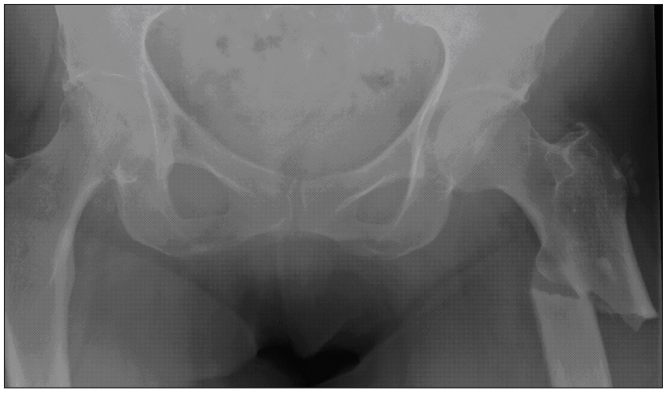


Figure 1: X-ray of pelvis

She had no other risk factors for osteoporosis aside from prolonged steroid therapy. There was no history of previous insufficiency fracture, she did not suffer with rheumatoid arthritis or other inflammatory condition, she had never smoked and drank minimal alcohol.

She had gone through menopause age 53 and not received hormone replacement therapy, there was no family history of femoral fracture and her BMI was 24. Dual energy X-ray absorptiometry (DEXA) scan 5 months prior to admission had shown osteopenia with T-scores of -1.6 in her lumbar spine, -2.0 in her left femoral neck and -1.8 in her right femoral neck.

Discussion

Bisphosphonates are analogues of inorganic pyrophosphate and inhibit farnesyl pyrophosphate synthase in the mevalonate pathway, which results in apoptosis of osteoclasts. They get incorporated in the bone matrix and inhibit bone resorption leading to increases in bone mineral density (BMD).

The most commonly used in practice are alendronate, risedronate, ibandronate and zoledronate, the latter being available as an intravenous preparation. They are first line therapies in treatment of primary and secondary osteoporosis. When deciding whether to treat a patient their risk factors should be assessed (outlined in table one). The WHO fracture risk assessment tool (FRAX) can then be used to guide the clinician on appropriate management. The ultimate decision is based on clinician and patient choice.

Risks independent of bone mineral density	Risks dependent on bone mineral density
Age	Drugs
Previous history of fragility fracture	Malabsorption
Parental history of hip fracture	Conditions resulting in prolonged immobility
Smoking	Untreated premature menopause, untreated hypogonadism
Alcohol intake of 4 or more units per day	Endocrine disease e.g. hyperthyroidism
Steroid use	Chronic liver disease
Rheumatoid arthritis	Chronic renal disease
Body mass index < 19 kg/m2	Chronic obstructive pulmonary disease
Low sunlight exposure	
Falls	

Table 1: Risk factors for decreased bone mineral density

This patient was a 56 year old female with a history of prolonged steroid use. There was no other significant medical, family or social history. Her BMI was 24.

In 2005 concern began regarding atypical fractures associated with use of prolonged bisphosphonates when an unusual type of femur fracture affecting the strongest part of the femur – the suntrochanteric and diaphyseal region began to be noted in patients who had been on bisphosphonate therapy for over 3 years (2). These are now referred to as 'atypical' fractures. It is a diagnosis of exclusion and is excluded if the fracture is intertrochanteric or affecting the neck of femur, spiral or comminuted, periprosthetic or secondary to malignancy.

Atypical fracture is a rare event, a large US healthcare database covering the period of 1996-2009 observed a low and stable rate of 5.9 atypical fractures per 100,000 person-years (3). A recent systemic review found that bisphosphonate therapy was associated with an increased risk of subtrochanteric, femoral shaft, and atypical femoral fracture with adjusted RR of 1.70 (95% CI 1.22–2.37) (4).

CASE BASED DISCUSSION - ATYPICAL FRACTURE

A Mason, R Armstrong

With the widespread use of bisphosphonate therapy it is a risk that physicians should be aware of and patients should be warned about prior to commencing treatment (5). Guidelines, as outlined in figure 2 below, suggest that once a patient has been on bisphosphonate therapy for 3-5 years they should be reassessed with bone mineral density (BMD) and if they are below the national osteoporosis guideline (NOGG) intervention threshold and have a BMD T-score > -2.5 a drug holiday should be considered.

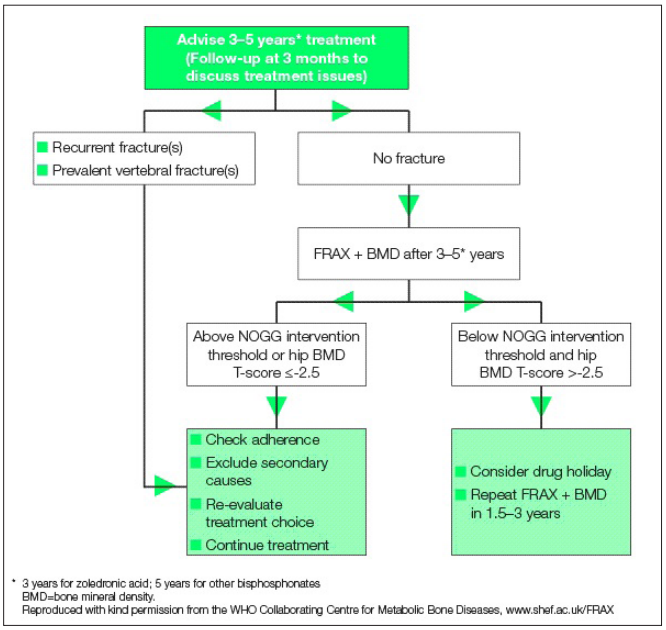


Figure 2: Algorithm for treatment monitoring with the use of bisphosphonates from the National Osteoporosis Guidelines Group (NOGG)

Patients with atypical fracture often present with prodromal thigh pain, as in this patient's case which may proceed the fracture by several weeks or months. The diagnosis should be suspected in any patient with unexplained thigh, groin or hip pain. Imaging of the femur (x-ray, MRI or isotope scanning) should be used to confirm the diagnosis. Circumferential thickening and cortical stress lesions can often be seen on x-ray preceding the complete fracture. In this case the pelvis had been imaged 2 days earlier and no abnormality was seen.

Details of previous osteoporosis treatment and BMD should be sought. In this case the lady had been on bisphosphonate therapy for 12 years. BMD measurements had revealed osteopenia and due to her recurrent use of steroids her bone protection treatment had been continued.

Atypical fracture requires admission and urgent review by the orthopaedic team. Surgical treatment with intramedullary nailing is often recommended. This patient underwent intramedullary nailing with proximal femoral nail antirotation (PFNA). Her post operative x-ray is shown below.

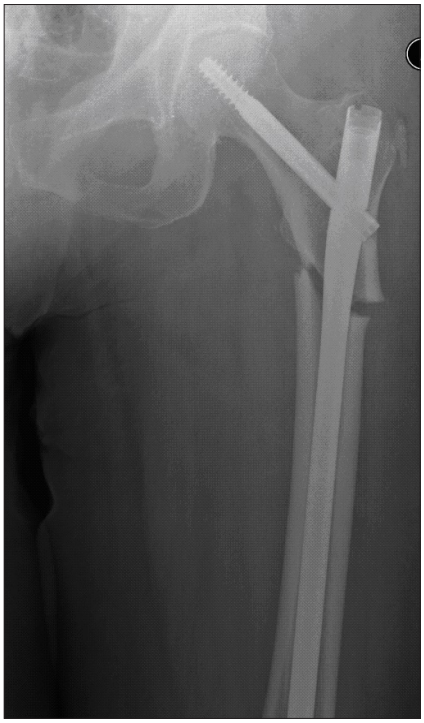


Figure 3: X-ray of left femur

Discontinuation of bisphosphonate therapy should be considered and alternative therapy options considered if appropriate. This patient was reviewed in hospital by the rheumatology team. Ibandronate was discontinued and she was commenced on strontium and vitamin D and calcium supplementation was continued. Subsequently she has been switched to terepatide as an outpatient when DEXA scanning after 2 years revealed deterioration in BMD.

Patients who have suffered atypical fracture should have the contralateral femur clinically assessed and imaged. The option of prophylactic intramedullary nailing is considered based on the patient's symptoms and imaging. Our patient had her right femur x-rayed and this demonstrated some stress reaction, likely secondary to her prolonged bisphosphonate use. The patient was completely asymptomatic on this side and it was decided to keep this under observation with the option of prophylactic nailing if it became painful.

CASE BASED DISCUSSION - ATYPICAL FRACTURE

A Mason, R Armstrong

Atypical fracture is a rare event. Overall bisphosphonates are a very good treatment for osteoporosis in postmenopausal women with a good safety profile (6, 7). Bisphonates prevent significantly more fracture than are caused (8, 9). This case highlights the importance of reassessing patients with osteoporosis and adjusting their therapy as appropriate.

Protocol for the use of Teriparatide

Treatment should be prescribed by doctors in the bone clinic, either from PRI or from Ninewells Hospital.

Treatment is distributed by the FORSTEO Homecare Programme – all registration forms to be sent to Ninewells Pharmacy fao Gordon Thomson.

Treatment should be considered only in postmenopausal women with WHO defined osteoporosis, i.e. T-score less than –2.5, and who ALSO fulfil the following criteria:

i) at least 2 vertebral fragility fractures with a Z-score of less than –2.0 (i.e. "severe osteoporosis")

OR

ii) fragility fractures despite having been on a bisphosphonate for at least 12 months.

Patient must be willing to take daily subcutaneous injection and should NOT HAVE any of the following conditions:

a) Hypercalcaemia

b) Severe Renal failure

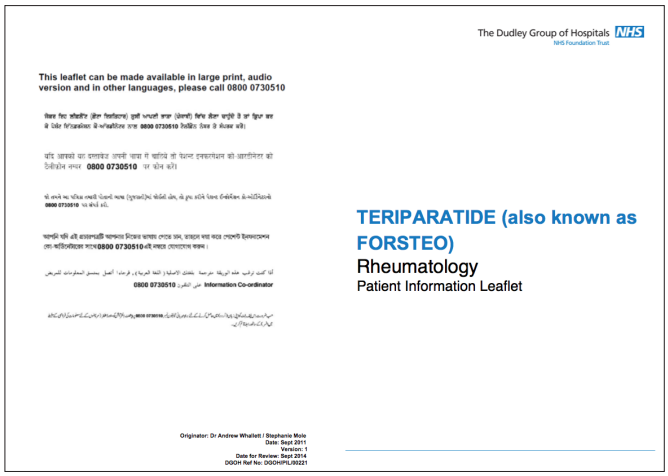
c) Metabolic bone disease or raised alkaline phosphatase

d) Previous skeletal radiotherapy

Notes

a) Whilst taking Teriparatide the patient should not be taking a bisphosphonate con-currently, but should be on calcium and Vitamin D unless there is a good reason to the contrary.

b) Treatment should be given for a maximum of eighteen months, and followed by a bisphosphonate or some other antiresorptive agent Tayside.



The Dudley Group of Hospitals NHS
NHS Foundation Trust

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TERIPARATIDE (also known as FORSTEO)
Rheumatology
Patient Information Leaflet

Originator: Dr Andrew Whallett / Stephanie Mole
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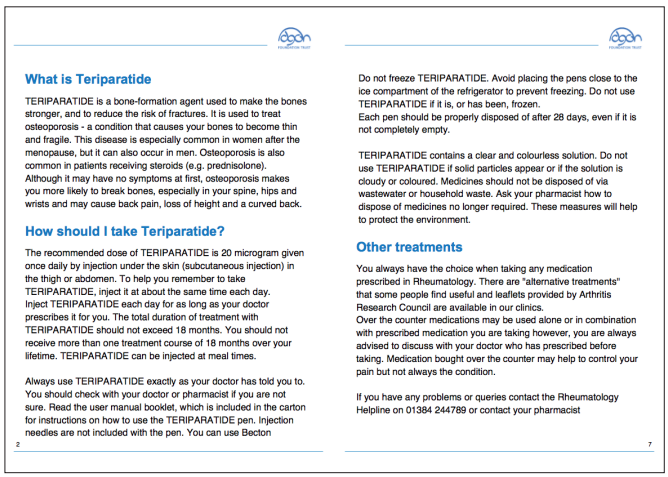

What is Teriparatide

TERIPARATIDE is a bone-formation agent used to make the bones stronger, and to reduce the risk of fractures. It is used to treat osteoporosis - a condition that causes your bones to become thin and fragile. This disease is especially common in women after the menopause, but it can also occur in men. Osteoporosis is also common in patients receiving steroids (e.g. prednisolone). Although it may have no symptoms at first, osteoporosis makes you more likely to break bones, especially in your spine, hips and wrists and may cause back pain, loss of height and a curved back.

How should I take Teriparatide?

The recommended dose of TERIPARATIDE is 20 microgram given once daily by injection under the skin (subcutaneous injection) in the thigh or abdomen. To help you remember to take TERIPARATIDE, inject it at about the same time each day. Inject TERIPARATIDE each day for as long as your doctor prescribes it for you. The total duration of treatment with TERIPARATIDE should not exceed 18 months. You should not receive more than one treatment course of 18 months over your lifetime. TERIPARATIDE can be injected at meal times.

Always use TERIPARATIDE exactly as your doctor has told you to. You should check with your doctor or pharmacist if you are not sure. Read the user manual booklet, which is included in the carton for instructions on how to use the TERIPARATIDE pen. Injection needles are not included with the pen. You can use Becton

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Do not freeze TERIPARATIDE. Avoid placing the pens close to the ice compartment of the refrigerator to prevent freezing. Do not use TERIPARATIDE if it is, or has been, frozen.
Each pen should be properly disposed of after 28 days, even if it is not completely empty.

TERIPARATIDE contains a clear and colourless solution. Do not use TERIPARATIDE if solid particles appear or if the solution is cloudy or coloured. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Other treatments

You always have the choice when taking any medication prescribed in Rheumatology. There are "alternative treatments" that some people find useful and leaflets provided by Arthritis Research Council are available in our clinics.
Over the counter medications may be used alone or in combination with prescribed medication you are taking however, you are always advised to discuss with your doctor who has prescribed before taking. Medication bought over the counter may help to control your pain but not always the condition.

If you have any problems or queries contact the Rheumatology Helpline on 01384 244789 or contact your pharmacist

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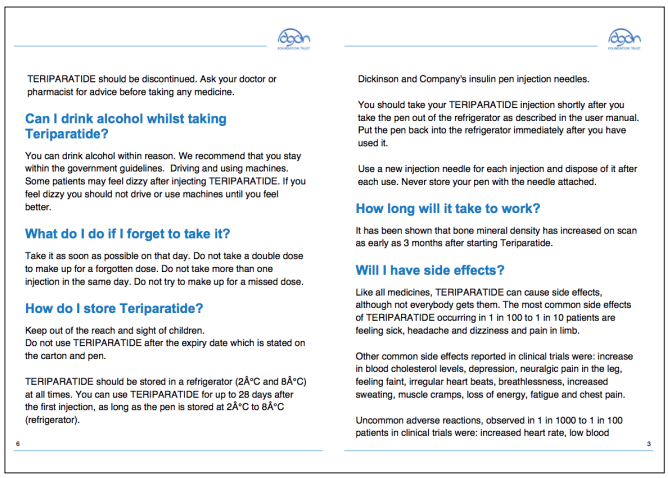

TERIPARATIDE should be discontinued. Ask your doctor or pharmacist for advice before taking any medicine.

Can I drink alcohol whilst taking Teriparatide?

You can drink alcohol within reason. We recommend that you stay within the government guidelines. Driving and using machines. Some patients may feel dizzy after injecting TERIPARATIDE. If you feel dizzy you should not drive or use machines until you feel better.

What do I do if I forget to take it?

Take it as soon as possible on that day. Do not take a double dose to make up for a forgotten dose. Do not take more than one injection in the same day. Do not try to make up for a missed dose.

How do I store Teriparatide?

Keep out of the reach and sight of children.
Do not use TERIPARATIDE after the expiry date which is stated on the carton and pen.

TERIPARATIDE should be stored in a refrigerator (2Â°C and 8Â°C) at all times. You can use TERIPARATIDE for up to 28 days after the first injection, as long as the pen is stored at 2Â°C to 8Â°C (refrigerator).

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Dickinson and Company's insulin pen injection needles.

You should take your TERIPARATIDE injection shortly after you take the pen out of the refrigerator as described in the user manual. Put the pen back into the refrigerator immediately after you have used it.

Use a new injection needle for each injection and dispose of it after each use. Never store your pen with the needle attached.

How long will it take to work?

It has been shown that bone mineral density has increased on scan as early as 3 months after starting Teriparatide.

Will I have side effects?

Like all medicines, TERIPARATIDE can cause side effects, although not everybody gets them. The most common side effects of TERIPARATIDE occurring in 1 in 100 to 1 in 10 patients are feeling sick, headache and dizziness and pain in limb.

Other common side effects reported in clinical trials were: increase in blood cholesterol levels, depression, neuralgic pain in the leg, feeling faint, irregular heart beats, breathlessness, increased sweating, muscle cramps, loss of energy, fatigue and chest pain.

Uncommon adverse reactions, observed in 1 in 1000 to 1 in 100 patients in clinical trials were: increased heart rate, low blood

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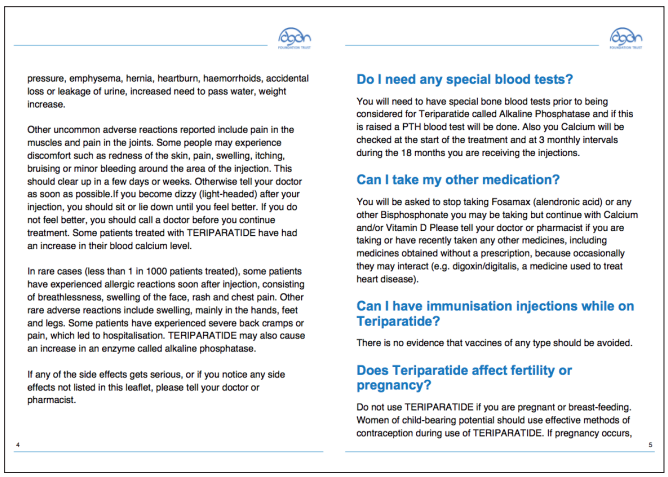
CASE BASED DISCUSSION - ATYPICAL FRACTURE

A Mason, R Armstrong



pressure, emphysema, hernia, heartburn, haemorrhoids, accidental loss or leakage of urine, increased need to pass water, weight increase.

Other uncommon adverse reactions reported include pain in the muscles and pain in the joints. Some people may experience discomfort such as redness of the skin, pain, swelling, itching, bruising or minor bleeding around the area of the injection. This should clear up in a few days or weeks. Otherwise tell your doctor as soon as possible.If you become dizzy (light-headed) after your injection, you should sit or lie down until you feel better. If you do not feel better, you should call a doctor before you continue treatment. Some patients treated with TERIPARATIDE have had an increase in their blood calcium level.

In rare cases (less than 1 in 1000 patients treated), some patients have experienced allergic reactions soon after injection, consisting of breathlessness, swelling of the face, rash and chest pain. Other rare adverse reactions include swelling, mainly in the hands, feet and legs. Some patients have experienced severe back cramps or pain, which led to hospitalisation. TERIPARATIDE may also cause an increase in an enzyme called alkaline phosphatase.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

4

Do I need any special blood tests?

You will need to have special bone blood tests prior to being considered for Teriparatide called Alkaline Phosphatase and if this is raised a PTH blood test will be done. Also you Calcium will be checked at the start of the treatment and at 3 monthly intervals during the 18 months you are receiving the injections.

Can I take my other medication?

You will be asked to stop taking Fosamax (alendronic acid) or any other Bisphosphonate you may be taking but continue with Calcium and/or Vitamin D Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, because occasionally they may interact (e.g. digoxin/digitalis, a medicine used to treat heart disease).

Can I have immunisation injections while on Teriparatide?

There is no evidence that vaccines of any type should be avoided.

Does Teriparatide affect fertility or pregnancy?

Do not use TERIPARATIDE if you are pregnant or breast-feeding. Women of child-bearing potential should use effective methods of contraception during use of TERIPARATIDE. If pregnancy occurs,

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Risks independent of bone mineral density	Risks dependent on bone mineral density
Age	Drugs
Previous history of fragility fracture	Malabsorption
Parental history of hip fracture	Conditions resulting in prolonged immobility
Smoking	Untreated premature menopause, untreated hypogonadism
Alcohol intake of 4 or more units per day	Endocrine disease e.g. hyperthyroidism
Steroid use	Chronic liver disease
Rheumatoid arthritis	Chronic renal disease
Body mass index < 19 kg/m2	Chronic obstructive pulmonary disease
Low sunlight exposure	
Falls	

5 MCQs

1. After what time period should patients on bisphosphoates therapies be reassessed?

a) 5 years for oral bisphosphonates, 3 years for zolendronte

b) Annual review with bone density measurements

c) No change need to be made unless patient has a further fracture

d) Drug holiday should automatically be taken after 3-5 years

e) There is currently no clear guidance and this is down to clinician choice

2. Which of the following are potential side effects of bisphosphonate use?

a) Atypical fracture, hypocalcaemia and Alzheimer's dementia

b) Atypical fracture, hypocalcaemia and increased rate of infection

c) Atypical fracture, osteonecrosis of the jaw and oseophagitis

d) Atypical fracture, osteonecrosis of the jaw and venous thrombosis

e) Atypical fracture, osteonecrosis of the jaw and cardiomyopathy

3. What proportion of the UK population will develop an osteoporotic fracture over their lifetime?

a) 1 in 10 women and 1 in 25 men will have an osteoporotic fracture in their lifetime.

b) 1 in 7 women and 1 in 12 men will have an osteoporotic fracture in their lifetime.

c) 1 in 5 women and 1 in 20 men will have an osteoporotic fracture in their lifetime.

d) 1 in 5 women and 1 in 5 men will have an osteoporotic fracture in their lifetime.

e) 1 in 3 women and 1 in 5 men will have an osteoporotic fracture in their lifetime.

4) What T-score on DEXA scanning constitutes osteopenia and osteoporosis?

a) T-score equal to 0 and > -2.5 = osteopenia, -2.5 or below = osteoporosis

b) T-score equal to -1 and > -3.5 = osteopenia, -3.5 or below = osteoporosis

c) T-score equal to 1.5 and > -2.5 = osteopenia, -3.5 or below = osteoporosis

d) T-score equal to -1 and > -4.5 = osteopenia, -4.5 or below = osteoporosis

e) T-score equal to -1 and > -2.5 = osteopenia, -2.5 or below = osteoporosis

T-score less than or equal to -1 and > -2.5 = osteopenia, -2.5 or below = osteoporosis

CASE BASED DISCUSSION - ATYPICAL FRACTURE

A Mason, R Armstrong

5) How is teriparitide given and over what time period?

a) By subcutaneous injection daily for 18 months to 2 years

b) By subcutaneous injection daily for 5 years

c) By subcutaneous injection 6 monthly for 2 years

d) Orally weekly for 5 years

e) Orally weekly for 2 years

Answers

1. After what time period should patients on bisphosphoates therapies be reassessed?

a) 5 years for oral bisphosphonates, 3 years for zolendronte. Guidance fro the National Osteoporosis Guidelines Group (NOGG) suggests that patients should be reassess after 5 years of treatment with oral bisphosphonates or after 3 years with zolendronte. If they have had an osteoporotic fracture then they should continue bisphosphonate or be switched to another therapy.

2. Which of the following are potential risk factors of bisphosphonate use?

c) Atypical fracture, osteonecrosis of the jaw and oseophagitis are potential risk factors of use of bisphosphonates and patient should be warned about this prior to use.

3. What proportion of the UK population will develop an osteoporotic fracture over their lifetime?

e) 1 in 3 women and 1 in 5 men will have an osteoporotic fracture in their lifetime10. This highlights the significant impact osteoporosis has on the health of the population.

4) What T-score on DEXA scanning constitutes osteopenia and osteoporosis?

e) T-score less than or equal to -1 and > -2.5 = osteopenia, -2.5 or below = osteoporosis. The T-score represents the number of standard deviations the patient BMD is away from a young healthy person of the same sex. The criteria of the World Health Organization are: Normal is a T-score of −1.0 or higher. Osteopenia is defined as between −1.0 and −2.5. Osteoporosis is defined as −2.5 or lower.

5) How is teriparitide given and over what time period?

a) By subcutaneous injection daily for 18 months to 2 years. Teriparitide is not currently recommended for longer than 2 years, partly due to an increased rate of osteosarcoma in rat models.

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TICK THE TICK: ARTHRITIS IN LYME DISEASE

I Biro, O Etomi, J Barret, H Tahir

Abstract

Over two thousand new Lyme disease cases are reported in the UK every year. Although a rare condition the annual reported incidence of laboratory-confirmed cases has increased three-fold in the last decade. Lyme disease is a complex condition with a pathophysiologic background suggesting genetic predisposition and autoimmune pathomechanism. It is induced by a bacterial infection *(i.e. Borrelia burgdorferi spp)* through tick bites.

Flu-like symptoms and skin rash are representative during the first weeks. Cardiovascular, neurologic and musculoskeletal symptoms occur months and years after the tick bite. In some cases chronic, destructive arthritis can develop despite adequate treatment. The knees are the most often affected and the clinical picture generally contains mono- oligoarthritis alongside constitutional symptoms. There is insufficient evidence linking chronicity and severity although a significant number of resistant arthritis cases have been reported.

The diagnosis is directed by a detailed medical history including a possible or confirmed exposure to ticks. Clinical examination is essential while imaging modalities, in particular ultrasound and MRI scans are adjunct investigations with the role of excluding other aetiologies. Lyme disease is confirmed by a two-tiered immunologic detection of anti-Borrelia IgM and IgG antibodies.

The management is simple and success rates are higher if treatment is given early. An essential step is primary prevention through patient education, management of host animals and vaccine development. If infection occurs the standard treatment for Lyme disease is a *14-21 day course of doxycycline 200 mg once a day.*

Introduction

There are between 2,000-3,000 new cases of Lyme disease in the UK every year. Although known as a rare condition a significant concern exists among patients and specialists due to the late increase in its prevalence.

In the early stages, the presentation is quite characteristic thus prompt diagnosis and treatment can prevent serious complications (i.e. meningitis, facial nerve palsy) and long-term sequelae. These can be debilitating and include chronic fatigue, forgetfulness, arthralgia, myalgia and chronic destructive arthritis. In later stages diagnosing Lyme can be difficult due to a plethora of non-specific clinical signs.

It is important to consider a *Borrelia spp* infection when seeing a patient with a mono or oligo-articular arthritis especially when this is accompanied by significant constitutional symptoms.

Background

Lyme disease was first recognised in 1975 in Lyme, Connecticut as a consequence of a large number of new diagnosis of juvenile rheumatoid arthritis. The symptoms typically presented in the summer months at the height of tick season and several patients reported a skin rash preceding the arthralgia. Since then it has earned international notoriety, causing mild to severe disease across the World.

Although a rare condition in the UK, the annual reported incidence of laboratory-confirmed cases has increased three-fold in the last decade. According to Public Health England there are 2000 to 3000 new Lyme cases in England and Wales annually. These are not all laboratory-confirmed and about 15% are acquired abroad (1,2).

Human infections occur through tick bites (3) however cases of other arthropods causing Lyme disease were reported (4). The tick population in some parts of the UK has increased and the endemic regions identified are widely spread across the country (5). (Table 1)

Canada (6), Mexico, the North-Eastern seaboard, California and Oregon in the US (7), Austria (8), the Netherlands (9) in Europe have the highest incidence of Lyme disease. Other states in the US, Europe, North Africa and East Asia are also recognized as endemic regions reporting significant incidence of Lyme borreliosis. (5) (Table 1)

Aetiology and pathogenesis

Lyme disease is the most common tick-borne infection in the Northern Hemisphere. It is caused by the spirochete, *Borrelia burgdorferi* whose normal reservoirs are small mammals (3). Whereas infection of the natural hosts does not lead to disease, the transmission to humans triggers an immune-pathological response to certain B. burgdorferi proteins leading to the clinico-pathological manifestation of Lyme disease (10,11).

In Europe *Borrelia Burgdorferi* sensu *lato spp* is responsible for Lyme disease cases (12) while the US reports infection with a single strain of Borrelia i.e. *Borrelia Burgdorferi sensu stricto (13).*

Reports of tick bites and Lyme disease are more frequent in the spring and early summer when the disease's vectors are in the final two stages of their life cycle. (14) Ticks (Ixodes spp) have four stages of development however attachment, blood –feed and subsequent spread of infection only happens after moulting into nymph and adult forms (15).

TICK THE TICK: ARTHRITIS IN LYME DISEASE

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Lyme Disease Endemic Regions			
America	**Europe**	**Asia**	**Africa**
USA	UK	Japan	Morocco
New England	New Forest	NW China	Algeria
Mid Atlantic	Exmoor	Nepal	Egypt
East-North Central	Dartmoor	Thailand	Tunisia
South Atlantic	Salisbury plain	Russia	
West North Central	Wiltshire		
Mexico	Berkshire		
South America	South Downs		
Brazil	Thetford Forest		
Bolivia	The Lake district		
Colombia	Scottish Highlands and Islands		
	Surrey		
	Kent		
	Herefordshire		
	London parks		
	Slovenia		
	Austria		
	Netherlands		
	Scandinavia, Germany		

Table 1. Lyme disease: Endemic regions

Gram-negative flagellated bacteria enter the body through the skin with the tick's saliva and reach several organs through haematogenous spread (10). The development of a multisystem disorder however depends largely on the infected individuals' innate immunity.

Many studies revealed that late Lyme disease is seen in people whose immune system's first line of defence fails to stop the spread of spirochetes beyond the skin layers (16). This evasion of the initial immune response and the invasion of the human body is possible through vector, bacterial and host factors. Tick salivary proteins, bacterial surface antigens, bacterial proteins and host adhesion molecules have been found to aid the initial infection, dissemination, special features and progression of the disease. Articular involvement is one of the later manifestations of Lyme disease (10).

Although there is insufficient evidence linking chronicity and severity in untreated cases there are reports of severe, resistant arthritis. Not all infected patients develop arthritis (17). This is attributable to the genetic diversity among *Borrelia burgdorferi* strains. While arthritis is the leading cause of Lyme disease-associated morbidity in the US (16), it is less frequently observed in Europe where neurological symptoms dominate the late stages of the disease. Reports of general musculoskeletal symptoms are better balanced between the two continents (13).

The subsiding and recurring nature of arthritis in Lyme disease is thought to be secondary to a repeat immune response to the spirochetes. The exact mechanism by which the bacterium causes arthritis is not fully understood however it has been aided by several animal models. These findings were correlated with human investigations and revealed a vast array of immunological pathways and biomarkers involved in the process of Lyme arthritis.

The lack of an efficient and coordinated response by macrophages, dendritic cells, and neutrophils against the infection permits the dissemination of the spirochetes (16). The late recovery and aggressive immune attack mediated by these cells contributes to the development of mild to severe arthritis and supports the proposition of Lyme arthritis being an autoimmune disorder.

Reports of a chronic arthritis in patients who received anti-microbial therapy exist (18) and a change in residency of the spirochetes to organs that are not fully penetrated by antibiotics along other immune-evasion mechanism (19) can explain these persisting symptoms. Although the lack of PCR evidence of Borrelia DNA did not support these hypotheses, concealed traces of bacterial protein have been found to persist in joints.

These proteins are thought to induce an immune-response at a level that is not detectable by contemporary techniques. Furthermore bacterial proteins (OspA) (20) as well as the role of not only Th-1 lymphocytes through IFN-µ (21), but also Th-17 lymphocytes through the production of IL-17 (22) were found to facilitate antibiotic-resistant arthritis. Patients who experienced arthritis after completing adequate treatment were found to possess HLA-DR4 and HLADRB1 antigens raising questions of a possible genetic background necessary to the occurrence of chronic arthritis following Borrelia infections (23).

Diagnosis and management

Lyme disease has three stages with distinct clinical features.

The *early* localized stage with its classic, patognomonic sign of a circular cutaneous lesion called erythema migrans (EM) starts 3-30 days after the tick bite and is associated with flu-like symptoms of low-grade fever, arthralgia, myalgia, headaches and general malaise (14). It is important to note that many non-specific presentations of EM have been described in the literature and as such the absence of "bull's eye" lesion with the central clearing should not exclude a diagnosis of Lyme's disease (24). The *early and late systemic stages* of the disease encompass symptoms and signs of cardiovascular, peripheral, central nervous system and musculoskeletal system involvement seen months to years after the tick bite in patients who have not received or have not responded to initial treatment (10, 14).

The clinical assessment supports the diagnosis in 60% of cases where a classic presentation of low-grade fever, malaise, arthralgia, myalgia, headaches and meningism are accompanied by a cutaneous lesion suggestive of EM and a history of exposure to ticks (10, 16).

TICK THE TICK: ARTHRITIS IN LYME DISEASE

I Biro, O Etomi, J Barret, H Tahir

The diagnosis in the early stages of the disease is based on clinical examination. Apart from arthritis the late clinical portfolio of Lyme disease contains cardiologic conduction defects (atrioventricular blocks, dysrhythmias), central nervous system disorders (encephalopathy, cognitive dysfunction, cranial nerve palsy, insomnia, depression, personality disorders) peripheral nervous system impairment (polyneuropathy affecting predominantly the lower limbs) and skin lesions (acrodermititis chronica atrophicans) (14, 17).

A study of 65 confirmed Lyme disease cases in the UK found that 51% of patients experienced musculoskeletal symptoms of myalgia and arthralgia while arthritis was at 28% (14). Another study from the UK based on positive serology tests found arthralgia and myalgia in 27% of the assessed patients (25), while a European study including 3317 cases detected joint problems in 15.8% of all cases (26).

Periarticular oedema, recurrent pain, swelling and stiffness of large joints are usually the presenting signs and symptoms of articular involvement in Lyme Borreliosis. More severe, persistent arthritis with cartilage and bone erosion causing permanent joint dysfunction was also recorded (10,17). If Lyme arthritis is suspected imaging, arthrocentesis of the affected joint and serologic blood tests can exclude other aetiologies. The majority of confirmed Lyme arthritis was seen in the knees, other large joint arthritis such as the ankle, elbows, wrists, hips and shoulders were also linked to this condition. Inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein are usually elevated (27).

Laboratory confirmation at the early stage was found misleading as cross-reacting antibodies and consequent false positive results led to unnecessary treatment with no resolution of symptoms (28).

All Lyme serology is processed at the Rare and Imported Pathogens Lab (RIPL) at Porton Down. This is usually a 2-tier methodology. The first test is screening to detect anti-Borrelia IgM antibodies via enzyme-linked immunosorbent assay (ELISA). If this is positive, a confirmatory Western blot (separate IgG and IgM) is performed. Serological tests can give negative result if employed too early as antibodies may not have formed. If the index of suspicion is high, we would advocate treatment and repeated test later. In both early and late stages of the disease false positive results are found to be caused by antibody cross-reactions from other infections, including Epstein-Barr virus, Cytomegalovirus or Herpes Simplex virus.

The rate of false positives is lower (1- 3%) compared to a false-negative rate (36%) in the early stages of infection using two-tiered testing (13,28). Polymerase chain reaction (PCR) for Borrelia Burgdorferi DNA-detection closes the array of diagnostic investigations. The high occurrence of false-positive results due to poor laboratory technique and the often seen false-negative result in both blood and cerebrospinal fluid rolled back the use of PCR in Lyme disease. A possible way of incorporating PCR in the diagnostic process would be by further developing the detection of the OspA DNA in synovial fluid specimens (13). The synovial fluid is predominated by neutrophil granulocytes in Lyme arthritis.

Radiography reveals joint effusion (29) and along with ultrasound and magnetic resonance imaging can aid the differential diagnosis.

An essential step in controlling and managing Lyme disease is primary prevention through patient education, management of host animals and vaccine development.

Treatment in the early stage of the disease is proven to be both health- and cost- effective. Highly favorable outcome of antibiotic treatment is seen in the late stages as well however a small percentage of patients will not respond to neither antibiotic nor anti-inflammatory agents. This refractory presentation characterized by chronic fatigue, joint or muscle pain, and neurocognitive symptoms can be caused by a co-infections with ehrlichiosis, babesiosis, or by a deregulated, defective immune system (1,15).

The standard treatment for Lyme disease is a *14-21 day course of Doxycycline 200 mg OD.* In children younger than 8 years of age and pregnant or breast-feeding women *Amoxicillin 500 mg* TDS for 14-21 days can be prescribed. Late and more severe presentations of the disease should be managed with Cefuroxime Axetil 500 mg BD or Azithromycin 500 mg OD administered for 21 days (29,30).

Conclusion

May, June and July are the time of the year when people are spending more time outdoors and the time when ticks are most active. As Borrelia infected ticks can cause Lyme disease it is important to educate the public about the importance of wearing long sleeves, long socks and boots, 20-30% DEET spray on skin and clothes when going on hikes in wooded, bushy areas with leaf litter and tall grassy meadows.

The diagnosis is based on clinical symptoms and objective signs elicited at physical examination. These findings are supported by a history of travel to a tick endemic region. The early stage of the disease is evident when systemic symptoms of fatigue, headaches and musculoskeletal complaints are backed by the presence of erythema around the port of bacterial entrance on the skin. Arthritis is a frequent late presentation of this condition and it occurs through a series of immune-modulated molecular processes supported by vector, bacteria and host-born factors.

The diagnosis at the late stages is based on serologic detection of antibacterial IgG, IgM antibodies and spirochete DNA.

Various pathomechanisms of Lyme arthritis are described in the literature signifying the complexity and intensity of the immune response generated by the spirochetes. These findings emphasize the importance of early appropriate antibiotic therapy and follow up of patients diagnosed with Lyme disease.

TICK THE TICK: ARTHRITIS IN LYME DISEASE

I Biro, O Etomi, J Barret, H Tahir

Questions

1. Lyme disease associated arthritis has a high incidence rate (60%) in :

A. USA

B. Netherlands

C. UK

D. East Europe

E. Egypt

2. Frequently seen late articular presentation of Lyme disease:

A. Small joint effusion of distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of the hands and feet

B. Polyarticular arthritis with predominant involvement of the hips

C. Mono- or oligoarticular arthritis affecting large joints

D. Arthritis associated with dactylitis and other soft tissue inflammation

E. Arthritis associated with enthesitis

3. The approved serologic tests to confirm a diagnosis of Lyme disease are:

A. Two-tiered: ELISA and Western Blot

B. Immunologic test confirmed by PCR

C. Two-tiered test and PCR detecting Borrelia OspA

D. ELISA detecting antibacterial IgG

E. Vector specific antigen antibody detection and anti-Borrelia IgM antibodies

4. The standard treatment for Lyme disease in children younger than 8 years and pregnant women is:

A. 200 mg Doxycycline OD for 14-21 days

B. 2 g of Cefuroxime Axetil OD for 21 days

C. 500 mg Azithromycin BD for 21 days

D. 500 mg Amoxicillin TDS for 14-21 days

E. 500 mg Cefuroxime Axetil OD for 21 days

5. Which is not a contributory factors to the development of Lyme arthritis:

A. Deficient host immunity

B. Bacterial surface proteins

C. Deficient host proteinase

D. Vector specific factors

E. Genetic predisposition (HLA-DR4, HLA-DRB1)

Answers

1. A

The USA reports infection with Borrelia Burgdorferi sensu stricto and the clinical picture in the late stages of the disease is predominated by articular involvement.

2. C

Lyme arthritis generally presents as mono- or oligoarthritis of large joints with the knees being the most frequently affected.

3. A

The currently approved diagnostic tool to confirm Borrelia infection is a two-tiered immunologic test. A positive screening ELISA for Borrelia IgM antibodies is followed by a confirmatory Western blot detecting anti-Borrelia IgG and IgM antibodies. The high occurrence of false-positive results due to poor laboratory technique and the often seen false-negative results rolled back the use of PCR in Lyme disease

4. D

The treatment for Lyme disease in pregnant women and children below the age of 8 is 500 mg Amoxicillin three times a days for 14-21 days.

5. C

Host specific proteinase enzymes have not yet been found to contribute to the development of arthritis in Lyme disease. A series of host, vector and bacteria specific antigens on the other hand alongside a deficient host immunity and the presence of HLA-DRB1 and HLA-DR4 major histocompatibility antigens have been proven to play an important role in the pathogenesis of arthritis in Borrelia burgdorferi infected mice models.

TICK THE TICK: ARTHRITIS IN LYME DISEASE

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CHRONIC PAIN: PATHOPHYSIOLOGY, PRESENTATION & MANAGEMENT

A Dawson, C Cooper, E Dennison

Introduction

Chronic pain is not an uncommon reason for referral for rheumatology review. It is defined as pain is pain persisting longer than expected past the normal time of healing, e.g. from an acute tissue injury [1]. Some definitions include a certain timeframe, for example persisting three months after resolution would have been expected [2]. It is a complex condition with interplaying physical, cognitive, emotional and behavioural elements [2].

Chronic pain represents a large international health burden. 96 million adults in Europe (approximately 1 in 5) and 56 million adults in America (28% of the adult population) suffer from chronic pain [3,4]. The economic cost is significant; in Europe direct and indirect costs are estimated at €300 billion annually including social security, welfare payments and lost productivity [4]. The figure for America is $100 billion, covering healthcare expenses, lost income and lost productivity [3].

Pathophysiology

The mechanisms behind chronic pain are complex and only partially understood. At a basic level, it is a maladaptive mechanism where physiological changes, which should be reversible once acute tissue healing is complete, remain intact. In a healthy state, tissue injury results in local and systemic inflammatory activation. If nociceptive stimulation however becomes continuous or repetitive, pain processing from the periphery to the brain is affected. Peripheral and central sensitisation occurs due to a prolonged inflammatory state and stimulatory thresholds become lowered, with escalated neuronal activity response [1]. Pain becomes persistent.

Transition From Acute To Chronic

From a physiological perspective early pain management targeted at various points along the pain pathways could seek to prevent the transition from acute to chronic pain. This is important for patient welfare and involves early identification, and in the case of surgical related pain, planning an individualised perioperative pain management strategy.

Not everyone develops chronic pain. Those with similar stimuli can exhibit wholly different responses. It is important to view the condition through a biopsychosocial lens and there are recognised risk factors associated with the development of chronic pain. They include mental health vulnerability including pre-existing depression, anxiety, PTSD, and catastrophising; female gender; raised BMI; younger age; social context and genetic factors [1,3].

The Patient Journey: Case Descriptions

Patients with chronic pain can be seen by a junior doctor in various clinical environments. Patients we have encountered recently describe individuals at different point along a recognisable but not inevitable journey in chronic pain. Maddy*, a 27 year old who works as a carer, with back pain. Suffers with anxiety and has had multiple episodes of time off work due to her back pain, which is causing her current employment difficulties. Has only encountered primary care.

Eleanor, a 22 year old office worker with diffuse pain and somatic symptoms of leg weakness for over one year for which she was referred into secondary care: no neurological or rheumatological cause has been found.

Sarah, a 38 year old with chronic pain which prevents her from working. She has osteopenia due to a previous eating disorder but no osteoporosis or inflammatory joint disease. Seen in a tertiary rheumatological professorial clinic after many clinical specialist encounters.

**all patients' names have been changed*

Physicians' Perspective

Seeing these patients is not always easy. Medical school has historically not prepared doctors well for chronic pain management and its attendant potential consultation conflicts [4,5]. Undergraduates spend a median of only thirteen (KRESS) hours of their training on pain management, far less than physiotherapists, whose input in chronic pain is often beneficial and yet they are involved in the treatment of less than 20% of European patients with chronic pain [4].

Many physicians report finding consultations with patients with chronic pain difficult and frustrating [5]. Recognition of these feelings is important, as is the need to reflect on their root cause. The perception of the chronic pain patient as difficult requires questioning. Assumptions we may have made about them, and about what has brought them here, must be interrogated. Time should be taken to examine our own agendas and recognise how it may be setting us up for potential conflict. A collaborative approach, with recognition of the importance of the patient's social history and context should be fostered [6].

Patients' Perspective

Patients report feeling frustrated with doctors who manage chronic pain. Concerns include time given to discussions of their pain, a preference for the underlying cause rather than treatment and control of the pain itself and perceptions that the physician is displaying frustration or disbelief [5].

Many patients struggle to accept any form of psychological element to their treatment, regarding it as an admission of failure or an implication that their problem is "all in their mind"[4]. Poor doctor patient communication erects barriers to shared understanding and a mutually negotiated and realistic expectation of treatment.

Management

There are tools available to assess patients' pain, which can help in understanding the impact on patients' lives and differentiate between neuropathic and nociceptive pain e.g.: Change Pain Scale; McGill Pain Questionnaire; DN4 [4].

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Pharmacological therapies aimed at the inflammatory process and at different targets along pain pathways are a crucial element of management. Anti-inflammatories can theoretically head off a degree of neurogenic inflammation, suppressing peripheral sensitisation.

Membrane stabilising anti-convulsant drugs have a role in decreasing excitatory neurotransmitters in the pain matrix, e.g. glutamate, noradrenaline and substance P. COX 2 inhibitors prevent breakdown of endocannabinoids, which decrease release of neurostimulators. Antidepressants such as TCAs and SNRIs work on descending modulation of pain [1,3]. Opioid drugs also continue to play a large role.

Psychological stressors are known to accentuate pain intensity [1]. If a patient is at risk from mental health concerns these need aggressive adjunctive treatment to their pain. CBT with an emphasis on coping skills is the non pharmacological therapy of choice in chronic pain. Patients whose journey in chronic pain is not diverted along the way, eased by medication or psychological therapy or in combination, have the option of a Pain Management Programme (PMP).

These are multidisciplinary collaborative programmes involving doctors, nurses, physiotherapists, occupational therapists and psychologists. It is a rehabilitative course structured on cognitive principles designed to educate on pain physiology, self management and healthy functioning as well as identifying and challenging unhelpful beliefs. It seeks to improve daily functioning without predicating this on pain reduction strategies alone.

Our Patients On Their Journey

Maddy: after discussing her anxiety and its negative effect on different areas in her life (her relationships; her pain tolerance and her view of the future) has decided to engage with psychological therapy alongside her predominantly codeine based analgesia.

Eleanor: is currently struggling with the lack of a certain underlying cause for her symptoms. She is hoping an awaited MRI will provide "the answer" and is unwilling to consider psychological intervention at present.

Sarah: currently awaiting a place on an intensive residential PMP after discussing it as an option at multiple clinical encounters.

Conclusion

The ideal goal is to avoid increasing disability in these patients through prompt acute treatment, early identification of those at risk of chronic pain, and timely implementation of psychological interventions. It is also to avoid a jaundiced view of patient encounters that can sometimes be difficult but which with self examination and reflection – the same thing we would ask of them - can be rewarding and uncover a shared pathway that is not inevitable.

MCQs

1. Patients with chronic pain may present to:

a. Rheumatology

b. Primary Care

c. Orthopedics

d. General medicine

e. All the above

2. Recent estimates of the annual economic cost of chronic pain in Europe (direct and indirect costs) are estimated at

a. 200 billion euros

b. 150 billion euros

c. 300 billion euros

d. 500 billion euros

e. 900 billion euros

3. Factors associated with the development of chronic pain include:

a. pre-existing depression

b. female gender

c. raised BMI

d. genetic factors

e. all the above

4. Management of a patient with chronic pain:

a. Is straightforward

b. Is well taught at undergraduate level

c. Requires insight regarding the doctor's own emotions, and good communication skills

d. Requires a patient to understand ' that it is all in their mind'

e. Is generally perceived to be good by the patient community

CHRONIC PAIN: PATHOPHYSIOLOGY, PRESENTATION & MANAGEMENT

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5. Management of a patient with chronic pain might include:

a. Anticonvulsants

b. Antidepressants

c. Antiinflammatories

d. Pain management programme

e. All the above

Answers

1. Correct answer – e.

2. Correct answer – c

3. Correct answer – e

4. Correct answer – c

5. Correct answer - e

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HOW TO APPROACH VASCULITIS: A CLINICAL GUIDE

A Pakozdi, MJ Lewis, H Tahir

Abstract

Vasculitis is inflammation within the blood vessels. Although vasculitis can affect a single organ, in clinical practice systemic disease with multi-organ involvement is more common. The severity of the disease depends on the size and the site of vessels involved. Histologically, the vasculitis may be necrotizing and granulomatous; some forms cause obliteration, ischemia and thrombosis, whilst other types result in aneurysm formation that carries the risk of rupture.

The aim of this article is to understand the nomenclature of primary vasculitides, to learn the different clinical presentations related to each entity, and to provide an approach to the patient with suspected vasculitis.

Case History 1

A 65-year old male presented to A&E with a 5-week history of severe headaches, pain on mastication, weight loss, low-grade fevers, night sweats, limb-girdle muscle stiffness and pain, and a 5-day history of double vision.

On examination he had tenderness of the scalp as well as the temples, temporal artery pulsation was reduced, he had right-sided ptosis with the eye deviating "down and out" but normal pupils (medical third nerve palsy). Laboratory tests revealed a raised ESR 91 mm/hour and CRP 46 mg/L. CT head scan was unremarkable as well as subsequent MRI brain (ruling out posterior communicating artery aneurysm).

Based on the history (constitutional symptoms, new onset severe headache with scalp tenderness, jaw claudication, polymyalgia) and clinical examination (temporal artery abnormality, mononeuritis multiplex affecting the oculomotor nerve) the patient was diagnosed with large vessel vasculitis, and treated with intravenous methylprednisolone 500 mg on 3 consecutive days, then oral Prednisolone 60 mg daily.

His headaches completely resolved after two days of corticosteroid treatment and his double vision has improved. The patient was discharged home. He underwent an outpatient temporal artery biopsy one week later, which showed inflammation of the artery with the presence of characteristic giant cells; hence the diagnosis was biopsy-proven giant cell arteritis.

Case History 2

A 44-year old female presented to A&E with 3 months history of crusty nasal discharge, oral ulcers and few days of worsening shortness of breath, hemoptysis and epistaxis. She also reported recent onset joint pains, and tingling of the fingers and toes. Examination of the nasal cavity showed erythematous granular appearance of the nasal mucosa with nasal crusting. Respiratory auscultation showed bilateral coarse crepitations.

Laboratory tests showed raised WBC 18 (neutrophilia), ESR 67 mm/hour, CRP 45 mg/L, creatinine 134 µmol/L. Urine analysis showed proteinuria and microscopic hematuria with red cell casts. Chest x-ray and subsequent CT revealed bilateral pulmonary nodules. CT of the sinuses showed diffuse mucosal thickening. On the basis of the involvement of the upper respiratory tract (nasal mucosa, epistaxis, sinusitis), lower respiratory tract (hemoptysis, lung nodules), renal involvement (raised creatinine, proteinuria and microscopic hematuria) a pulmonary-renal syndrome was suspected.

Immunofluorescence staining was positive for ANCA with a cytoplasmic staining pattern, and anti-PR3 antibodies were elevated. Despite patient was treated with intravenous methylprednisolone 500 mg on three consecutive days, the hemoptysis worsened and her urine output diminished. Repeat chest x-ray revealed diffuse pulmonary infiltrates and the serum creatinine rose to 622 µmol/L.

Bronchoalveolar lavage revealed hemosiderin containing macrophages suggesting diffuse alveolar hemorrhage. Patient was commenced on hemodialysis and treated with plasmapheresis, and then received intravenous cyclophosphamide 15 mg/kg. She showed gradual resolution of the respiratory and renal failure. She underwent a kidney biopsy confirming a crescentic necrotizing glomerulonephritis. The clinical presentation, the presence of c-ANCA with histological evidence of a necrotizing glomerulonephritis is characteristic of granulomatosis with polyangiitis (formerly named Wegener's granulomatosis, a form of ANCA-associated small vessel vasculitis).

Discussion

Nomenclature of primary vasculitides

There are about 15-20 distinct entities of primary vasculitides. The Chapel Hill nomenclature was first published in 1994 and revised in 2012 (Table 1).(1) Although it is not intended for diagnosing vasculitis, and certainly does not provide a classification system, it is an invaluable tool to understand the different entities. Although the nomenclature system is primarily based on vessel size, the revised version has recognized that some conditions could not be classified by vessel size or anti-neutrophil cytoplasmic autoantibody (ANCA) status. It no longer uses eponyms; instead, the new names reflect the pathology and/or the etiology.

HOW TO APPROACH VASCULITIS: A CLINICAL GUIDE

A Pakozdi, MJ Lewis, H Tahir

Large vessel vasculitis
Takayasu arteritis (TA)
Giant cell arteritis (GCA)
Medium vessel vasculitis
Polyarteritis nodosa (PAN)
Kawasaki disease (KW)
Small vessel vasculitis
ANCA-associated vasculitis
Microscopic polyangiitis (MPA)
Granulomatosis with polyangiitis (GPA)[1]
Eosinophilic granulomatosis with polyangiitis (EGPA)[2]
Immune complex vasculitis
Anti-glomerular basement membrane disease (anti-GBM)
Cryoglobulinaemic vasculitis (CV)
IgA vasculitis (IgAV)
Hypocomplementaemic urticarial vasculitis (HUVS)
Variable vessel vasculitis
Behçet's disease (BD)
Cogan's syndrome (CS)
Single-organ vasculitis
Cutaneous leukocytoclastic vasculitis
Cutaneous arteritis
Primary central nervous system vasculitis
Isolated aortitis
Vasculitis associated with systemic disease
Lupus, Rheumatoid, Sarcoidosis, etc.
Vasculitis associated with probable etiology
HCV, HBV, syphilis, drugs, malignancy, etc.
[1]Formerly known as Wegener's granulomatosis [2]Formerly known as Churg-Strauss syndrome

Table 1. Vasculitis nomenclature by the Chapel Hill Consensus Conference

Large vessel vasculitis

Takayasu arteritis (TA) predominantly affects females under the age of 40. It is an arteritis involving large vessels, the aorta and its major branches. (2) Symptoms are related to the sites of vessels involved, and include limb claudication (ischemic pain in the arms or legs related to mechanical use), or chest pain. Examination findings may include reduced arterial pulses, bruit over large peripheral arteries (carotid, subclavian, femoral vessels), and blood pressure difference between arms.

In contrast to TA, giant cell arteritis (GCA) is uncommon below the age of 50, and mostly occurs in Caucasians. It also affects the aorta and its major branches, but with a predilection to the extracranial branches of the carotid artery.(3) Patients therefore often present with severe headache, scalp tenderness and jaw or tongue claudication.

Polymyalgic symptoms (limb girdle muscle pain and stiffness) are common. Blindness due to anterior ischemic optic neuropathy is a severe complication. On examination, there is tenderness in the scalp including the temples, the temporal arteries may be palpable with nodularity but pulsation may be reduced or absent.

Systemic/Multisystem disease
Infection (bacterial endocarditis)
Malignancy (metastasis, paraneoplastic)
Others (Sweet syndrome, scurvy)
Occlusive vasculopathy
Embolic (cholesterol, atrial myxoma, infection)
Thromboembolic (APS[1], TTP[2], sickle cell disease)
Others (Ergot induced vasospasm, radiation, Degos disease, severe Raynaud's)
Angiographic mimics
Aneurysmal (fibromuscular dysplasia, neurofibromatosis)
Occlusion (coarctation)
[1] antiphospholipid syndrome [2] thrombotic thrombocytopenic purpura

Table 2. Vasculitis mimics

Medium vessel vasculitis

Polyarteritis nodosa (PAN) is a necrotizing arteritis of medium sized vessels causing vessel narrowing and dilatation, internal organ and digital infarcts, as well as aneurysm formation with rupture.(4) Patients may present with abdominal pain secondary to mesenteric ischemia. Kidney impairment is due to renal artery involvement, whilst glomerulonephritis is not a feature.

It often goes undiagnosed for many months due to the relatively non-specific symptoms (remember it as a differential diagnosis for pyrexia of unknown origin). ANCA is always negative. PAN may be associated with current or previous hepatitis B virus (HBV) infection. The incidence of PAN may have decreased due to more effective HBV treatments.(5)

Small vessel vasculitis

Small vessel vasculitides are divided into two groups: one group is associated with ANCA autoantibodies whilst the other one with immune complex formation.

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Granulomatosis with polyangiitis (GPA) (formerly known as Wegener's granulomatosis)(6) is a necrotizing granulomatous inflammation of the small vessels. It most commonly affects the upper respiratory tracts causing a chronic ulcerative inflammation of the nasal and sinus mucosa, the lungs with pulmonary infiltrates, granuloma formation and pulmonary hemorrhage; and the kidneys resulting in glomerulonephritis.(7) ANCA is nearly always positive on immunofluorescence staining (95%), which most commonly shows a cytoplasmic staining (c-ANCA).

Eosinophilic granulomatosis with polyangiitis (EGPA) (formerly named Churg-Strauss syndrome) (8), similarly to GPA, is a necrotisising granulomatous small vessel vasculitis.(9) Marked eosinophilia (>10%) not only in the peripheral blood but also on tissue biopsy, allergic rhinitis, late onset or worsening preexisting asthma are cardinal features.

Neuropathy secondary to ischemia is common and can lead to mononeuritis multiplex or peripheral neuropathy. Myocardial involvement is present in a fifth of patients and is the major cause of death. Although much less common than in GPA, EGPA can also cause glomerulonephritis. ANCA is positive in up to 40% of the cases.

Microscopic polyangiitis (MPA) is a necrotizing vasculitis without granulomatosis and is another cause for pulmonary-renal syndrome. MPA causes pulmonary haemorrhage (dyspnoea, anaemia, haemoptysis), which may progress to diffuse alveolar haemorrhage, and rapidly progressing glomerulonephritis. Arthralgia and myalgia are common even months or years before diagnosis. Other complications are purpura, peripheral polyneuropathy, mononeuritis multiplex and interstitial lung fibrosis. ANCA is nearly always detected (90%) with p-ANCA and anti-MPO in the majority of the cases.

Immune complex vasculitides include anti-glomerular basement membrane disease (Goodpasture syndrome) that causes pulmonary renal syndrome and is associated with the presence of anti-GBM autoantibodies. IgA vasculitis (Henoch-Schönlein purpura) is associated with IgA dominant immune deposits typically involving the skin, the gastrointestinal tract and the kidneys.(10)

In essential cryoglobulinaemic vasculitis, the skin and the kidneys are most commonly affected with cryoglobulin immune deposits.(11) The most common underlying cause is active Hepatitis C infection. Hypocomplementaemic urticarial vasculitis (HUVS) is characterized by recurrent urticaria, hypocomplementaemia (low C1q, and often C3 and C4) associated with anti-C1q autoantibodies. Arthritis, uveitis, glomerulonephritis are common manifestations.

Variable vessel vasculitis

Behçet's disease presents with mouth and genital ulcerations, skin lesions, panuveitis, and retinal vasculitis. Vasculitis involves both arteries and veins of all sizes; although predominantly affects the venous system resulting in deep vein thrombosis, whilst arterial lesions are typically aneurysmal.

Cogan's syndrome is often associated with systemic vasculitis; it causes interstitial keratitis and vestibuloauditory inflammation leading to sensorineural hearing loss. Associations with aortitis have also been described.

Cutaneous vasculitis

The skin is a highly vascularized organ and therefore cutaneous involvement in vasculitis is very common. In cutaneous leukocytoclastic vasculitis the only organ affected is the skin, although it is crucial to assess patients for systemic disease. In addition, the most common causes of isolated cutaneous vasculitis are drugs (Table 3.), in which case withdrawal of the drug usually resolves the problem. In practice, it is therefore important to interpret leukocytoclastic vasculitis as a clinical sign rather than a diagnosis.

Propylthiouracil
Methimazole
Carbimazole
Rifampicin
Isoniazid
Cefotaxime
Minocycline
Indomethacin
Penicillamine
Allopurinol
Clozapine
Phenytoin
Leukotriene antagonists
Cocaine

Table 3. Drugs associated with vasculitis

The hallmark clinical sign of leukocytoclastic vasculitis is palpable purpura. The lesions commonly affect dependent and trauma-prone body parts as opposed to thrombocytopenic purpura that shows a more random distribution and involves the mucosal surfaces as well.

A variety of rashes have been associated with small vessel vasculitides. The urticarial rash of HUVS is persistent (>24 hours) with a predilection to the trunk and proximal extremities; it is burning or painful rather than itching, as opposed to the common urticaria that comes and goes and has marked pruritus.

Although ulceration is most likely to be the consequence of medium to large vessel involvement, necrotic papules or nodules are often found in GPA, as well as pyoderma gangrenosum. Digital gangrene suggests larger vessel involvement like PAN. Livedo reticularis may be a feature of PAN and cryoglobulinaemia but can rarely occur in ANCA associated vasculitides as well.

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Diagnostic approach to vasculitis: the principles.

1. Perform a laboratory screen to differentiate between entities:

RF, ANA, ANCA, anti-GBM, anti-C1q, cryoglobulin, complements C1q, C3 and C4.

2. Consider the appropriate imaging:

CT PET for large vessel vasculitis, as shown on Figure 1. (12); angiogram for large vessel or medium vessel vasculitis, e.g. cerebral or visceral angiogram. High resolution Doppler ultrasound is increasingly used to assess the involvement of the large branches of the aorta in large vessel vasculitis, and can detect inflammation before stenosis would occur. Even smaller arteries, like the temporal arteries can be assessed using ultrasound.

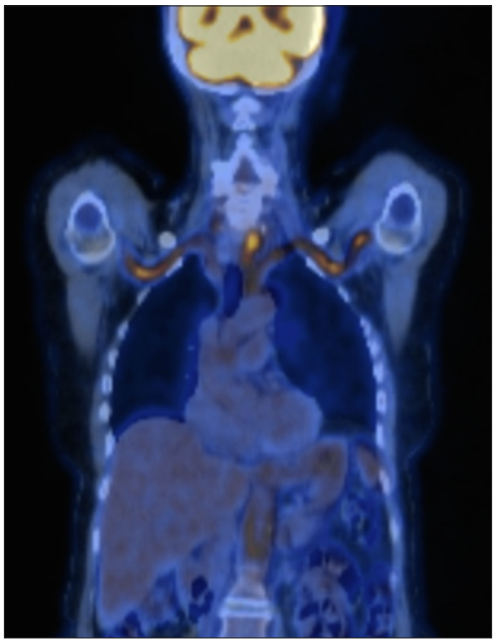

Figure 1. PET scan showing increased uptake in the ascending aorta and subclavian arteries in a patient with large vessel vasculitis

3. Remember, vasculitis is a histological diagnosis! Biopsy the affected area: temporal artery, nasal or sinus mucosa, lung nodule, kidney, skin.

4. Rule out secondary causes and vasculitis mimics listed in Table 2.: infection screen, blood cultures, viral hepatitis and HIV screen, TB, ECHO etc.

Treatment

In large vessel vasculitis the mainstay of treatment is corticosteroids. The optimal dosage is not evaluated in trials but most clinicians would start at 0.5-1 mg/kg/day (max 60 mg/day) maintained for a month then tapered gradually by monitoring the clinical and laboratory (ESR, CRP) response. Pulsed intravenous methylprednisolone is given to patients with visual symptoms. Immunosuppressive therapy is considered only for patients who relapse despite corticosteroid treatment.

There is scarce evidence on the first choice of second line immunosuppressive agent, but methotrexate is often preferred based on its efficacy in small open labeled studies. Azathioprine can be an alternative option. Cyclophosphamide is reserved for life threatening disease. There is emerging data that the IL-6 inhibitor tocilizumab may be useful in steroid refractory cases. All patients should be prescribed aspirin unless contraindicated. Osteoporosis is a well-known consequence of prolonged high dose corticosteroid treatment, and therefore bisphosphonates should be considered in all cases. (13)

In contrast, the treatment of ANCA-associated vasculitides is a combination of corticosteroids and immunosuppressive therapies.(14) The relapse rate in patients treated with corticosteroids alone is high. The choice of immunosuppressive agent depends on the severity of disease. In severe cases cyclophosphamide or rituximab (a monoclonal antibody against CD20 found on B cells) is used to induce remission.

Cyclophosphamide can be given either orally continuously or pulsed intravenously with comparative efficacy, however the intravenous therapy is associated with lower cumulative dose and hence lower toxicity, but may carry a higher risk of relapse. For prevention of opportunistic infections, such as Pneumocystis jiroveci, co-trimoxazole is prescribed concomitantly. Rituximab has been shown no inferiority to cyclophosphamide for achieving remission in ANCA-positive GPA and MPA in two large randomized controlled trials (15, 16), however, the role of rituximab in ANCA-negative cases is unclear.

Once remission is achieved, patients are switched to maintenance immunosuppressants commonly methotrexate, azathioprine or mycophenolate mofetil. Plasma exchange is often used in patients with pulmonary hemorrhage. Intravenous immunoglobulins (IvIg) have a relatively lower side effect profile and can be given to patients with severe infection; and although some good response has been shown with IvIg in GPA, EGPA and MPA, the benefit seems to be temporary.

Cutaneous small vessel vasculitis without systemic features, other organ involvement and without an identifiable secondary cause is usually self-limiting and needs no specific treatment. Symptomatic relief can be achieved with anti-histamines and NSAIDs. Persistent or recurrent cutaneous vasculitis may respond to colchicine or dapsone.

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MCQs

1. The causes of large vessel vasculitides are:

a. GCA

b. Cogan's syndrome

c. Behçet's disease

d. Takayasu arteritis

e. HBV infection

2. Pulmonary-renal syndrome is characteristic to these small vessel vasculitides:

a. GPA

b. EGPA

c. MPA

d. PAN

e. Anti-GBM disease

3. MPA is most commonly associated with these autoantibodies:

a. Anti-MPO

b. Anti-PR3

c. c-ANCA

d. p-ANCA

e. ANA

4. The features of EGPA include:

a. Late onset asthma

b. Granulomatous myocarditis

c. Eosinophilia

d. Peripheral neuropathy

e. Urticaria

5. Cutaneous involvement is common in the following vasculitides:

a. IgA vasculitis

b. GPA

c. Takayasu arteritis

d. HUVS

e. Cutaneous PAN

ANSWERS

1. Answer a. b. c. d.

Large vessel vasculitides include GCA and Takayasu arteritis. Behçet's disease and Cogan's syndrome can cause vasculitis of any sized vessels including large vessels. Another rare autoimmune cause is IgG4 disease. Secondary causes of large vessel vasculitis include infections such as bacterial infections (staphylococcus, streptococcus, salmonella, TB), spirochaetal infections (treponema, syphilis), fungal infections (coccidiomycosis).(17) HBV infection is classically associated with the medium vessel vasculitis PAN.(5)

2. Answer a, b, c, e.

Pulmonary-renal syndrome is a combination of pulmonary capillaritis causing diffuse alveolar hemorrhage and rapidly progressive glomerulonephritis. Causes are:

60% ANCA associated small vessel vasculitides (GPA, MPA, EGPA)

20% Anti-GBM disease

20% others (e.g. SLE, antiphospholipid syndrome, thrombotic thrombocytopenic purpura)

Although PAN can cause renal involvement via vascular nephropathy, glomerulonephritis is not a feature and it does not affect the lungs.

3. Answer a, d.

MPA patients most commonly have p-ANCA and anti-MPO autoantibodies. ANCAs are autoantibodies against the cytoplasm of neutrophil granulocytes and can be divided into patterns when visualized by immunofluorescence staining: cytoplasmic ANCA (c-ANCA), perinuclear ANCA (p-ANCA) and atypical ANCA. c-ANCA is mainly antibodies against proteinase-3 (PR3) and p-ANCA mostly reacts to myeloperoxidase (MPO). PR3-ANCAs occur in the majority of GPAs, whilst MPO-ANCAs are less frequent.

In contrast, MPO-ANCAs are the predominant type of autoantibodies in both MPA and EGPA. Up to 10% of GPA and MPA patients and 60% of EGPA patients can be ANCA negative.

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4. Answer a. b. c. d.

EGPA is strongly associated with an atopic habitus; allergic rhinitis, asthma, eosinophilia, high IgE levels are cardinal features. Granulomatous myocarditis affects up to 20% of patients and is the leading cause of mortality. Cutaneous features include palpable purpuras or necrotic nodules with eosinophilic dermal infiltrates on biopsy.

5. Answer a. b. d. e.

Cutaneous involvement predominates IgA vasculitis (palpable purpura) and cutaneous PAN (mostly livedo reticularis). Small vessel vasculitides like GPA, EGPA or MPA can affect the skin but in combination with other systemic features. Large vessel vasculitides like GCA or TA rarely cause cutaneous lesions.

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HOW WELL DO WE IDENTIFY & TREAT BONE DISEASE IN PATIENTS ADMITTED WITH ALCOHOL-RELATED HARM?

L Moyles, E Archer, C Kelly

Abstract

The number of alcohol related admissions to hospital is growing. One complication of alcohol excess is fracture, and there is minimal evidence base to guide therapeutic intervention in such patients who often fail to appreciate their increased risk of fragility fractures. The risk of fracture may also be underestimated by medical staff in this patient group. We examined Inpatients with alcohol related harm and interviewed them, reviewing their medical notes and laboratory results. We assessed the indication for further action on the basis of the National Osteoporosis Guidance Group (NOGG) recommendations.

Out of 50 inpatients over 5 weeks, 29 required medical intervention to reduce fracture risk according to FRAX scores and the NOGG. DXA scans were recommended in 22 patients, while 7 warranted immediate treatment without DXA. Half of the patient group had experienced a previous fragility fracture but only 4% had had a previous DEXA scan and while 28% were prescribed bone active treatment, half were non-compliant. Patients who misuse alcohol have a high incidence of fragility fractures. We found that they were grossly under investigated and under treated. Improvements must be made by reminding medical staff of the value of the FRAX tool and its pivotal role risk assessment in patients who misuse alcohol.

Introduction

Two brothers, aged 37 and 39, were admitted via ambulance on a Monday afternoon. They lived and drank together, and had derived most of their calorie intake from alcohol over the preceding decade. They had attended a betting shop that morning, and while the elder brother stood outside, the other went in to place a bet.

While in the queue, he suffered a tonic-clonic seizure and his brother was summoned inside. Unfortunately, he tripped over his sibling, sustaining a fractured neck of femur. On arrival in hospital, the younger brother recovered sufficiently from his post-ictal state to complain of severe posterior mid-thoracic pain. X-ray confirmed compression fractures of T12 and L2 which were felt to have been precipitated by opisthotonus.

In January 2016 the chief medical officer proposed new guidelines to reduce the level of harm caused by excessive drinking (1). In the same month, Public Health England issued the guidance "Health matters: harmful drinking and alcohol dependence" to illustrate the harm caused by excessive drinking and discuss methods to reduce alcohol misuse (2).

Harmful drinking and its consequences are far-reaching, indifferent of socio-economic group, age and gender. Many of the public health campaigns to reduce excessive drinking highlight the negative impact alcohol has on the body. Health issues identified regularly include liver disease, cancer and a negative impact on mental health. A clinical consequence not mentioned in either of these new guidelines is the impact excessive drinking has on bone mineral density and fracture risk.

A literature review carried out by Kelly et al. found that fractures are globally four times more prevalent in chronic alcohol abusers compared to age matched controls. A low bone mass is frequently found in alcoholics, and this is associated with increased fracture incidence, delayed healing and increased complication rates (3). This is a significant cost to the NHS and a cause of morbidity for the patient.

The pathogenesis of this low bone density is multifactorial. Alcohol has been shown to induce osteocyte apoptosis and lipid infiltration of osteocytes, bone marrow and bone micro-vessels in rodents (4). Other indirect associations include the effect of alcohol on the liver, pancreas, parathyroid and sex hormones, which can lead to a reduction in osteoblastic activity, or an increase in osteoclastic activity overall reducing bone mineral density.

Patient factors such as malnutrition, reduced exposure to sun light, poor motor control whilst intoxicated and an increased propensity to experience violence also increase fracture risk. When this is combined with a low bone mineral density, the global four-fold increased risk of a fracture is understandable. Hip and vertebrae are the main fracture sites, followed by rib and wrist fracture (3).

The Bone Mineral Density (BMD) of patients who abuse alcohol and sustain a fragility fracture tends to be in the osteopenic range rather than the World Health Organisation (WHO) osteoporosis definition. This may be explained by this group's demographics of a low mean age and a preponderance of males (3). In a study examining younger patients undergoing surgery for hip fractures, half of all patients were abusers of alcohol (5). This study highlighted the need for osteoporosis to be considered in working age alcohol abusers.

The effect of alcohol on BMD is acknowledged by the WHO Fracture Risk Assessment Tool or FRAX. Patients score additional points on the FRAX tool if they drink more than 3 units of alcohol daily. FRAX acknowledge the affect is dose dependent so those that drink a lot more than 3 units could be at additional risk (6). Whilst FRAX is a validated international tool, we felt it was being underused in this patient group.

On admission to hospital with alcohol related harm, patients are treated for withdrawals and possible Wernicke's encephalopathy, but an assessment of their bone health is not always considered even when the patient is admitted with fragility fractures. The authors wished to investigate this and examine ways in which we could improve current standards in secondary care.

Methods

The study was carried out at the Queen Elizabeth Hospital in Gateshead over five weeks. Fifty inpatients were identified by the authors with help from the alcohol liaison nurses. Patients included in the study were:

- *Any patient admitted with a condition related to alcohol excess and drinking more than 3 units a day*
- *Any patient with diagnosed alcoholic liver disease who may or may not be drinking excessively*

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A pro-forma was developed to collect information relating to the patients:

- *Demographics (age, sex, body mass index)*
- *Previous medical history*
- *Alcohol intake*
- *Fracture history*
- *Previous investigations and treatment for reduced BMD*
- *Other risk factors associated with osteoporosis according to the FRAX tool*

Only fractures deemed to be fragility fractures were included in the study. Patients were seen either on inpatient wards or the Emergency Assessment Unit. The information was gathered from speaking to the patients. Their inpatient notes and laboratory results were also analysed, this included results from DEXA scans and vitamin D levels. A FRAX score was then calculated for each patient.

Results

Patient Demographics	
Gender	11 women, 39 men
Age range	30-85 years
Mean Age	58 years
BMI range	16-37
Mean BMI	24.4

Table 1: Patient Demographics

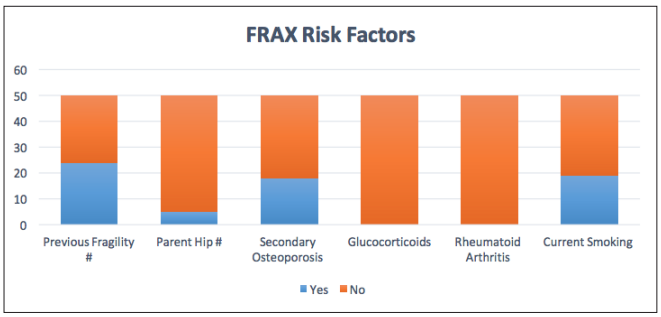
11 patients experienced a classic fragility fracture of the hip, vertebrae or wrist. The most common fracture site was the rib.

Site	No. of Patients
Hip	3
Vertebral	4
Rib	5
Wrist	4
Ankle	2
Shoulder	1
Hand	3
Clavicle	1
Humerus	1

Table 2: Site of fragility fracture

The rate of fracture was reflected in the increased FRAX scores calculated for this group. Out of the 50 patients, 20 patients had a 10-year probability of a major fracture above 10% with the range varying from 2.6% - 36%. The average was 10.6. The average 10-year probability of a hip fracture was 3.9.

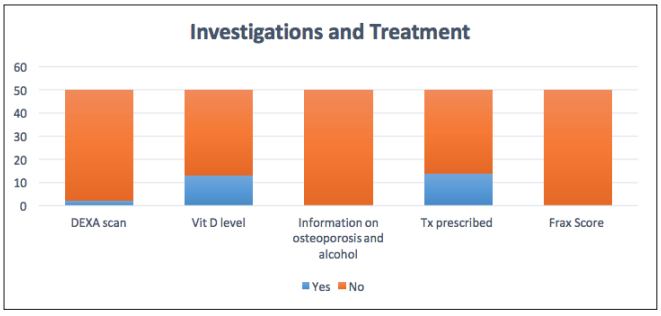
The risk factors used to assess fracture risk were those used by the internationally recognised FRAX tool. On examination of the risk factors that this patient group had 48% had had a previous fragility fracture, 38% were current smokers and 36% were classified as having secondary osteoporosis. No one in our study group had rheumatoid arthritis or took regular glucocorticoid treatment.



Bar chart 1: FRAX Risk Factors

When these patients FRAX scores were applied to the National Osteoporosis Guideline Group, 58% of patients required an intervention. 44% required a DEXA scan to assess if treatment would be beneficial and 14% had risk factors so high they required immediate treatment.

When we studied the group's previous investigations for low BMD or high fracture risk we discovered intervention rates were very low and patient knowledge of the condition was non-existent. Only 4% had had a previous DEXA scan and none had a documented FRAX score in their notes. 28% were prescribed calcium and vitamin D treatment and 2% were prescribed alendronic acid, however only half of the group prescribed medications were compliant with treatment. Some patients denied they were prescribed any treatment at all and this was only discovered from looking at information provided by their GP on admission.



Bar chart 2: Investigations and Treatment

Discussion

Out of the 50 inpatients studied, 24 had experienced a fragility fracture. The National Osteoporosis society report in those aged over 50, 1 in 5 men and 1 in 2 women will experience a fragility fracture (7). Given the high proportion of men in the study group there was an above normal incidence of fracture. Hip, vertebrae, wrist and rib fractures were the most common sites of previous fragility fractures in our study group. This correlates with the results by Kelly et al in a literature review of fracture patterns in patients who abuse alcohol.

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The most common risk factors for fracture in our study group were previous fragility fracture, secondary osteoporosis, current smoking and increased alcohol intake. Interestingly none of the patients had rheumatoid arthritis or took regular glucocorticoid treatment. This indicates that life style choices such as smoking and heavy drinking played a greater role in this group's previous fragility fractures and increased their risk of future fragility fractures. A large proportion of our patients scored for secondary osteoporosis. This was also linked to increased alcohol intake, as many suffered from associated chronic malnutrition, malabsorption and chronic liver disease.

It is important to acknowledge the limitations of this study. Some of the information taken from patients regarding their height and weight may have been inaccurate, with patients often refusing to be weighed or measured. Also some patient's weights were misrepresented due to the presence of ascites. Due to the intoxicating effects of alcohol, some patients were not able to accurately recall the mechanism of injury of their previous fractures.

If they could not recall their fracture, it was not documented as a fragility fracture. Examination of inpatient notes was also difficult, as this group of patients are frequent attenders to hospital and may have many volumes of notes. Therefore, previous calculations of FRAX scores and trials of preventative treatment may have been missed. Finally, three of our patient group were under the age of 40 which is outside the age range for the FRAX assessment tool.

When we examined the group for previous investigation and treatment to prevent alcohol related fractures, there was an overall low rate of intervention. This correlates with our belief that osteoporosis related to alcohol is not acknowledged by medical staff working in secondary care. Patients admitted with alcohol misuse tend to present with symptoms relating to liver pathology or alcohol withdrawal.

A significant number however do present with injury, often due to poor mobility and co-ordination whilst under the influence. Given that fracture is so common amongst this group we feel that more should be done to protect these patients from osteoporotic fractures. As highlighted previously this group are known for poor compliance and follow up may be complicated. However, preparations such as zoledronic acid which is given as an annual IV infusion could address this issue of concordance, while 6 monthly subcutaneous injections of the rank ligand inhibitor are an excellent alternative.

If patients are being admitted for treatment with IV High Potency Vitamin B and C, (pabrinex) an opportunity is available for treatment with bisphosphonate or a denosumab once a bone profile has been completed. Further efforts should be made to encourage all grades of medical staff to consider osteoporosis in patients who misuse alcohol. Simple evaluation of fracture risk using the FRAX score with the follow up of a DEXA scan can be completed at ward level and prevent costly future admissions to A+E and hospital.

Conclusion

The brothers each required a prolonged hospital stay occasioned by a combination of immobility as a consequence of pain from their fractures and the need for high doses of chlordiazapoxide during prolonged withdrawal features. FRAX scores indicated that each required a DEXA scan. This revealed osteoporosis at the spine (T score -2.9) in the younger sibling and in the hip (T score -2.6) in his older sibling.

Each needed treatment with bisphosphonates to relieve pain in the short term and reduce fracture risk in the longer term. Investigations also revealed each brother had established alcohol related liver disease with oesophageal varices. The risk of oral bisphosphonates causing gastrointestinal haemorrhage was felt to be high, so intravenous zoledronic acid was administered to each brother after vitamin D levels were normalised to prevent hypocalcaemia being induced by therapy.

The infusions were repeated annually for three years with an excellent response as assessed by change in bone density at the spine, which improved by 5% per annum in each brother. Neither sibling recorded further fractures during this follow up period and each reduced their alcohol intake sufficiently to prevent progression of underlying liver disease.

In conclusion fracture risk assessment and treatment for alcohol associated osteoporosis is underperformed in secondary care. If treatment is implemented it may produce positive results, reducing the risk of fractures that are associated with considerable mortality, morbidity and cost to the NHS. Prevention is better (and cheaper) than cure, but if patients have already sustained one or more fragility fractures at presentation, secondary prevention of further fractures is essential. Do not leave this to the Orthopaedic Department – it will only happen if YOU make it happen!!

Multiple choice questions

1. Which if the following is not a factor used in the fracture risk assessment tool FRAX?

a. Smoking status
b. Weight
c. Parental hip fracture
d. Increased rate of falls
e. Premature menopause

2. Which of the following fracture sites are commonest in alcoholics?

a. Hip
b. Rib
c. Vertebra
d. Clavicle
e. Metatarsal

HOW WELL DO WE IDENTIFY & TREAT BONE DISEASE IN PATIENTS ADMITTED WITH ALCOHOL-RELATED HARM?

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3. Which of the following is a risk factor for secondary osteoporosis?

a. Type 1 (insulin dependent) diabetes mellitus
b. Old age
c. Female gender
d. Low weight
e. Smoking

4. Which of the following patients would score higher due to glucocorticoid use on a FRAX risk assessment?

a. A child taking regular corticosteroids for Duchene muscular dystrophy.
b. A 75 year old male COPD patient using an emergency pack of prednisolone 30mg/day for five days twice in the last 3 months.
c. A 60 year old lady with polymyalgia rheumatica on 5mg daily for the past 6 months.
d. A 25 year old male with ulcerative colitis using a prednisolone foam enema
e. A 57 year old lady using clobetasol propionate cream (dermovate) daily for contact dermatitis.

5. Which of the following therapies are best in alcoholics with osteoporosis?

a. Alendronate
b. Raloxifene
c. Strontium
d. IV bisphosphonate
e .SC Denosumab

Answers

1. Answer D – Increased rate of falls.
A patient meets the criteria for secondary osteoporosis if they start the menopause before the age of 45 years.

2. Answer A, B and C.
Answers D and E are far less common in this group.

3. Answer A.
According to FRAX insulin dependent diabetes is strongly associated with osteoporosis. Answers B-E are associated with osteoporosis but not secondary osteoporosis.

4. Answer C.
A and E are false as FRAX only applies to patients over 40 years. B is incorrect as the average daily dose over 3 months is 3.33mg and only a dose of 5mg or more per day is included in the FRAX score. D and E are incorrect as FRAX only score glucocorticoids taken via the oral route.

5. Answer D and E.
Parenteral therapies are best for both safety and compliance.

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MANAGEMENT OF COMMON SOFT TISSUE DISORDERS

I Biro, O Etomi, A Pakozdi, H Tahir

Abstract

Soft tissue disorders are caused by a combination of etiologic factors including a series of tensile stresses, micro-trauma and maladaptive physiological responses. Poor biomechanics, inadequate exercise-technique and inappropriate use of special equipment can also contribute to the pathogenesis of the disease.

The diagnosis is based on detailed medical history and clinical examination. Imaging modalities, in particular ultrasound and MRI scans can be useful to confirm the findings and exclude other causes.

The mainstay of managing symptoms caused by soft tissue disorders is most commonly conservative. Acute injuries are treated with a short period of rest, icing, compression, elevation and protection followed by physiotherapy. Injection therapies can offer a short term symptomatic relief but are not considered to be therapeutic. Invasive surgical procedures are rarely required.

Although considered self-limiting conditions, soft tissue disorders can have a significant impact on patients' lives. Those affected come from all walks of life and as such it is important to provide education about preventative measures. Adequate use of special equipment, proper manual handling and exercise technique alongside appropriate footwear and progressive, regular physical activity can prevent the development of such conditions.

Introduction

Musculoskeletal disorders are common and represent 30% of all presentations to general practitioners. (1) The management of these conditions is particularly challenging for a number of reasons:

1. Patients often present with poorly localised and non-specific symptoms of pain.

2. Poor biomechanics are common underlying issues. They are often not considered and difficult to correct.

3. Limited understanding of anatomical structures results in poor examination technique.

4. Investigations often reveal non-specific abnormalities and rarely guide the therapeutic approach.

5. Treatment requires self-motivation and commitment to often prolonged and sustained exercise therapy.

It is important to recognise that there is a complex interplay between the body's anatomical structures and the biomechanical forces that govern movement. Disequilibrium in the musculoskeletal system leads to pain, functional loss and disability. Soft tissue disorders can affect anyone but are more likely to occur in certain professions (e.g. athletes, craftsmen and office workers).They are often seen in combination and are inter-related.

Disruption to normal biomechanics in combination with tensile stresses, microtrauma and abnormal adaptive responses are risk factors for overuse syndromes. Limb misalignments, muscular imbalance and an increase in traction loads acting on different joints are all well known biomechanical risk factors. The sliding motion of tendon fascicles as well as the shear forces at interfaces are mechanical factors considered in the pathophysiology of a common soft tissue disorder affecting tendons. Obesity or more specifically, excess adiposity has also been linked to the incidence of tendinopathies.

Acute soft tissue injuries (sprains, strains) are caused by traumatic events and represent contusions. If managed appropriately, they have a favourable outcome. In contrast, chronic soft tissue disorders resulting from repetitive micro-trauma and overuse are more difficult to treat. Soft tissue disorders can be categorized based on their anatomical location.

Synoviopathies and bursopathies affecting the synovium and bursal tissues can be classed as intra-capsular articular soft tissue disorders. Tendinopathies, enthesopathies and ligamentopathies are pathological conditions of fibrous bands that are located outside the joint capsule and as such can be called extra-capsular articular soft tissue disorders. Pathologies affecting the musculoskeletal fascia and its annexes are a group of non-articular soft tissue disorders. (Table 1) The causes of these musculoskeletal abnormalities can be broadly classified as: traumatic, degenerative, inflammatory, vascular, neurogenic, metabolic and malignant.

The purpose of this article is to describe the common soft tissue disorders, highlight their aetiology, clinical findings, and diagnostic investigations while providing a practical approach to their management.

General perspective

Regardless of the affected anatomical structure or its location the symptoms are often non-specific and are predominantly characterised by pain, swelling and restricted range of movement (ROM) leading to loss of function. The diagnosis is based on a careful history as well as a thorough examination using a 'look, feel, move' approach.

Inspection looking for asymmetry, swelling and obvious deformity is followed by palpation over the anatomical structures revealing tenderness and confirming swelling. In most cases, active movements are painful and limited whilst passive movements are preserved. The clinical examination is completed by provocative manoeuvres to reproduce symptoms.

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SOFT TISSUE DISORDERS		
INTRACAPSULAR	EXTRACAPSULAR	NON-CAPSULAR
ynoviopathy	Ligamentopathy	Fasciopathy
Synovitis	Patellar tendinitis	Fasciitis(nodular, necrotizing, eosinophilic
Tenosynovitis (calcific, stenosing tenosynovitis, trigger finger, DeQuervain)	Hypermobility	Fibromatosis/contracture
Transient synovitis	Entesopathy	Dupuytren contracture
Ganglion cyst	Tendinopathy	Plantar fibromatosis
Synovial chondromatosis	Adhesive capsulitis	Aggressive fibromatosis
Villonodular synovitis(Pica syndrome)	Impingement syndrome	Knuckle pads
Giant cell tumor of tendon sheath	Rotator cuff tear	
ursopathy	Golfers' elbow	
Bursitis	Tennis elbow	
Synovial cyst (Baker)	Iliotibial band syndrome	
Calcific bursitis	Patellar tendinitis	
	Calcaneal spur	
	Metatarsalgia	
	Bone spur	
	Tendinitis/Tendinosis	

Table 1. Common Soft Tissue Disorders

Regional soft tissue disorders

Shoulder

The most commonly affected structure in the shoulder is the rotator cuff. The rotator cuff is a group of muscles and tendons that arise from the scapula and insert on the head of the humerus. They stabilize the glenohumeral joint and have multiple functions. The four muscles of the rotator cuff include:

- *Supraspinatus (shoulder abduction)*
- *Infraspinatus (external rotation)*
- *Teres minor (external rotation)*
- *Subscapularis (internal rotation)*

Aging and activities that require frequent overhead lifting, throwing and rowing with the arm being above the horizontal position predispose to rotator cuff abnormalities including various tendinopathies, impingements and tears. Painful arc (abduction 60 to 120 degrees), pain on specific movements and positive impingement signs are features of rotator cuff pathology.

Subacromial bursitis is a condition often related to microtrauma affecting the supraspinatus tendon. Pain can be reproduced by resisted abduction due to the pinching of the bursa as the deltoid contracts. It is often related to rotator cuff disorders and inflammatory conditions.

Tenderness over the bicipital grove and pain on resisted elbow flexion is a feature of bicipital tendinopathy. Adhesive capsulitis (frozen shoulder) is caused by an irritation of the glenohumeral joint capsule. Special features of adhesive capsulitis include severe pain which is worse at night and in cold temperatures. The pain is increased on external shoulder rotation and abduction.

Elbow

The elbow is a common place of tendon injuries. Lateral epicondylalgia (tennis elbow) is frequently associated with activities related to excessive extensor carpi radialis brevis and extensor digiti minimi muscle work. Histopatology shows granulation tissue, microrupture and degenerative changes. No signs of inflammation were detected, labelling this condition an angio-fibroblastic tendinosis or tendinopathy. Pain is located around the lateral epicondyle, and can be precipitated by resisted wrist extension.

The medial epicondyle is the origin of the forearm's flexor and pronator tendons. The tendon sheath of these muscles is susceptible to repetitive strain injury leading to a condition commonly referred to as golfers elbow or medial epicondylalgia.

Unaccustomed strenuous activity, decreased mental chronometry and lack of controlled lengthening of forearm muscles (eccentric muscle contraction) as well as direct injury to the elbows can cause epicondylopathies. Golfers, rock-climbers and those with a grip-intensive occupation that requires torsion of the wrist and forearm may suffer from chronic, gradually worsening pain, tenderness, swelling and restriction at this level. Pain is aggravated by resisted wrist flexion and pronation.

Wrist

Another frequently encountered repetitive strain injury is DeQuervain tenosynovitis. It causes pain at the radial side of the wrist, spasm, burning sensation in the hand, mild swelling over the thumb and difficulty gripping. Activities that require the thumb to be held in abduction and extension as well as hormonal changes, fluid retention and frequent lifting are thought to be causative factors. Histological specimens found non-inflammatory thickening and myxoid degeneration of the extensor pollicis brevis and abductor pollicis longus muscles' tendons and synovial sheaths.

The diagnosis is confirmed with the provocation manoeuvre termed Finkelstein's test (patient places the thumb inside the fist, whilst the examiner gently flexes the wrist towards the ulna). Conditions mimicking DeQuervain syndrome include first carpo-metacarpal joint osteoarthritis, intersection syndrome (inflammation at the site of intersection of the 1st and 2nd dorsal muscle compartment of the forearm), Wartenberg's syndrome (cheiralgia paraesthetica-radial nerve compression) and carpal tunnel syndrome (medial nerve compression).

Compression neuropathy of the median nerve at the level of the carpal tunnel causes pain in the wrist and the hand and is associated with paraesthesia of the lateral three fingers. Carpal tunnel syndrome may be secondary to inflammatory arthritis but it is also recognised in pregnancy, diabetes, hypothyroidism and acromegaly.

Symptoms are generally worse at night and can be reproduced by percussion above the carpal tunnel (Tinel's sign) or by prolonged forced flexion of the wrist (Phalen's sign). A long-standing compression can lead to wasting and weakness of the thenar muscles. Nerve conduction study can indicate the severity of the disease and therefore guide therapy.

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Hips

The gluteus medius and minimus muscles insert into the greater trochanter of the femur. Pain at this site is commonly described as greater trochanteric pain syndrome (GTPS). Causes include anatomical variations (uneven leg length), trochanteric bursitis, gluteal tendinosis, iliotibial band syndrome or weakness of hip abductor muscles.

It is important to differentiate GTPS from more severe conditions including fracture, slipped upper femoral epiphysis, avascular necrosis of the femoral head, infections, inflammatory arthritis, osteoarthritis, psoas abscess or other retroperitoneal and testicular pathology. In younger patients transient synovitis of the hip (toxic synovitis), Legg-Calve-Perthes disease and developmental dysplasia should also be considered.

The iliotibial band is the fibrous reinforcement of the tensor fascia lata and the gluteus maximus muscle and it has a role in stabilizing the knees. It runs on the lateral side of the thigh and inserts to the lateral epicondyle of the tibia. Iliotibial band syndrome is considered to be an overuse fasciopathy and it commonly affects runners, cyclists, hikers and weight lifters due to repeated flexion and extension of the knees causing continuous rubbing of the band over the lateral femoral epicondyle.

Knee

Patellofemoral pain syndrome, otherwise called as anterior knee pain is a common problem in young adults especially in females. It is attributed to various causes and is often a result of complex biomechanical changes including stiff ankles, weak gluteal muscles, tightness in the calf, quadriceps and hamstring muscles.

Predisposing factors for primary patellofemoral instability include increased genu valgum resulting in increased Q-angle (angle between the transfers line crossing the centre of the patella and tibial tuberosity and the line connecting the middle of the patella and the anterior superior iliac spine; normal between 10-14o in men and 15-17o in women), increased ligamentous laxity and shallow trochlear groove.

Maltracking of the patella can be an obvious sign on examination. Degenerative patellar tendinosis is caused by chronic overload of the extensor mechanism and is common in activities that require jumping, hence the term jumpers' knee. Other soft tissue disorders that can occur in the context of overuse are prepatellar bursitis (housemaids' knee), infrapatellar bursitis (plumber's knee or clergymen's knee), pes anserine bursitis, synovial cysts (e.g. Baker's cyst), and synovial plica syndrome.

Ankle

Soft tissue disorders of the ankle are often seen in patients with a high body mass index (BMI), biomechanical dysregulation, limb malalignments and poor muscle tone. They include damage to the Achilles, peroneal, flexor hallucis longus and the tibialis posterior muscle tendons.

The Achilles tendon and the patellar tendon are specifically sensitive to damage caused by overuse or improper use. Achilles tendinitis manifests itself as swelling and burning pain around the ankles that is worse with activity. Improper exercise load and training habits, sedentary lifestyle, obesity and worn down footwear all represent causative factors. Frequent lunging and jumping especially with excessive foot pronation in the subtalar joint can affect the Achilles tendon.

Foot

Plantar fasciitis is the main site for overuse fasciopathy. The plantar fascia is a thick fibrous band that runs from the calcaneus to the metatarsal heads. Risk factors include a high body mass index, high arched feet, pes planus and leg length discrepancy. Differential diagnosis of heel pain include calcaneal fracture, calcaneal bursitis, calcaneal spurs, fat pad syndrome, tarsal tunnel syndrome, medial calcaneal nerve impingement and L5/S1 nerve root lesions. Differential diagnosis of forefoot pain includes Morton's neuroma, intermetatarsal bursitis, and plantar plate disruption, stress fracture of the metatarsals and osteonecrosis of the second or third metatarsal (Freiberg's infarction).

Investigations

In the majority of cases careful history taking and clinical examination can elucidate the diagnosis. Imaging techniques should only be used as an adjunct to the clinical assessment.

X-Ray may reveal anatomical variations, osteophytes and calcification. Although cheap and readily available, it is important to consider the suspected underlying diagnosis as the x-ray is often normal. Frankel et al reviewed 312 patients seen in an A&E department with shoulder pain. They found the strongest predictors for a therapeutically informative x-ray were the history of trauma or the presence of a deformity on examination.

Ultrasonography is extremely advantageous as it is non-invasive, cheap and can be used by the bedside in real-time, assessing the anatomical structures in a static and more dynamic action. It can reveal active synovitis and cortical erosions related to inflammatory arthritis.

For assessing tendon related abnormalities including tenosynovitis, impingement and partial or complete tendon tears, ultrasound is often considered to be the most reliable tool. In addition, ultrasounds can guide local corticosteroid injections however inter-operator variability and the lack of available equipment limits its use in every-day practice.

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MRI scans provide a higher resolution of the soft tissues and are able to detect fluid accumulation within and around the joint. They can also reveal thickening and damage to the synovial bursa, tendons and ligaments. Disorganized collagen matrix as well as fluid and cysts can be picked up by both ultrasound and magnetic resonance images.

Management

The backbone of treatment for musculoskeletal disorders is focused on education, correcting biomechanical discrepancies, physiotherapy and weight loss. Sport and work related soft tissue injuries can be minimized by empowerment of patients with adequate training and basic education on the body's biomechanical properties.

A graduated exercise programme can avoid injuries in those who are unaccustomed to regular exercise. Performing adequate and consistent physical activity improves the elasticity and strength of tendons and ligaments, the tensile resistance of muscles, the metabolic turn-over of bones, cartilage and synovium. Stretching, warm-up before starting an exercise session and taking regular resting periods between sessions is essential. Proper footwear is crucial to provide longevity to the tendons and other musculoskeletal structures.

Different treatment options have been developed and trialled for overuse syndromes with varying success. The general consensus in our department and in the literature is a three-step plan which should be followed when dealing with soft tissue problems of non-specific aetiology.

1. Conservative treatment modalities.

In case of acute injuries, a (P)RICE approach (protection, rest, icing, compression and elevation) has been demonstrated beneficial however insufficient evidence is available from randomized controlled trials to determine the relative effectiveness of this therapy.

To alleviate pain, oral paracetamol and non-steroidal anti-inflammatory (NSAIDs) medications can be taken. When caring for people with chronic soft tissue disorders however there is a role for other therapists such as osteopaths, chiropractors, physiotherapists and podiatrists. Alternative treatments include massage therapy, daily extensive stretching, eccentric exercises and the use of special orthoses (braces, taping, splints, in-soles).

Physiotherapists provide tailored exercise regimes with focus on gentle improvement of motion and gradual strengthening. Low intensity pulsed ultrasound (LIPUS), shockwave therapy, cryotherapy, deep heat-treatment, electrotherapy, TENS, iontophoresis, phonophoresis are alternative methods of managing overuse musculoskeletal disorders.

2. If symptoms persist, corticosteroid injections can be beneficial.

The use of steroids for soft tissue injuries has been demonstrated to be more effective for pain management when compared to placebo or placebo in combination with NSAIDs. Steroid injections have also been shown to help increase the range of movement, enhance physiotherapy and can be used as a diagnostic tool. Corticosteroids provide analgesia in the short term (6 weeks) although the evidence of long-term effectiveness is controversial.

It is important to highlight that the controversy arises as the presented data originates from individual studies on soft tissue disorders that have a small sample size and are poorly structured. A recent meta-analysis found no long term benefit to corticosteroid therapy over placebo for the treatment of tendinopathies. Repeated corticosteroid injections for lateral epicondylalgia have been proven to result in poorer long term outcomes, with worse pain, loss of function and increased relapse.

In case of trochanteric bursitis, exercise therapy and shockwave therapy seem to be more beneficial compared to corticosteroid injections over the long term. Whilst there is some benefit in injecting the patellar tendon in overuse syndromes, other treatment modalities seem more beneficial in Achilles tendinopathy. Side effects of corticosteroid injections include reduced tendon strength and tendon ruptures, subcutaneous atrophy and cartilage damage.

3. For selected patients, the final step in the management of refractory soft tissue disorders would be surgical intervention.

They can be minimally invasive such as ultrasound guided percutaneous needle release or thread dissection for trigger fingers or more complex, open excisions with correction and reconstruction of disrupted anatomical structures.

Conclusion

Soft tissue disorders differ from soft tissue injuries as they occur as a consequence of a long, improper physical activity or repetitive movement and have a tendency to become chronic. Pain and restriction are common symptoms. It is important to have a general knowledge about these soft tissue disorders as they are relatively difficult to treat and have significant negative effect on the ability to work and on patients' quality of life.

Preventative measures and patient education is pivotal. Raising awareness about the importance of proper posture, correct use of equipment, adequate manual handling, appropriate footwear and supportive accessories for specific activities with the addition of regular muscle strengthening and conditioning exercises should be the principle approach to avoid the occurrence of overuse syndromes.

Management starts with non-surgical, non-invasive methods of rest, physiotherapy and analgesia. Furthermore corticosteroid injections and other injectable treatment as well as surgical intervention can be considered for symptomatic relief or with curative purpose.

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Questions

1. Bursopathies are part of which group of soft tissue disorders:

A. Intracapsular

B. Extracapsular

C. Non-articular

D. Tendinopathies

E. Non off the above

2. Which symptom /sign is not seen in soft tissue disorders:

A. Restricted active mobility of affected joint

B. Unrestricted passive mobility of affected joint

C. Pain and narrowed ROM

D. Significant joint effusion

E. Small fluid collections

3. Where is the pain localized in De'Quervain tenosynovitis:

A. Radial side of the forearm along the proximal end of extensor hallucis brevis and abductor hallucis longus muscles

B. The radial side of the wrist

C. Over the 1st carpo-metacarpal joint

D. Thenar muscle region

E. All of the above

4. The pain experienced in lateral epycondilitis (i.e. tennis elbow) can be reproduced through:

A. Resisted abduction of arms

B. Resisted flexion of the wrist

C. Resisted extension of the wrist

D. Resisted pronation of the wrist

E. Internal forearm rotation

5. Which is not a conservative treatment modality in soft tissue disorders:

A. ESWT

B. Rest

C. Phonophoresis

D. Autologous blood injections

E. Structured exercises

Answers

1. A

Explanation: the synovial bursa is a continuation of the synovial membrane located between bones, tendons or muscles around a joint and is considered a part of the articular capsule.

2. D

Explanation: pain, narrow ROM, restricted active and fairly preserved passive mobility are generally present in soft tissue disorders. Small effusions can also accompany them however large effusion are hardly ever present.

3. E

Explanation: generally speaking the exact location is the radial side of the forearm, however tenderness can be experienced along the radial side of the wrist at the level of the radiometacarpal and 1st carpo-metacarpal joint with radiation to the thenar region.

4. C

Explanation: resisted extension of the wrists in lateral epycondilitis produces pain due to a tensile pressure of the extensor carpi radialis tendon caused by the counter-force of the examiners hands.

5. D

Explanation: extracorporeal shock wave therapy, phonophoresis, structured exercises and rest are all conservative treatments and are at the forefront of managing soft tissue disorders. They are effective, non-invasive treatment modalities and are better tolerated than injection therapies.

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SEROSAL INFLAMMATION & ITS DIAGNOSTIC CHALLENGES: A CASE STUDY OF SYSTEMIC LUPUS ERYTHEMATOSUS

E Fisken, M Ahuja, C Kelly

Abstract

Inflammation of the pleura, pericardium or peritoneum is recognised as serositis. This is often associated with systemic illness and pyrexia. It can be precipitated by infection and patients may be treated empirically with antibiotics. However, inflammatory disorders may also present in this way, particularly when more than one organ is involved.

We present the case of a 65 year old lady who developed breathlessness, arthralgia, fever and chest pain. She was initially treated for infection but speciality input led to a revised diagnosis of serositis related to systemic lupus erythematosus (SLE). This case highlights the diagnostic challenge that autoimmune conditions present. We developed a protocol to aid the diagnosis and treatment of patients presenting with serositis.

Case history

Mrs W is a 65 year old lady who has a history of well controlled asthma and haemolytic anaemia for which she was under the care of the Haematology team. She had previously been treated with steroids and Rituximab therapy, suggesting an auto immune aetiology.

She presented with a history of gradual onset lethargy, fevers and breathlessness. She had coarse crackles on auscultation and received Amoxicillin for a presumed lower respiratory tract infection. Unfortunately her breathing deteriorated and she presented to hospital where she also reported pleuritic chest pain, abdominal pain and arthralgia.

The initial investigations are shown below:

Test	Result	Reference Range
Hb	71	115 – 165
WBC	3.6	4 – 11
Platelets	139	150 – 450
Neutrophils	2.7	1.8 – 7.5
Lymphocytes	0.7	1 – 4.5
Urea	3.8	2.5 – 7.8
Creatinine	57	45 – 85
Bilirubin	47	1 – 21
ALT	120	0.1 – 40
ALP	147	30 – 130
GGT	140	0.1 – 45
LDH	1728	240 – 480
PT	15	11 – 15
APTT	34	25 – 35
Fibrinogen	4.7	1.5 – 5
CRP	77	0 – 5
Urine dip	Negative	
CXR	Bilateral pleural effusions	

Table 1: Initial investigations upon admission to hospital

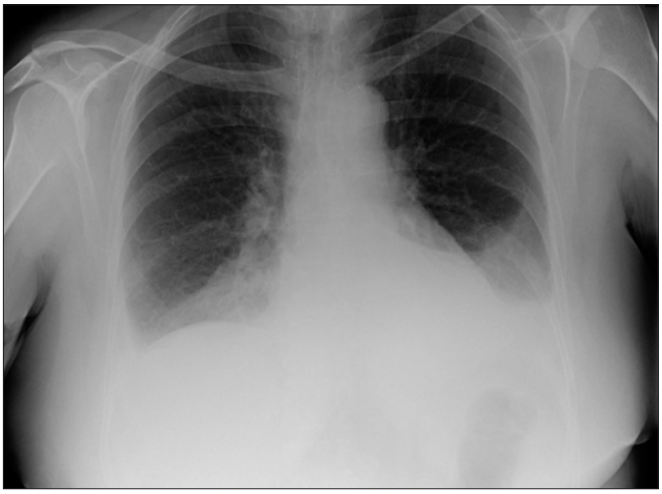

Figure 1: Bilateral pleural effusions seen on the chest X ray.

She was commenced on intravenous antibiotics but unfortunately she soon required admission to intensive care due to increased oxygen requirements. A CT of the chest, abdomen and pelvis demonstrated a small pericardial and bilateral pleural effusions with no evidence of infection or malignancy. Blood cultures and MSU were negative and she showed no significant improvement from antibiotics. Given the pericardial, pleural effusions and arthralgia she was reviewed by the Rheumatology team.

She had a number of auto-antibodies tested with the following results:

ANA	Positive (levels 640 with homogenous HEp 2 pattern)
Liver Autoantibodies	Negative
Anticardiolipin	Positive
Lupus anticoagulant	Positive
ANCA	Negative
dsDNA	Negative
ENA	Negative
Complement	Normal levels
Direct Coombs test	Positive
HIV	Negative
Hepatitis screen	Negative
CMV	IgM Negative
EBV	IgG detected – consistent with infection more than 8 weeks ago
Legionella antigen	Negative
Pneumococcal antibodies	39 (20 – 200)
Echo	Mild MR, normal LV size with mild post wall hypokinesia and small pericardial effusions

Table 2: Second line investigations in ITU

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The combination of serositis with a pancytopaenia and a previous Coombs positive haemolytic anaemia suggested SLE in spite of negative dsDNA. Her positive ACL antibodies raised the possibility of thrombosis but D Dimers were negative. At this point a trial of oral Prednisolone 30mg daily was started and she had further Rituximab.

Within two days she had significant improvement in her arthralgia, abdominal pains and breathing, with clinical and radiological resolution of the pleural effusions. She was able to leave hospital to receive the 2nd infusion of Rituximab as an outpatient. Haemoglobin rose steadily from discharge. This lady met the American College of Rheumatology (ACR) criteria for a diagnosis of SLE with arthralgia, serositis, positive ANA and antiphospholipid antibodies.

Discussion

What features should make you consider an autoimmune aetiology?

Autoimmune aetiologies could be considered in the following set of patients:

- *Patients with persistent fever in whom treatment with antimicrobials has not worked.*
- *Patients with persistent or cyclical abdominal or chest pains with no alternative diagnosis.*

In this case, our patient presented with serositis, in particular, pleural and pericardial effusions. Abdominal pain was also a feature which could have been due to peritoneal irritation. Other symptoms that run commonly with autoimmune flare ups can include fever, arthralgia and rashes.

Inflammatory markers can also be raised making it difficult to distinguish between infective and inflammatory causes. We have therefore created a diagnostic flow chart that can aid clinicians in making a diagnosis when presented with a patient with serositis.

This is shown below:

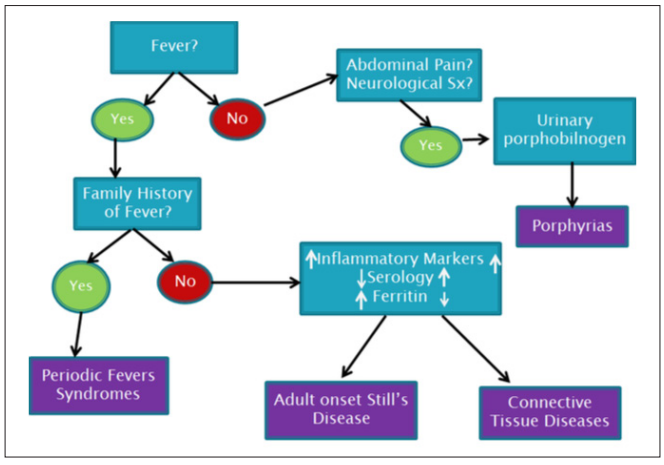

Figure 2: Diagnostic flow chart considering autoimmune aetiology in patients with serositis.

So using this flow chart, we would reach a diagnosis of connective tissue diseases, when presented with the symptoms in our case study. Our patient had fever, with no family history, raised inflammatory markers and positive serology.

How do we diagnose SLE?

SLE is a multi-system disease that can present in a variety of ways and affect different organ systems. This can sometimes make it challenging to reach a diagnosis. The mnemonic "SOAP BRAIN MD" can be useful in remembering the diagnostic criteria for SLE as per the American College of Rheumatology (1). There needs to be 4 of the 11 criterion present for a positive diagnosis.

- *Serositis*
- *Oral ulcers*
- *Arthritis*
- *Photosensitivity*
- *Blood disorders*
- *Renal involvement*
- *Antinuclear antibodies*
- *Immunologic phenomena (eg, dsDNA; anti-Smith [Sm] antibodies)*
- *Neurologic disorder*
- *Malar rash*
- *Discoid rash*

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There is also discussion about a new proposed criterion by the SLICC2 (Systemic Lupus International Collaborating Clinics) which includes histological confirmations as a criterion as shown below:

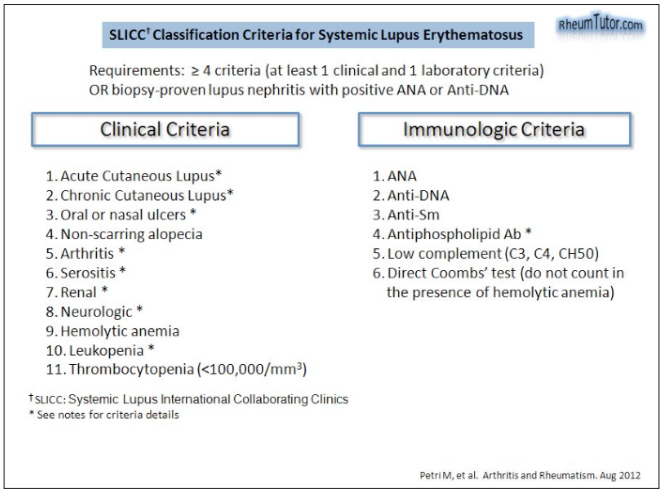

Figure 3: Diagnostic criteria proposed by the SLICC

The management of SLE varies greatly based on disease severity and organ involvement. In this case, our patient had severe systemic involvement and required a combination of short term steroids and biological DMARDS (B cell depletion with Rituximab) as a rescue therapy.

MCQs: Teach Yourself

Q1. This lady has a past history of haemolytic anaemia and from her blood tests she is anaemic. Which blood tests from the following list can be performed to help aid the diagnosis of haemolysis

a. Ferritin

b. LDH

c. Bilirubin

d. Reticulocyte count

e. Transferrin saturations

Q2. Which types of anaemia are associated with autoimmune conditions?

a. Iron deficiency anaemia

b. Haemolytic anaemia

c. Pernicious anaemia

d. Folate deficiency

e. Anaemia of chronic disease

Q3. Which group of people are more predisposed to having SLE?

a. AfricoAmerican Men

b. AfricoAmerican women

c. Caucasian men

d. Caucasian women

e. Asian women

Q4. Which of the following auto-antibodies have a role in disease monitoring, in patients with SLE?

a. Anti-nuclear antibodies

b. Anti-Sm antibodies

c. Anti dsDNA antibodies

d. Anti phospholipid antibodies

e. Rheumatoid factor

Q5. A 32 year old lady with SLE gives birth to a baby who has congenital heart block. Which of the following antibodies are likely to be present in the maternal serum?

a. Anti nuclear antibodies

b. Anti dsDNA antibodies

c. Anti Ro/SSA antibodies

d. Anti endomyosial Antibodies

e. Anti Sm Antibodies

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Answers

1. Answer: B, C and D

If haemolysis is suspected, a number of blood tests can aid your diagnosis. Bilirubin will naturally be raised as a byproduct of red cell breakdown. The reticulocyte count is a measure of immature red cells in the body, which will be increased in response haemolysis. However this can also be raised in other conditions. Serum LDH elevation is very sensitive for haemolysis, but is also not specific as it is released from neoplastic cells and other damaged organs.

2. Answer: B, C and E

There are a number of causes for haemolytic anaemias, including genetic, autoimmune and non immune (for example trauma, haemolytic uraemic syndrome and disseminated intravascular coagulation). Autoimmune haemolytic anaemia can be further classified into warm antibody type, cold antibody type or drug related. SLE is an example of a warm antibody type autoimmune haemolysis.

Pernicious anaemia causes Vitamin B12 deficiency due to failure of gastric parietal cells to produce sufficient intrinsic factor. It is an autoimmune disorder with the presence of anti-parietal cell antibodies in 90% of patients.

3. Answer: B

SLE is more common in women than men and Afro American women are three times more likely to have SLE than Caucasian women.

4. Answer: C

Although all of the above can be present in SLE, only Anti dsDNA can be used for disease monitoring. It is important to note that they are not present in all patients. They are highly specific (>99%) but less sensitive (70%). Anti phospholipid antibodies are associated with an increased risk of early recurrent miscarriage and venous and arterial thrombosis, associated with throbocytopaenia.

5. Answer: C

There is a strong risk of maternal autoantibodies crossing the placenta during pregnancy to cause neonatal lupus erythematous. One of the complications of this condition is congenital heart block which could require pacemaker insertion. This condition is strongly linked to Anti Ro/SSA antibodies. Careful monitoring of foetal cardiac function is needed during the latter stages of pregnancy to reduce the risk of intra uterine death.

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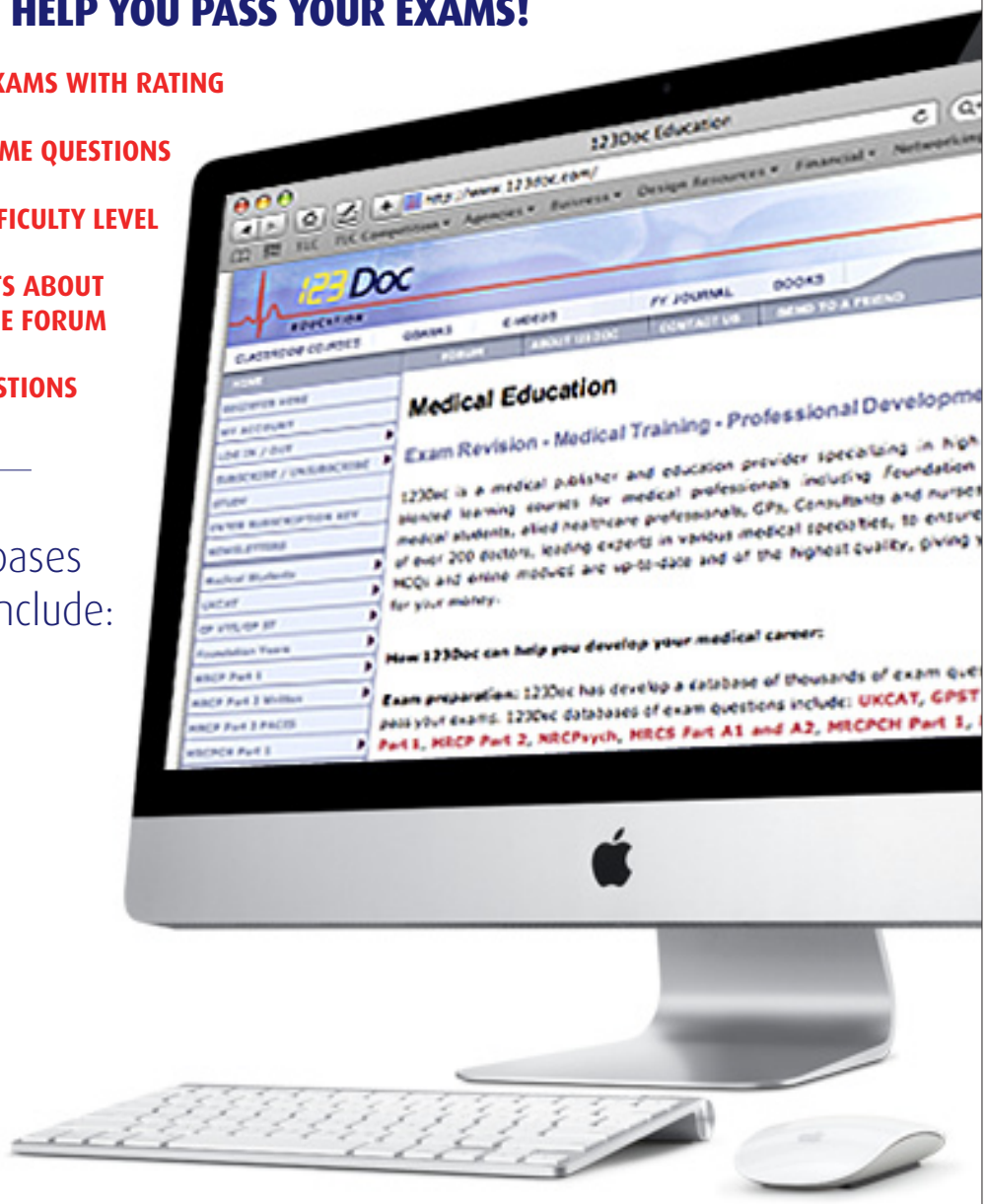

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