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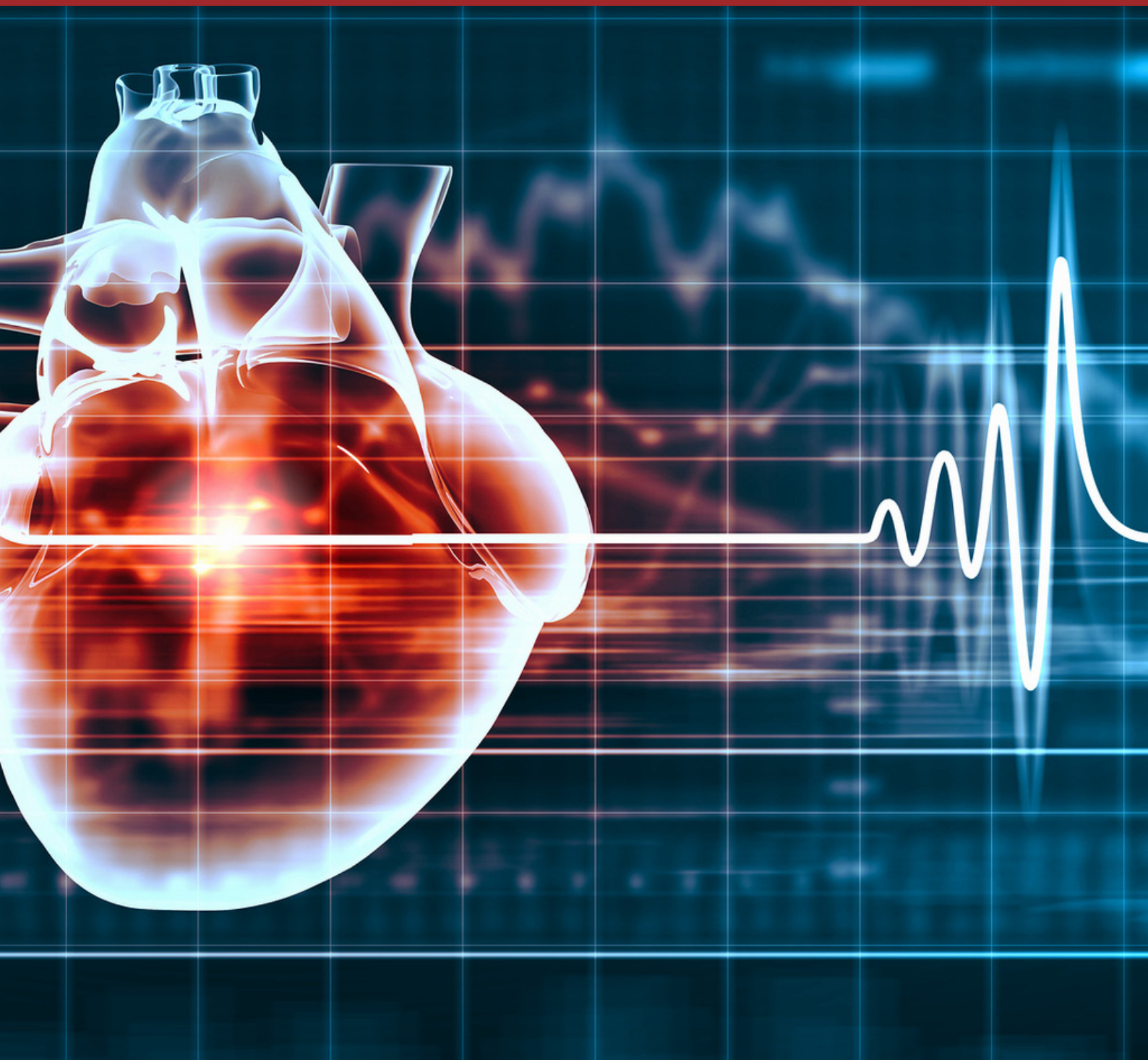

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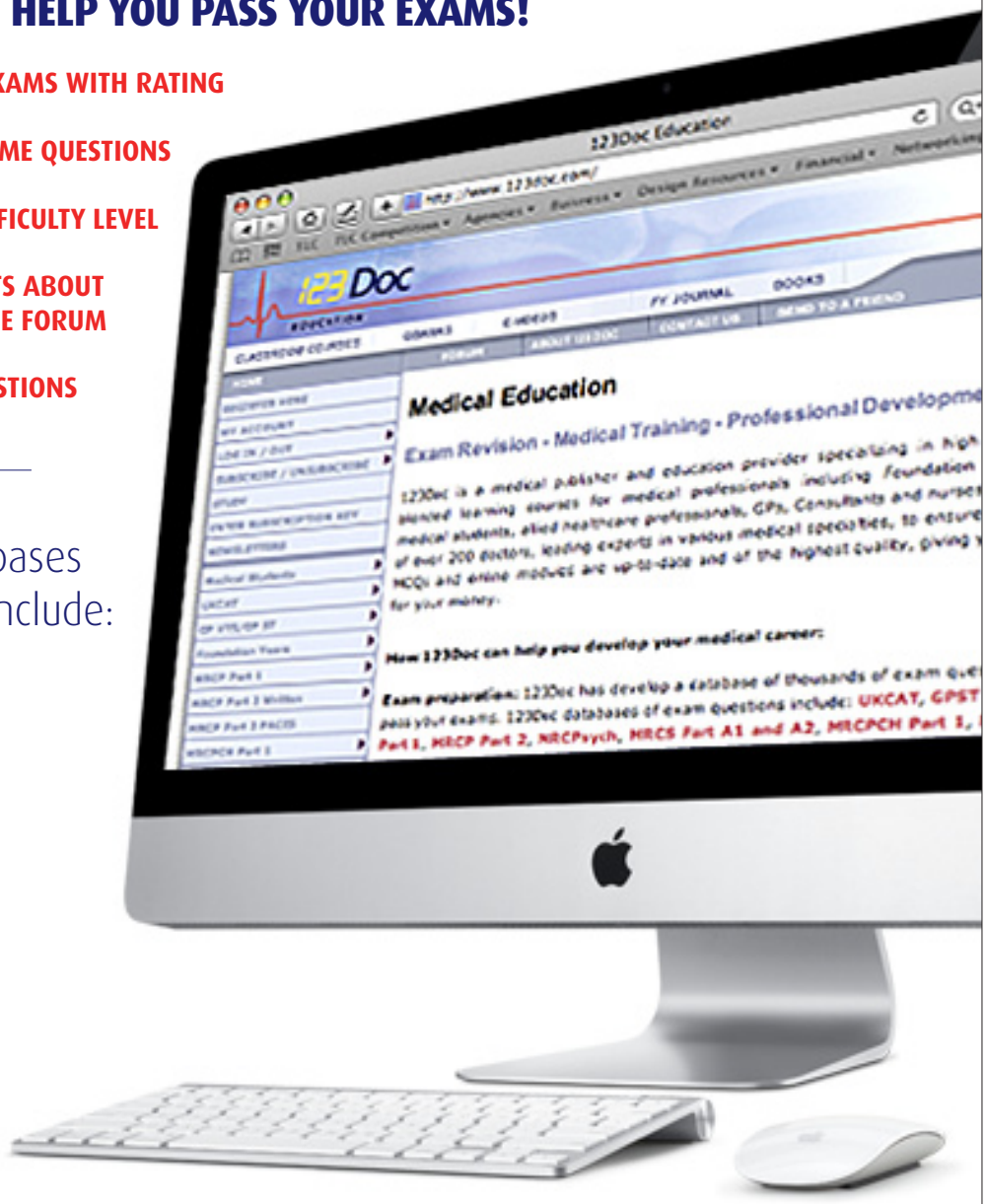

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Volume 10

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A CASE OF LATE PRESENTING ACUTE MYOCARDIAL INFARCTION

R Antony, D Rasoul, A Khalatbari, A Rao

Abstract

We report a case of late presenting anterior myocardial infarction (MI) developing acute ventricular septal rupture. Mechanical complications post MI are rare but serious, often leading to patient death and should be looked for carefully in the immediate presentation period. Early detection, stabilisation and intervention is the key to reduce the already significantly high mortality in this patient group. Guidelines for device therapy in severe left ventricular systolic dysfunction and cardiac transplantation are also discussed.

Case History

A 59 year old male patient presented a week after onset of central chest pain. His ECG (Figure1) showed anterior ST segment elevation with established deep Q waves indicating late presenting acute myocardial Infarction (AMI). He was taken to cardiac catheter laboratory and a left heart catheterisation (LHC) was performed which revealed occluded left anterior descending artery (LAD) and no other significant coronary artery disease (CAD). The following day he became acutely unwell with cardiogenic shock. An echo revealed ventricular septal defect (VSD) (Figure 2, 3).

He was taken that day urgently to the cardiac theatre and a patch operation was performed to close the VSD. He subsequently improved initially but developed acute pulmonary oedema 3 days later, requiring intubation and ventilation along with intra-aortic balloon pump insertion. Though improved and eventually weaned off from ventilator, he developed right toe ischemia.

A CT angiogram of his lower limbs revealed extensive peripheral vascular disease. He had a trans-oesophageal echocardiogram (TOE) which revealed clot in the left atrial appendage (LAA) for which he was started on warfarin. His left ventricular function remained poor with normal right ventricular systolic function. He slowly improved and was optimised on low dose angiotensin receptor inhibitor (ACE inhibitor) and beta blockers. He subsequently had an implantable cardio-defibrillator (ICD) implanted and was referred to cardiac transplantation centre for assessment as an outpatient.

Discussion

Mechanical complications post AMI carries a very high mortality. Our patient suffered from acute VSD whilst the other two mechanical complications are left ventricular free wall rupture and acute mitral regurgitation (MR) due to papillary muscle rupture or displacement.

Ventricular free wall rupture though uncommon post MI (<1%) is associated with a high mortality in this cohort (14-26%) (1, 2).

Percutaneous intervention (PCI) may help in resolution of acute ischemic MR (3,4), surgery is often required for papillary muscle rupture (5,6,7) but with an operative mortality of around 50% (8). Around 50% of acute ischemic MR is not audible (9-12). It is thought to be due to early equalisation of left atrial and left ventricular pressures subsequent to low systemic blood pressure and elevated left atrial pressures.

Acute VSD post MI is an infrequent complication, though more likely to occur in late-presenting MI. Mortality in acute VSD is very high, with a significant percentage of patients not reaching the theatre for a repair. Acute VSD may develop anywhere between 24 hours to up to 2 weeks.

Risk Factors for VSD

Interventricular septum is predominantly supplied by left anterior descending artery (LAD). Generally, inferior one-third of the septum is supplied by right coronary artery (RCA). In individuals with a "wrap-around" LAD, which wraps around left ventricular apex and supply the inferior septum and distal inferior wall, the occlusion of this artery puts them in very high risk for developing a VSD. Other risk factors are poor septal collaterisation and extensive myocardial damage.

Site of VSD

VSD could be seen equally post anterior and non-anterior infarcts (13).With inferior MI, the defect is at the basal septum, whilst the defect is at apical septum in anterior MI. The size of the defect determines the volume of shunt and in-turn, the prognosis.

Investigations

Following clinical suspicion after an episode of cardiogenic shock and finding a pansystolic murmur at the lower left sternal edge, an echocardiogram with colour doppler often helps in confirmation. Further diagnostic investigations include coronary angiography with right heart catheterisation and shunt assessment. Occasionally trans-oesophageal echocardiography may be required to assess the anatomy fully.

Management

In patients with cardiogenic shock, death is certain without surgical intervention. Vasodilators and early intra-aortic balloon counter pulsation (IABP) reduces afterload, thereby reducing left ventricular pressure and subsequently left- right shunt, is useful in stabilising the patient. Other agents used are inotropic agents to increase cardiac output and diuretics to offload the ventricle. Once stabilised, LHC is done to assess coronaries preceding VSD repair. Percutaneous trans-catheter closure of VSD is another approach that could be considered; particularly in the absence of coronary disease and with smaller size VSD's (14).

Prognosis

In the GUSTO-I trial, 0.2 % developed a ventricular septal defect. Surgical repair was performed in 40% of these patients at a median of 3.5 days after the onset of infarction symptoms. Survival at 30 days (53 versus 6%) and one year (47 versus 3%) was significantly higher in those undergoing surgery compared to those treated medically (15). A delayed approach to surgical approach though with unpredictable outcomes could be considered in patients without heart failure and shock, but will have to be carefully monitored. Survival is better in those patients who also had coronary artery bypass grafts along with VSD repair (16).

A CASE OF LATE PRESENTING ACUTE MYOCARDIAL INFARCTION

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Learning Points

In the case discussed above, though patient survived the acute event and had a successful patch repair of the VSD, his left ventricular systolic function remained poor. Introducing and up-titrating his heart failure medications were a challenge due to low blood pressure and onset of acute renal failure. He subsequently had an implantable cardio-defibrillator implanted as an outpatient for protection from sudden cardiac death (Table 1).

He was also referred to the regional cardiac transplantation centre for assessment for a heart transplant in view of his poor left ventricular function and relatively young age, though extensive peripheral vascular disease is a relative contra-indication (Tables 2,3).

It is imperative to keep a close eye on patient's post AMI even after initial successful revascularisation, especially in those presenting late. Trainees should not forget their auscultation skills as an early detection of a new pan-systolic murmur post-acute MI should lead to early echocardiogram and diagnosis of potential life threatening mechanical complications discussed.

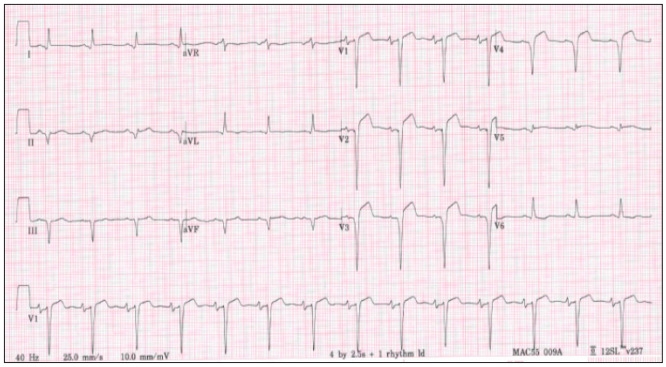

Figure 1: 12 lead ECG showing completed anterior infarct with deep Q waves in anterior leads.

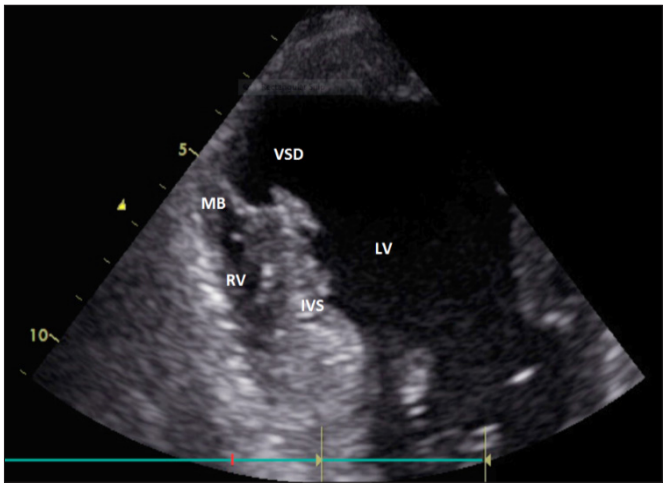

Figure 2: Echo image showing Cardiac chambers and VSD
RV: Right Ventricle; LV: Left Ventricle; MB: Moderator Band; VSD: Ventricular Septal Defect; IVS: InterVentricular Septum.

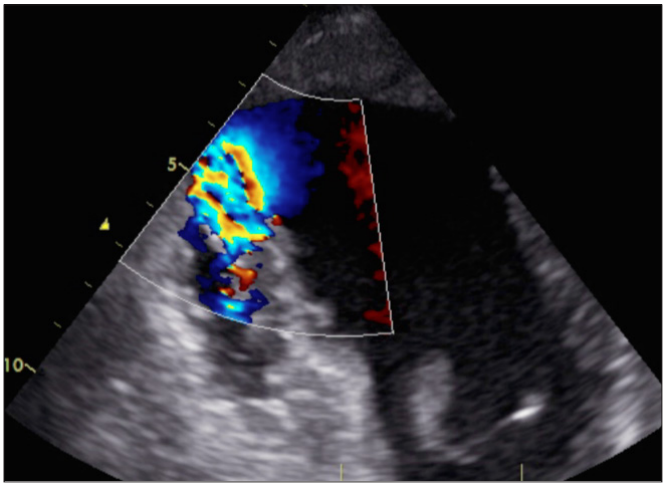

Figure 3: Same Echo image as above, showing colours flow across the defect.

	NYHA class			
QRS	I	II	III	IV
<120MS	ICD	ICD	ICD	ICD/CRT not indicated
120-149ms with LBBB	ICD	CRT-D	CRT-P/D	CRT-P
120-149ms without LBBB	ICD	ICD	ICD	CRT-P
>150ms with or without LBBB	CRT-D	CRT-D	CRT-P/D	CRT-P

Table 1: National Institute for Health and Care Excellence (NICE) 2014 (TA314) indications for implantable cardiac defibrillator (ICD) and cardiac resynchronisation therapy (CRT) devices in patients with a left ventricular ejection fraction (LVEF)≤ 35%.

Key: CRT-D: Cardiac Resynchronisation Therapy with Defibrillator, CRT-P: Cardiac Resynchronisation Therapy with Pacemaker, LBBB: Left Bundle Branch Block, NYHA: New York Heart Association Class.

A CASE OF LATE PRESENTING ACUTE MYOCARDIAL INFARCTION

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Absolute Indications in Appropriate Patients
For hemodynamic compromise due to HF
•Refractory cardiogenic shock •Documented dependence on IV inotropic support to maintain adequate organ perfusion •Peak VO_2 less than 10 mL per kg per min with achievement of anaerobic metabolism
Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention
Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities
Relative Indications
Peak VO_2 11 to 14 mL per kg per min (or 55% predicted) and major limitation of the patient's daily activities
Recurrent unstable ischemia not amenable to other intervention
Recurrent instability of fluid balance/renal function not due to patient noncompliance with medical regimen
Insufficient Indications
Low left ventricular ejection fraction
History of functional class III or IV symptoms of HF
Peak VO_2 greater than 15 mL per kg per min (and greater than 55% predicted) without other indications

Table 2: Indications for cardiac transplantation.

Absolute contraindications
Irreversible severe pulmonary hypertension (PVR> 5wood units, Transpulmonary gradient >15)
Age >70 years
Active systemic infection
Active malignancy or recent malignancy with high chance of recurrence
Relative Contraindications
Diabetes Mellitus with end organ damage
Obesity with BMI>30
Severe peripheral vascular disease not amenable to revascularisation
Irreversible renal, hepatic or pulmonary disease
Recent or unresolved pulmonary infarction
Psychosocial factors that may prevent patient from following a complex medical regimen
Active peptic ulcer disease
Creatinine >2.5 mg/dL or creatinine clearance <25 mL/min*
Bilirubin >2.5 mg/dL, serum transaminases >3X, INR >1.5 off warfarin
Severe pulmonary dysfunction with FEV_1 <40 percent normal
Recent pulmonary infarction within six to eight weeks
Difficult-to-control hypertension
Irreversible neurological or neuromuscular disorder
Drug, tobacco, or alcohol abuse within six months
Heparin-induced thrombocytopenia within 100 days

Table 3: Contraindications for cardiac transplantation.

MCQ's

1) 66 year old male presents with severe left ventricular systolic dysfunction (EF 30%) and an ECG showed sinus rhythm with LBBB and a QRS width of 160ms. He is established on good heart failure therapy and is currently NYHA class 3. What device therapy should he have?

a. CRT-P
b. CRT-D
c. CRT-P/D
d. ICD
e. None of the above

2) The 1 year survival rate post VSD repair in GUSTO-1 trail versus medical treatment was

a. 3%
b. 47%
c. 53%
d. 6%
e. 18%

3) Compared to anterior infarcts, VSD in non-anterior infarcts is

a. 25 %
b. 50%
c. 75%
d. 60%
e. 15%

4) A 50 year old female was seen 2 months after a severe anterior MI. Echocardiogram showed severe LVSD with EF of 27%. A 12 lead ECG showed sinus rhythm with a QRS width of 118 ms. She is established on good heart failure therapy. What device therapy should she have?

a. CRT-P
b. CRT-D
c. CRT-P/D
d. ICD
e. None of the above

5) A 48 year old male was seen in heart failure clinic 18 months after a severe anterior MI. His echocardiogram showed severe left ventricular systolic dysfunction (EF 15%). He had an ICD implanted 9 months ago. A 12 lead ECG showed sinus rhythm with a QRS width of 90ms. He is established on good heart failure therapy and is currently NYHA class 3 with 3 recent hospital admissions for decompensated heart failure. What is the next step in the management of this patient?

A CASE OF LATE PRESENTING ACUTE MYOCARDIAL INFARCTION

R Antony, D Rasoul, A Khalatbari, A Rao

a. Palliative care
b. Upgrade to CRT-D
c. Refer to cardiac transplant centre
d. Check medication compliance
e. c and d

Answer key

1. D

As per 2014 NICE guidelines he is a candidate for CRT-P or D. The decision on P or D is often made by clinicians after reviewing co-morbidities and discussion with the patient regarding both procedures.

2. B

In GUSTO-1 trial 1 year survival was 47% in those who had successful repair compared to 3% who only had medical therapy.

3. B

The incidence is equal in anterior and non-anterior infarcts.

4. D

This patient has a narrow QRS (<120ms). Therefore she should have an ICD.

5. E

This patient has severe LV impairment and has a narrow QRS. He does not qualify for CRT upgrade. He is already established on good heart failure therapy. It is imperative to check compliance in someone with repeated hospital admissions, but a young patient with severe LVSD and recurrent admissions after established heart failure therapy should prom

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A TALE OF TWO CUSPS

A Das, E Joy, R Crook

Abstract

A 55 year old man with type 2 diabetes mellitus (DM) and hypertension, who presented with critical limb ischaemia secondary to undiagnosed atrial fibrillation (AF). An ejection systolic murmur was noted. Echocardiography confirmed severe (bicuspid) aortic stenosis and he was subsequently shown to have a severe coarctation of the aorta.

This case highlights several issues:

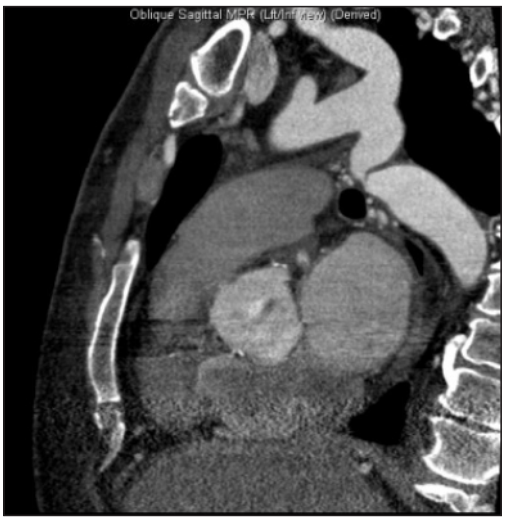
Thromboembolic risk in AF; the need to consider secondary causes of hypertension, and the importance of identifying bicuspid aortic vales and their associated aortopathy.

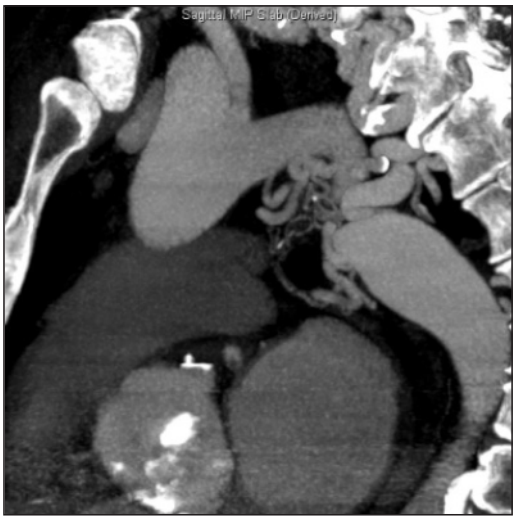
Case History

We present a 55 year old gentleman with a past medical history of type 2 DM and hypertension. He was admitted with a pale, cold and pulseless right hand and was admitted under the vascular surgeons. On examination his pulse was irregular and there was an ejection systolic murmur at the upper right sternal edge. An ECG confirmed AF and he underwent successful embolectomy of his critical limb ischaemia.

He was duly anti-coagulated with Warfarin, and rate controlled on a combination of beta-blocker and digoxin. Outpatient echocardiography demonstrated severe aortic stenosis of a bicuspid aortic valve (BAV) with a peak pressure drop of 88mmHg. He was seen in clinic and gave a history of increasing shortness of breath on exertion, and therefore he began surgical work up for an aortic valve replacement.

His coronary angiogram was performed via the right femoral artery, which was noted to be weak. We were unable to advance the guide wire past the aortic arch. The procedure was therefore converted to the right radial artery and calcified, non-obstructive coronary artery disease was noted. In order to confirm our suspicion of coarctation, he underwent magnetic resonance angiography (MRA) of the aorta, which demonstrated severe coarctation of the aorta (Figure 1). He was referred for aortic valve replacement and resection of the coarctation but tragically died before this could be undertaken.





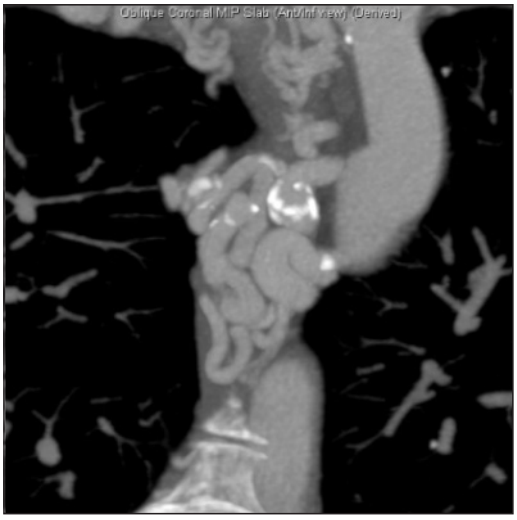


Figure 1: MRA thoracic aorta showing severe coarctation with impressive collaterals.

Discussion

Younger patients with AF should ideally have an echocardiogram to look for structural abnormalities that might increase the thromboembolic risk. There is perhaps too much emphasis on the left ventricular function, whereas patients with significant valve disease and dilation of the left atrium are also at increased risk.

Essential hypertension (primary cause unknown) accounts for 95% of cases of hypertension. Coarctation of the aorta (COA) is a rare cause of secondary hypertension [1]. This case highlights the importance of taking history from and examining all patients presenting with persistent hypertension, especially younger patients, and exploring the possibility of a secondary cause (Table 1). The femoral pulses should always be palpated (weak femorals rather than radio-femoral delay should prompt further investigation).

A TALE OF TWO CUSPS

A Das, E Joy, R Crook

Renal	Endocrine	Other
Intrinsic Renal Disease - glomerulonephritis - chronic pyelonephritis - polycystic kidney disease	Cushing's	Coarctation of Aorta
Reno-vascular Disease -renal artery stenosis	Conn's	Pregnancy
Fibromuscular Dysplasia	Acromegaly	Drugs (steroids, contraceptive pill, etc)
	Pheochromocytoma	Obstructive Sleep Apnoea

Table 1: Secondary causes of Hypertension.

Aortic stenosis in younger patients suggests the possibility that the valve is bicuspid. BAV are the most common congenital cardiovascular abnormality, occurring in 1-2% of the population. 20% of patients with BAV have an associated COA [2], with a nine-fold increased risk of thoracic aortic dissection. COA also shares an association with Turner's syndrome and intracranial aneurysms [3].

Echocardiography remains the gold standard investigation in picking up COA in infants and children. In adults however, the echocardiographic views of the aorta are often suboptimal. Computerised Tomography (CT) or MRA provide superior images and information regarding the site and anatomy of the coarctation [3], which occur in the descending aorta, most commonly just distal to the origin of the left subclavian artery.

There are ongoing randomised control trials taking place comparing surgical correction with endovascular balloon dilatation and stent placement. After correction, patients will require annual follow up with a cardiologist. Special attention is required towards addressing hypertension, which often persists despite correction possibly as a result of decreased aortic wall compliance and abnormal blood flow. They will require repeat imaging every 5 years to assess for aneurysms and restenosis [4]. It is also recommended to screen first degree relatives of patients with a bicuspid aortic valve with associated aortopathy or a family history of valvular heart disease or aortopathy for a bicuspid aortic valve [5].

Test Yourself

1. Which of these conditions is not known to be a cause of secondary hypertension?

a) Coarctation of the aorta

b) Conn's Syndrome

c) Acromegaly

d) Obstructive Sleep Apnoea

e) Addison's Disease

2. Which feature on examination may be present in severe Aortic Stenosis?

a) Loud second heart sound

b) Narrow pulse pressure

c) Corrigan's sign

d) Early diastolic murmur

e) A murmur that is louder on inspiration

3. Which congenital syndrome is associated with coarctation of the Aorta?

a) Down's syndrome

b) William's syndrome

c) Turner's syndrome

d) Holt-Oram syndrome

e) Alagille syndrome

4. If a 59 year old lady who is a smoker, with hypercholesterolaemia, asthma and epilepsy presents with Atrial Fibrillation, what is her CHA2DS2VASC score?

a) 0

b) 1

c) 2

d) 3

e) 4

5. Which of the following is not associated with an ejection systolic murmur?

a) Aortic Stenosis

b) Patent Ductus Arteriosus

c) Hypertrophic Obstructive Cardiomyopathy

d) Williams Syndrome

e) Aortic Sclerosis

A TALE OF TWO CUSPS

A Das, E Joy, R Crook

Answers

1 – e) Addison's disease

This is associated with hypotension. There are many causes of secondary hypertension, broadly categorised into renal (e.g. chronic renal failure, renal artery stenosis), endocrine (e.g. Conn's syndrome, Cushing's syndrome, Acromegaly, Hyperparathyroidism), iatrogenic (e.g. NSAIDs, steroids, oral contraceptives), pregnancy, obstructive sleep apnoea and coarctation of the aorta to name a few.

2 – b) Narrow Pulse Pressure

Severe aortic stenosis is also associated with a quiet second heart sound, ejection systolic murmur which is louder of expiration and a slow rising pulse.

3 – c) Turner's Syndrome

Down's syndrome is associated with atrioventricular septal defects and ventricular septal defects. William's syndrome is associated with supravalvular aortic stenosis. Holt-Oram is associated with atrial septal defects and Alagile syndrome is associated with Tetralogy of Fallot.

4 – d) 0

If the only risk factor is female, the score remains zero. If she were to develop one other risk factor, her score would become 2. CHA2DS2VASC stands for – Chronic Heart Failure, Hypertension, Age, Diabetes Mellitus, Previous Stroke or Transient Ischaemic Attack, Vascular disease (previous myocardial infarction, peripheral artery disease or aortic plaque), Sex

5 – b) Patent Ductus Arteriosus

This is associated with a continuous machinery murmur. The others are all associated with an ejection systolic murmur.

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ACUTE MYOCARDIAL INFARCTION FOLLOWING ROAD TRAFFIC ACCIDENT

AA Faraj, P Silverton

Abstract

A young male adult sustained traumatic myocardial infarction, following road traffic accident. The diagnosis and treatment of this was difficult, the case is highlighted to learn from and put in the differential diagnosis of patients with chest pain following trauma.

Keywords: *Trauma, myocardial infarction, coronary artery, thrombolysis.*

Introduction

Blunt thoracic injuries are serious. Approximately 33% of these injuries require hospital admission. 20-25% of all deaths caused by blunt trauma are directly caused by thoracic trauma (1).

Myocardial contusion is more common than myocardial infarction following blunt anterior chest wall trauma (1-6). We report an unusual case of acute infero-apical myocardial infarction following a high velocity road traffic motor vehicle collision to make the trauma surgeon aware of this otherwise fatal condition.

Case Report

A healthy, non-smoking 20-year-old student unrestrained driver of a car was involved in a high velocity head on collision with another car, at a combined speed of 110mph. At the scene, he was found in the front of the driver's seat with his left forearm bent and locked between the seat and the dashboard. The front of the car had sustained severe damage. He presented to our Accident and Emergency department with a closed fracture of the left radius and ulna. On admission, he had mild central chest discomfort with difficulty in breathing when lying supine but relieved on sitting up. There were no external signs of chest wall or abdominal injuries. On auscultation there were no murmurs and neck veins not distended. There was no history of drug abuse hence no drug screen was performed.

CT scan of the chest (Fig 1) showed no lung contusion or heart abnormality.

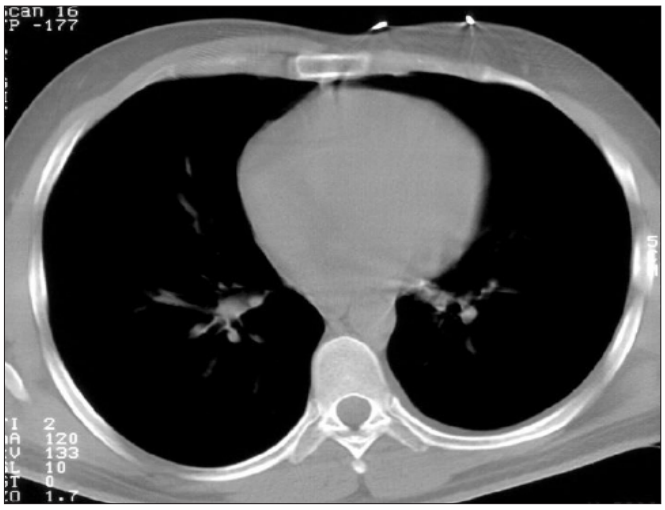

Fig 1: CT scan of the chest showing no gross abnormalities.

The initial ECG revealed hyper-acute ST segment elevation in the inferior and lateral leads compatible with an acute myocardial infarction. (Fig 2)

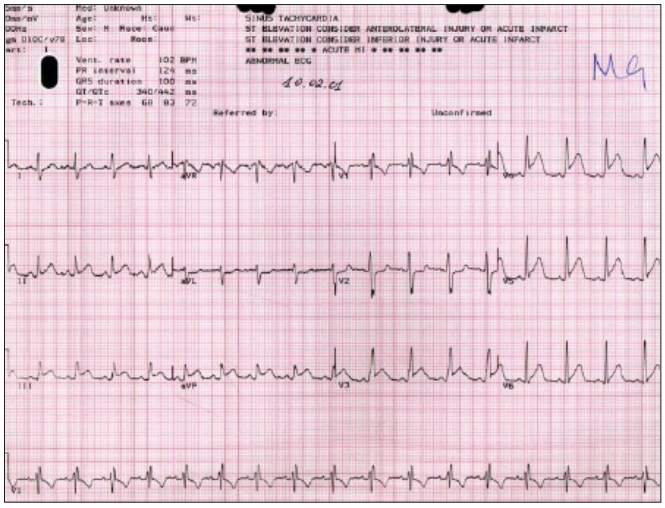

Fig 2: ECG on admission showing hyperacute ST elevation in infero-lateral leads.

Thrombolysis was contraindicated in view of his recent injury. He was treated with Aspirin and a low dose beta-blocker. He was admitted to the coronary care unit for observation. ECG at 48hrs post-injury, revealed pathological Q waves in leads II, III, AVF and V6 and the ST segment elevation decreasing. (Fig 3).

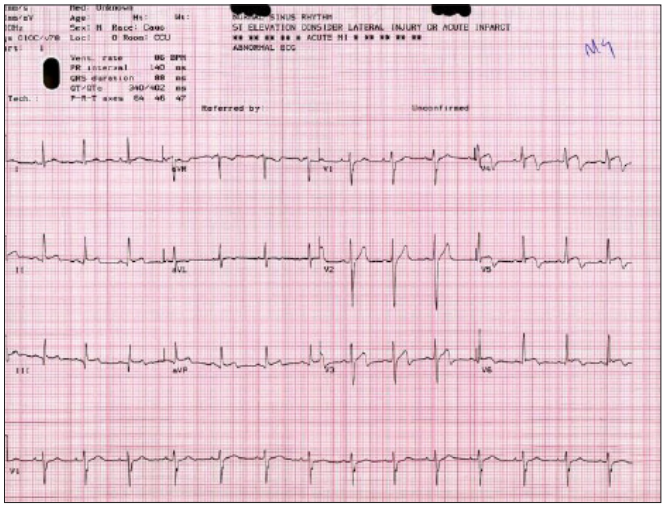

Fig 3: ECG 48-72 hrs after the injury, showing small pathological Q waves in leads II, III, AVF and V6 as the ST segment elevation.

ACUTE MYOCARDIAL INFARCTION FOLLOWING ROAD TRAFFIC ACCIDENT

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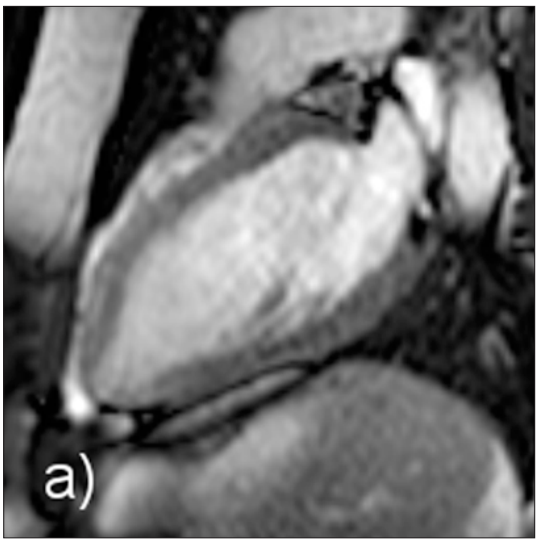
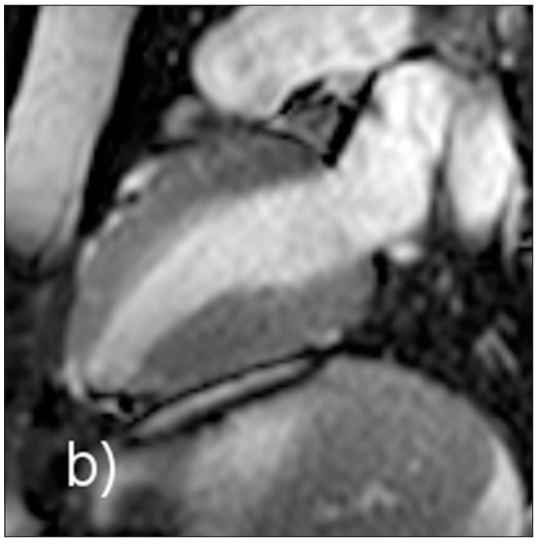
T wave inversion developed by seventy-two hours in the affected leads. These findings were strongly suggestive of infero-apical myocardial infarction secondary to right coronary and or left circumflex artery involvement. Cardiac catheterisation was not performed, as it was not indicated in this clinical scenario. A cardiac magnetic resonance scan was carried out, which confirmed the presence of an infero-apical myocardial infarction (Fig 4). He made satisfactory recovery without any further cardiac complications.

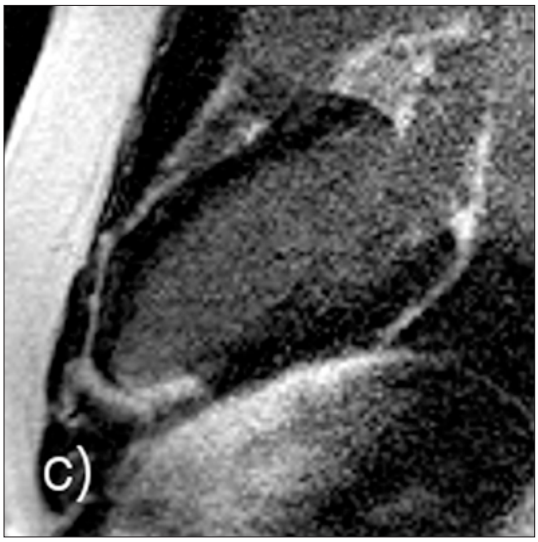
Fig 4: MRI scan of the heart.



(a) Diastolic.



(b) Systolic showing an area of akinesia in the inferior apex.



c) T1 weighted inversion recovery radient echo images acquired 15 minutes after intravenous administration of Gadolinium showing hyper-enhancement of the same infero-apical region.

Nine days after the injury, open reduction and internal fixation of radius and ulna fracture was performed under brachial plexus block. There were no intra or post-operative complications. He was discharged home eleven days following the admission.

Discussion

Myocardial contusion is a recognized injury following blunt chest trauma (1). The right ventricle is the chamber more likely to be involved as it is situated immediately behind the sternum (2). Very few cases of myocardial infarction secondary to traumatic coronary artery thrombosis have been reported in the literature (1-4). The left anterior descending artery, being in proximity to the sternum, is commonly involved (4).

The incidence of traumatic acute inferior myocardial infarction due to right coronary artery involvement is very rare (2, 6). Our patient did not undergo cardiac catheterisation which may demonstrate an abnormality in the left anterior descending artery. He appears to have experienced a traumatic acute infero-apical myocardial infarction, secondary to a lesion either involving the right coronary and or left circumflex artery distribution.

ACUTE MYOCARDIAL INFARCTION FOLLOWING ROAD TRAFFIC ACCIDENT

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The inferoapical myocardial infarction in this case could still be caused by blunt trauma to distal LAD, which is anatomically more likely. In some people, the LAD is longer than usual and wraps around the apex, going up in the posterior interventricular groove for a fair distance, and giving blood to the distal inferior wall. Trauma to distal LAD at the tip of apex can cause infarction in the apical inferior wall; like this patient.

The normal course of coronary arteries is such that they are rarely involved in blunt anterior chest wall trauma. The injury can however be the result of a deceleration injury rather than direct blunt trauma to the artery.

When considering blunt cardiac injuries, nonperforating injuries are the most common and the usual mechanism for these is deceleration, with the relatively mobile heart striking the chest wall. The perforating blunt cardiac injuries are the ones more associated with a crush-type mechanism and these are less frequently encountered (2). This could result in rib fractures and anterior chest wall bruises. Interestingly our patient did not have any anterior chest wall injuries, despite the combined velocity of 110 mph.

It has to be noted that the finding of hyper-enhancement on late-contrast enhanced Magnetic Resonance images is not specific for myocardial infarction. However, the distribution of the abnormality in this patient was highly suggestive of Myocardial Infarction. There were also no features in the cardiac magnetic resonance images to suggest myocardial contusion, which is an important differential diagnosis, such as pericardial effusion or myocardial oedema.

The chance of car occupant mortality from chest injuries following high velocity road traffic accidents is high, especially if the car speed is more than 55 mph (3). This particular case has been characterised by survival following a very high velocity impact (110mph).

Conclusion

The clinical presentation, the site of myocardial infarction and the survival of our patient makes this case unique. Even without external chest wall signs, in high velocity deceleration trauma to the chest, a high index of suspicion of myocardial damage and low threshold for appropriate diagnostic evaluation is necessary.

Questions: Which of the following is true?

1: In regards to sternal fracture:

a. Mortality rate of up to 1%.

b. Incidence of cardiac dysrhythmia requiring treatment is 1.5%.

c. Isolated sternal fracture is a closed fracture.

d. All patients with sternal fracture need admission to intensive care unit.

2: In car collisions:

a. Three point restrained occupants, reduces the incidence of thoracolumbar fracture.

b. The combined speed in car collision is the summation of the speed of two vehicles colliding with each other.

c. Seat belt usage reduces the severity of injury, hospital stay, and number of operations in injured patients.

d. Road traffic injuries are the leading cause of death globally.

3. In regards to anatomy of sternum:

a. The sternum develops as three distinct parts: the manubrium, the body of the sternum (sometimes called the gladiolus), and the xiphoid process.

b. The name manubrium means "handle," gladiolus means "sword," and xiphoid means "sword-shaped."

c. The xiphoid process ossifies only during childhood.

d. Regardless of its degree of ossification, the xiphoid process serves as an important attachment point for the tendons of the diaphragm, rectus abdominis, and transverse abdominis muscles.

e. During open heart surgery, the sternum must be cut in half along its long axis to provide access to the heart.

ACUTE MYOCARDIAL INFARCTION FOLLOWING ROAD TRAFFIC ACCIDENT

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4. Regarding traumatic myocardial infarction:

a. Is synonym to myocardial contusion.

b. In non-perforating blunt cardiac trauma, the mechanism of injury is an acceleration.

c. Anterior descending coronary artery can be injured following sternal fracture.

d. Cardiac arrhythmia can be the presenting feature.

5. Regarding diagnosis of myocardial infarction following chest trauma:

a. The electrocardiogram (ECG) may present nonspecific abnormalities in up to 70% of cases.

b. Abnormal ST segment and T wave associated with sinus tachycardia is the most frequent electrocardiographic findings.

c. The increase of the cardiac enzyme CKMB [creatine kinase and its MB isoenzyme] is considered to be specific for the diagnosis of infarction in patients with trauma.

d. The echocardiogram can show segmental deficits and it must be requested in suspected cases of cardiac trauma.

Answers

1. A: T

1. B: T

1. C: F Answer

Isolated sternal fracture may be defined as a sternal fracture without any other thoracic injury such as rib fracture, hemothorax, or pneumothorax.

1. D: F Answer

Recent studies have commented on the poor clinical yield of this approach and suggested that in patients with a normal ECG, benign chest X-ray (CXR), and stable hemodynamic parameters, significant cardiac injury is unlikely and post-ED discharge could be recommended.

2. A: T

2. B: T

2. C: F

2. D: F Answer

RTAs are the eighth leading cause of death globally, and the leading cause of death for young people.

3. A: T

3. B: T

3. C: F Answer

The Xiphoid process ossifies slowly ossifies throughout childhood and adulthood until around age 40 when all of its cartilage is replaced by bone.

3. D: T

3. E: T

4. A: F Answer

Myocardial infarction is myocardial damage as a result of coronary artery occlusion, while myocardial contusion is direct muscle damage.

4. B: F Answer

It is a deceleration one

4. C: T

4. D: T

5. A: T

5. B: T

ACUTE MYOCARDIAL INFARCTION FOLLOWING ROAD TRAFFIC ACCIDENT

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5. C: F Answer

The cardiac enzymes cannot be considered specific for diagnosis of infarction in patients with trauma, due to its presence in the skeletal muscle and in other organs. Serum measurements of troponins T or I is more specific in the diagnosis of post-traumatic myocardial infarction

5. D: T

5. E: T

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AN UNUSUAL PRESENTATION OF ENDOCARDITIS

A Kalra, A Khan

Abstract

A 65 year-old gentleman with a bioprosthetic aortic valve replacement presented with central crushing chest pain and was diagnosed with a myocardial infarction. During his hospital admission, he showed clinical signs of systemic infection and was suspected to have endocarditis.

He experienced left flank tenderness which, after thorough investigation, was diagnosed as a large splenic abscess presumably secondary to septic emboli from the infected aortic valve. After long term intravenous antibiotic therapy and ultrasound guided drainage of the abscess, the patient made a full recovery.

Case History

A 65 year old gentleman presented to accident and emergency with central, crushing chest pain radiating to his left arm associated with sweating and nausea. These symptoms were on a background of a two day history of worsening chest pain while climbing stairs.

He had no respiratory, urinary, or gastrointestinal symptoms. His past medical history consisted of a Nissen fundoplication five years previously for a hiatus hernia and a previous bioprosthetic aortic valve replacement three years ago due to calcific degeneration of the valve.

On examination, he had a slow-rising pulse, an ejection systolic murmur audible at the aortic area which radiating to his carotids, and no other significant findings. He had normal inflammatory markers and an unremarkable ECG, but had a troponin I of 0.07 which rose to 13.08 at 12 hours.

A diagnosis of non-ST elevation myocardial infarction (NSTEMI) was made and he was started on medical management for acute coronary syndrome and listed for primary percutaneous coronary intervention.

Three days after admission, the patient complained of dysuria and left flank pain. He was pyrexial and a temperature of 39°C was recorded. Venous blood cultures were taken and inflammatory markers were elevated. The patient's urine dipstick was found to be positive in leucocytes and nitrites, and treatment was started for a suspected ascending urinary tract infection.

An abdominal ultrasound was performed to investigate for pyelonephritis which showed normal kidneys, a distended bladder, and an enlarged spleen. His transthoracic echocardiogram revealed an ejection fraction of 65% with no wall motion abnormality.

However, moderate restenosis of bioprosthetic aortic valve with no obvious vegetation was noted. His subsequent transoesophageal echocardiogram re-confirmed no vegetation or paravalvular leak of the aortic prosthesis with normal LV function.

Over the next day, the inflammatory markers continued to rise and a careful history uncovered a three month history of slowly worsening shortness of breath, fatigue, weight loss, and loss of appetite. Furthermore, around that same time, he had undergone scaling of his teeth. To exclude endocarditis, a further transoesophageal echocardiogram was performed which was also unable to detect valvular vegetations.

After detailed discussions with the hospital microbiology team, antibiotics were stopped as there was no objective evidence of endocarditis. However, on the following day blood cultures taken earlier in the week grew Streptococcus viridans.

Therefore, as per sensitivities, the patient was started on a six-week course of intravenous benzylpenicillin, with the plan of further imaging in the form of positron emission tomography (PET) to determine a definitive diagnosis of infective endocarditis. PET scanning was indicated due to the need for a higher specificity investigation than the modalities of echocardiography that had already been used.

The patient continued to suffer from left flank and left upper quadrant tenderness, and further abdominal imaging was requested to investigate this. An abdominal ultrasound and CT (figures 1-3) showed an enlarged 13cm spleen with a lobulated collection within its body measuring 6cm x 8.5 cm. Finally, the PET scan (figures 3 and 4) showed markedly increased uptake over the aortic valve as well as an avascular lesion in the spleen surrounded by increased uptake indicating this collection was an abscess.

AN UNUSUAL PRESENTATION OF ENDOCARDITIST

A Kalra, A Khan

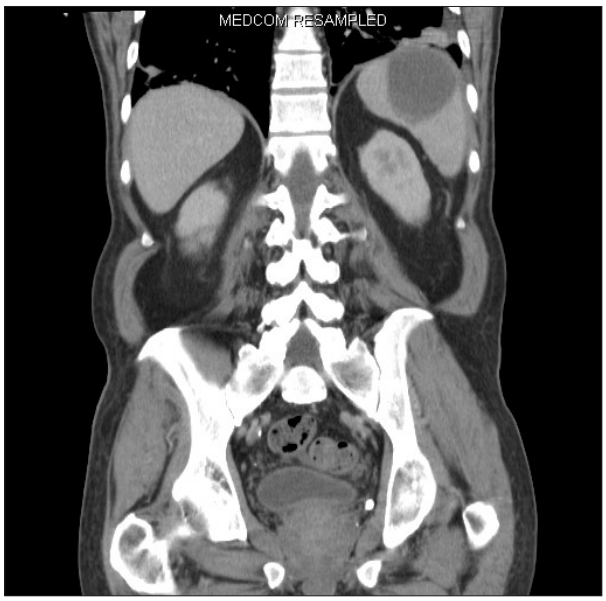

Fig 1: CT cor.

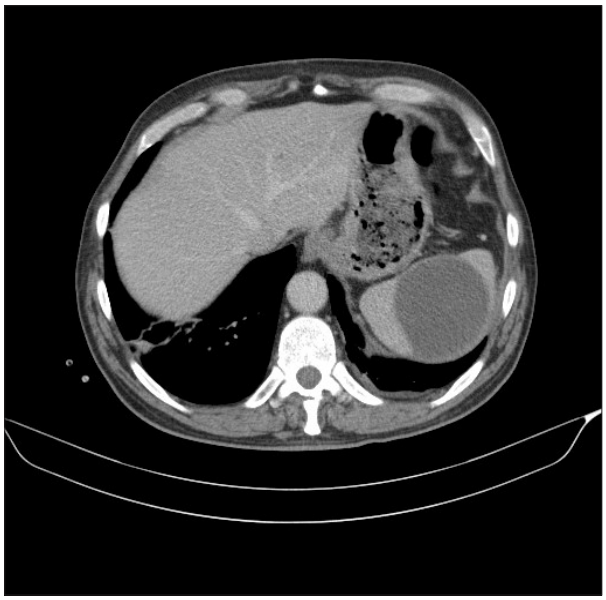

Fig 2: CT trans.

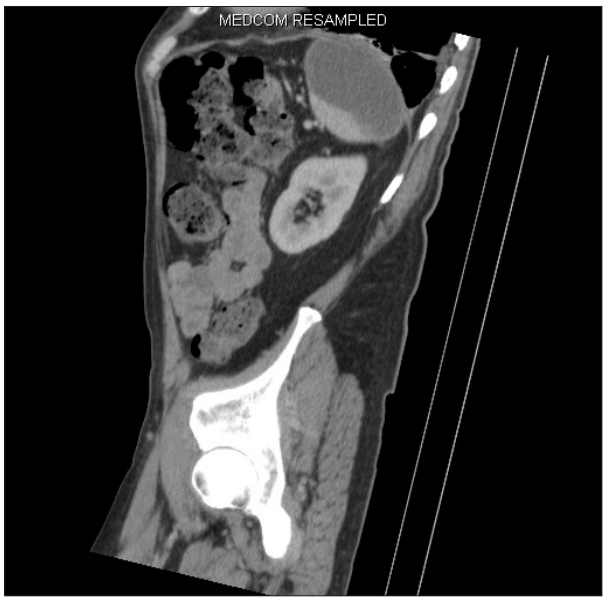

Fig 3: CT sag.

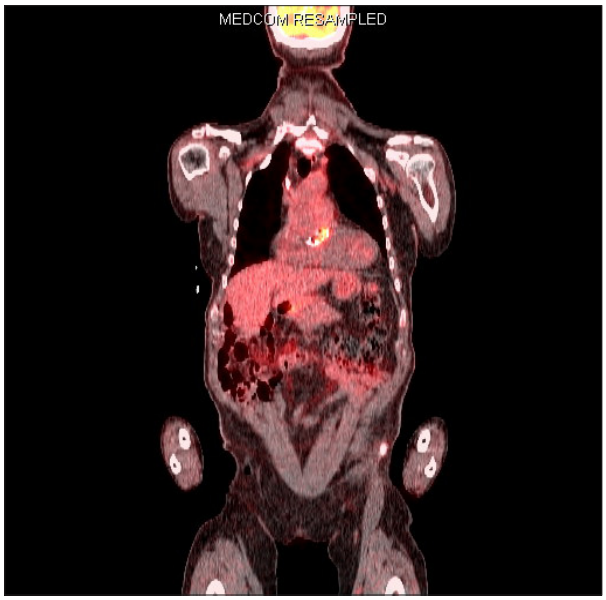

Fig 4: PET AVR cor.

AN UNUSUAL PRESENTATION OF ENDOCARDITIST

A Kalra, A Khan

The endocarditis was successfully treated by six weeks of IV benzylpenicillin followed by a further six weeks of oral amoxicillin. The splenic abscess, thought to be seeded by a septic embolus from the infected aortic valve, was treated by the insertion of a drain which drained green and brown fluid over the span of two weeks and was monitored by regular ultrasound scans until resolution.

This case was discussed in MDT meeting with cardiothoracic surgeon and decided to keep under follow up with no immediate intention of surgery as all inflammatory markers, cultures and clinical features were satisfactory.

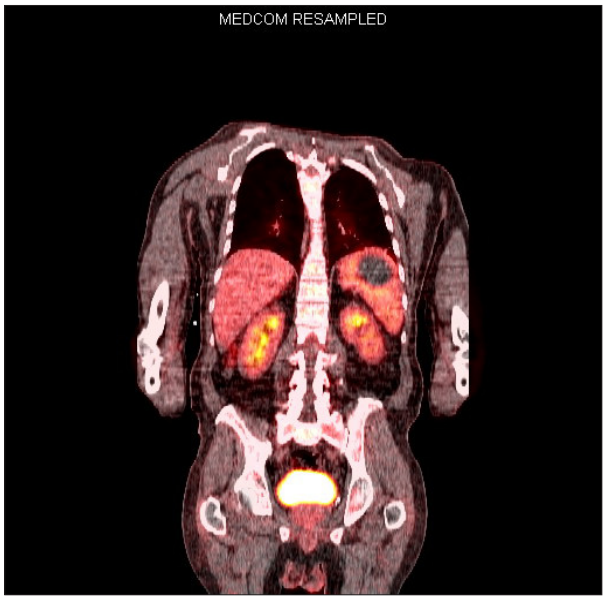

Fig 5: PET spl cor.

Discussion

A recurring theme in this case was the competing relevance of the clinical features of the patient versus useful information gained by investigations. At times, both aspects were prioritised over each other based on the clinical risk and benefit of relying on each resource.

Early before the patient's diagnosis of endocarditis, the patient presented as a strong clinical case of subacute bacterial endocarditis, yet both the transthoracic and transoesophageal echocardiograms were found to be negative.

At this time, the clinical symptoms, the audible murmur on auscultation, and the history of a previous aortic valve replacement proved more useful than negative investigations which have inherent imperfect sensitivities. Furthermore, the risk in this case for stopping treatment altogether proved much greater than the benefit of potentially unnecessary antibiotic therapy.

At another point in this case, this theme was again exemplified while investigating the patient's urinary symptoms and loin pain. While at that point pyelonephritis was the most likely explanation for the clinical picture, the patient's personal risk factors and recent myocardial infarction required a firmer diagnosis than his presentation alone.

This paid dividends with the radiological diagnosis of a splenic collection which was an unlikely differential but potentially catastrophic if missed. In this case, risk and benefit was correctly weighed to result in thorough radiological investigations which served to recognise and eventually treat this abscess. Long-term, this patient was potentially saved from a splenectomy or a catastrophic perforation.

A thorough history and clinical examination are always important in accurate diagnosis.

Foundation doctors often are required to make decisions outside their previous experiences. In these cases, decisions based on potential risk and potential benefit serve as the foundation of safe clinical practice.

Questions

1. What is the most commonly affected valve in infective endocarditis in intravenous drug users?

a. Mitral

b. Aortic

c. Pulmonary

d. Tricuspid

e. Both right-sided heart valves are equally affected

2. Which of the following is a major criterion in the Modified Duke's criteria?

a. Janeway lesion

b. Venous blood culture positive for Streptococcus bovis

c. Predisposing heart condition

d. Fever >38 degrees Celsius

e. Pulmonary infarct

AN UNUSUAL PRESENTATION OF ENDOCARDITIST

A Kalra, A Khan

3. Which of the following conditions would be least associated with a higher risk of developing vegetations?

a. Large ventricular septal defect

b. Bicuspid aortic valve

c. Previous endocarditis

d. Mitral valve prolapse

e. Repaired cyanotic heart disease

4. Indications for surgery in infective endocarditis:

a. Whenever a valve grows a vegetation

b. Fungal infective endocarditis

c. Persistent sepsis after 72 hours of appropriate antibiotic treatment

d. Rupture of an aneurysm of the sinus of Valsalva

e. Conduction disturbances caused by a septal abscess

5. Mycotic aneurysms:

a. Only occur in cerebral vessels

b. Are always due to fungal infection

c. Never occur in the abdominal aorta

d. Are produced by embolization to the vasa vasorum

e. Can be found in pulmonary arteries.

Answers

1. D

While left-sided heart valves are predominantly affected in endocarditis overall, endocarditis in patients who use intravenous drugs most commonly affects the tricuspid valve. This is thought to be due to the tricuspid valve being the first valve encountered by systemic blood flow from the systemic circulation.

Any potential septic emboli from potentially infected injection sites or contaminated instruments will therefore have the opportunity to seed to this valve first. The tricuspid valve is the most frequently affected (60%-70%), followed by the mitral and aortic valves (20%-30%). Pulmonary valve infection is rare (< 1%).

2. B: In the Modified Duke's criteria used to establish a diagnosis of infective endocarditis, major criteria consist of either:

a. a positive blood culture for infective endocarditis (Strep. viridans, Strep. bovis, HACEK organisms, Staph. aureus without another primary site of infection, or enterococci species) from two separate blood cultures or two positive cultures from samples drawn >12 hours apart

b. evidence of endocarditis evident on an echocardiogram such as an oscillating intracardiac mass on a valve or a supporting structure, an abscess, partial dehiscence of a prosthetic valve, or a new valvular regurgitation

The full Modified Duke's criteria are as follows:

For diagnosis of infective endocarditis the requirement is:

- *2 major and 1 minor criteria or*
- *1 major and 3 minor criteria or*
- *5 minor criteria*

Major criteria

- *Positive blood cultures for infective endocarditis*
- *Typical microorganism for infective endocarditis*

from 2 separate blood cultures.

- *Viridans streptococci, Streptococcus bovis, and HACEK group or*
- *Community-acquired Staphylococcus aureus or enterococci in the absence of a primary focus or*
- *Persistently positive blood cultures, defined as recovery of a microorganism consistent with infective endocarditis from:*
- *2 blood cultures drawn 12 hours apart or all of 3 or most of 4 or more separate blood cultures, with first and last drawn at least 1 hour apart*
- *Evidence of endocardial involvement*
- *Positive echocardiogram for infective endocarditis*
- *Oscillating intracardiac mass on valve or supporting structures or in the path of regurgitant jets or on implanted material in the absence of an alternative anatomical explanation or*
- *Abscess or*
- *New partial dehiscence of prosthetic valve or*
- *New valvular regurgitation*

AN UNUSUAL PRESENTATION OF ENDOCARDITIST

A Kalra, A Khan

Minor criteria

- *Predisposing heart condition or intravenous drug use*
- *Fever: ≥38°C*
- *Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway lesions*
- *Immunologic phenomena:*
- *Glomerulonephritis*
- *Osler nodes*
- *Roth spots*
- *Rheumatoid factor*
- *Microbiologic evidence: positive blood culture but not meeting major criterion as noted previously or serologic evidence of active infection with organism consistent with infective endocarditis*
- *Echocardiography findings consistent with infective endocarditis but not meeting major criterion as noted previously*

3. A: Vegetations occur when a high-pressure jet enters a low-pressure cavity through a narrow orifice. In B and D, this is the cause of the increased incidence of infective vegetations. In A, the large ventricular septal defect is too large a channel to cause a significant increase in pressure.

Despite repairing congenital cyanotic heart defects, patients remain at an increased lifetime risk for developing infective endocarditis. Previous endocarditis is a well-established risk factor for developing infective endocarditis.

4. B: Indications for surgery include:

a. Congestive cardiac failure caused by vegetations or severe valvular incompetence caused secondary to vegetations
b. Persistent sepsis including systemic symptoms lasting longer than 5-7 days, relapsing infective endocarditis, or most patients with abscess, fistula, or pseudoaneurysm formation
c. Systemic emboli
d. Pathogens that are particularly aggressive (including Brucella and Staph. lugdunensis), multidrug resistant, or specifically Pseudomonas or fungal pathogens.
e. Prosthetic valve endocarditis

5. E: Mycotic aneurysms are infected aneurysms either caused by septic emboli into pre-existing aneurysms or are caused themselves by septic emboli becoming impacted into vessel walls causing inflammatory aneurysm formation.

Despite their name, they are never due to fungal pathogens. They are often due to embolization from infected valves and can exist wherever septic emboli can reach.

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NEW ONSET ATRIAL FIBRILLATION

DE Harding, SD Rosen

Abstract

This case based discussion describes the management of a 64 year old patient with new-onset, fast atrial fibrillation secondary to influenza. Our article aims to guide foundation trainees in the inpatient management of this common arrhythmia (Fig 1).

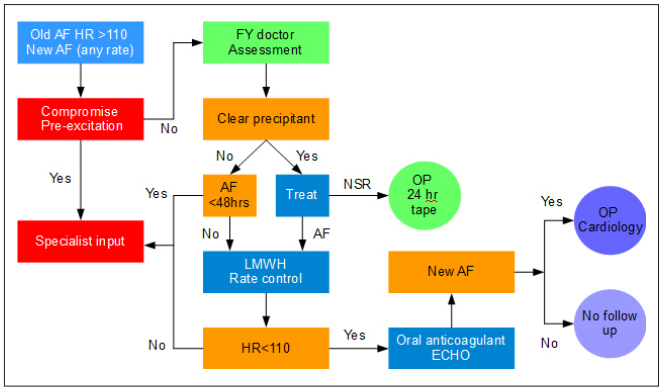

Figure 1: Flow chart for management of fast or new onset atrial fibrillation (AF). HR = heart rate; FY = foundation year; NSR = normal sinus rhythm; OP = outpatient; LMWH = low molecular weight heparin (treatment dose); ECHO = echocardiography.

Case history

Patient A (a 64 year old female) presented with a 24 hour history of palpitations and chest pain. She had been unwell for four days with coryzal symptoms and was referred by her GP with fast atrial fibrillation (AF). Her medical background included irritable bowel syndrome and urinary urgency, but she did not take any regular medications. The patient denied alcohol use and there were no cardiovascular risk factors.

Assessment in A&E showed the patient to be clinically stable (BP 98/63, RR 15, SaO2 99% on air, T 36.1) but in AF with a fast ventricular rate (HR 171). The physical examination was otherwise unremarkable, as were a chest x-ray and venous blood gas. Bloods including electrolytes, renal function and thyroid profile were normal. The patient was resuscitated with intravenous (IV) fluids, rate controlled with oral and IV ß-blockers, and anticoagulated with low molecular weight heparin (LMWH). She was subsequently loaded with IV digoxin by the on-call medical team and monitored overnight.

Following referral to cardiology, the ß-blocker dose was increased, digoxin stopped and empirical treatment given for sepsis (IV antibiotics and fluids). Swabs were taken for viral influenza and blood and urine sent for microbial culture and sensitivities. Despite antibiotic therapy and regular anti-pyretics, the patient continued to spike temperatures. Blood and urine cultures were negative, but the viral swabs confirmed influenza A (H1N1). Antibiotics were switched to the antiviral oseltamavir and the patient was isolated in a side room.

After four days of inpatient therapy the patient was fit for discharge. Her ventricular rate was adequately controlled with oral bisoprolol (10mg OD) and anticoagulation was continued with apixaban. Outpatient review was arranged (4 weeks) with a view to electrical cardioversion (DCCV). Prior to discharge, echocardiography (ECHO) demonstrated a small pericardial effusion around the right atrium and right ventricle and mild bi-atrial dilatation (Fig 2). Left ventricular volume and systolic function were normal.

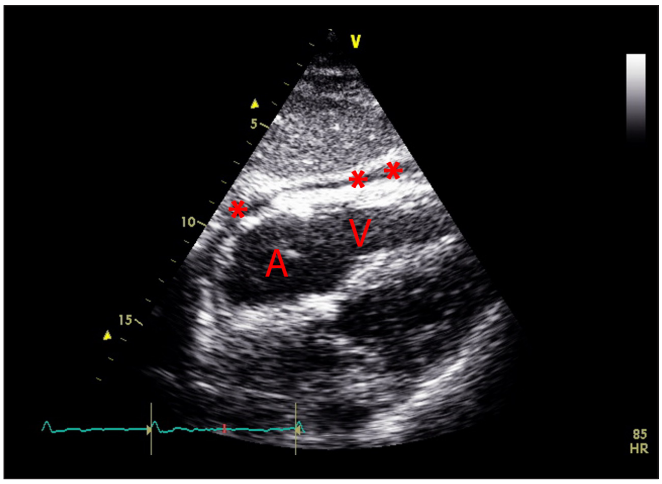

Figure 2: Echocardiography demonstrating a pericardial effusion (*) around the right atrium (A) and right ventricle (V).

The patient re-presented two weeks later with decompensated left ventricular failure (Fig 3). She was treated with IV diuretics and chemically cardioverted with amiodarone. Apixaban was stopped, bisoprolol reduced (2.5mg OD) and low dose aspirin started. The patient was discharged after 24 hours and remains well.

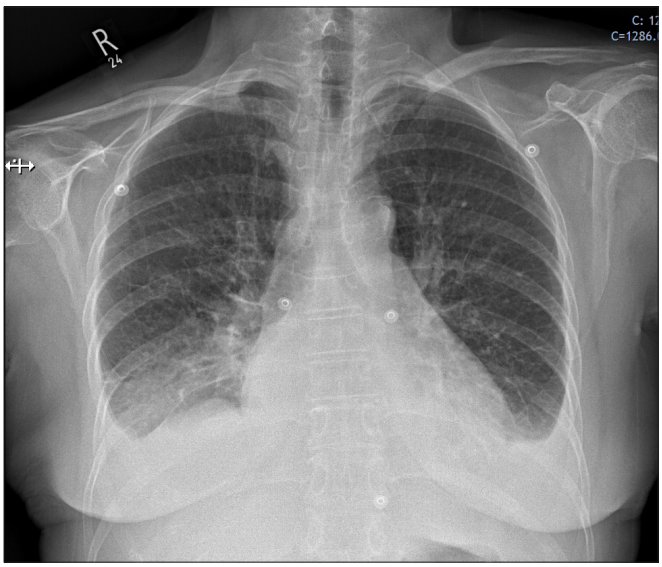

Figure 3: Chest x-ray performed at re-presentation demonstrating bilateral pleural effusions and mild interstitial oedema.

NEW ONSET ATRIAL FIBRILLATION

DE Harding, SD Rosen

Discussion

In any patient presenting with an abnormal cardiac rhythm, the key question is whether they are haemodynamically compromised. Fast AF with evidence of compromise requires urgent referral and senior support. Clinical features include reduced conscious level; severe hypotension; acute pulmonary oedema and cardiac ischaemia.

If these are absent, it is safe for foundation trainees to proceed with independent assessment and management (Fig 1). Pre-excited fast AF (short PR interval, slurred QRS upstroke e.g. Wolff Parkinson White) should also be referred urgently, but will not be covered in this article.

After clinical examination, an ECG, chest x-ray and bloods should be requested. An arterial blood gas may be indicated if there are signs of respiratory compromise. This will help to confirm or exclude common precipitants of AF such as infection, electrolyte disturbance and tissue hypoxia. It will also guide management and identify patients in acute heart failure.

Information should be sought about the patient's active medical problems, co-morbidities and any other relevant investigations (e.g. old ECGs and ECHO reports) should be reviewed. It is also helpful to establish the timing of AF onset, because if it is <48 hours the patient can be cardioverted with specialist support.

The first element of the management of fast AF is to address the underlying cause where possible. Patients who are clinically dehydrated should be resuscitated with fluids, electrolyte derangements should be corrected and infection treated with antibiotics (or antivirals). Serum magnesium should be kept >1mmol/L and potassium >4.0mmol/L.

No early attempt at rate control is usually necessary if there is a clear precipitant and no haemodynamic compromise. Unless contraindicated (e.g. CHA2DS2VASC score not 2 or more points greater than HAS-BLED score and no intention of DCCV), all patients in AF should receive therapeutic dose LMWH, which should be converted to an oral anticoagulant when clinically appropriate.

Patients who remain tachycardic (>100-110) despite resuscitation should be treated with rate limiting drugs. These can be given oral or IV, depending on access to cardiac monitoring and the urgency of rate control. ß-blockers and calcium channel antagonists (CCBs) are used first line (1,2).

Digoxin is usually reserved for patients in fast AF with decompensated heart failure, but it can supplement maximal dose ß-blocker/ CCB therapy if required (1). Patients who are not controlled with two agents (ß-blocker/ CCB + digoxin) can be loaded with amiodarone (1). This drug requires cardiac monitoring for IV initiation and should not be started without specialist support.

At the point of discharge, patients with AF should be rate controlled to a target HR <110 bpm (3). They should have undergone ECHO and been referred to outpatient cardiology if the AF is of new onset. Patients who have reverted to normal sinus rhythm should undergo a 24 hour tape in the community to confirm cardioversion.

Case Evaluation

There are three aspects of fast AF management in this case that could be improved: electrolyte optimisation, ventricular rate control and anticoagulation on discharge.

Serum magnesium was not normalised before starting rate limiting drugs. The magnesium level on admission was 0.76mmol/L, which should have been corrected to a target of >1.0 mmol/L. Magnesium has an established safety profile and reduces the ventricular rate in AF (4). It also increases the likelihood of successful cardioversion with anti-arrhythmic drugs (5).

The ventricular rate was initially controlled with metoprolol (5mg IV) and bisoprolol (2.5mg PO). Digoxin (1mg IV loading dose) was started two hours later for additional rate control, in the absence of heart failure or haemodynamic compromise (BP 115/70). It would have been more appropriate to increase ß-blocker therapy to the maximum tolerated dose before starting digoxin.

At re-presentation the patient was cardioverted with amiodarone and apixaban was switched to low dose aspirin. The European Society of Cardiology recommends that all patients should continue an oral anticoagulant for four weeks after successful DCCV or chemical cardioversion unless low risk (CHA2DS2VASC <2) (1). The patient's CHA2DS2VASC score on discharge was 2 (age ≥65, female sex) and HAS-BLED was 0, making her moderate-high risk and suitable for an oral anticoagulant.

NEW ONSET ATRIAL FIBRILLATION

DE Harding, SD Rosen

Best of 5

Q1. A patient presents in fast AF with no clear precipitant. They have been initially treated with IV metoprolol. On review the HR is 145 and BP 75/50. How would you proceed?

A. Give 2.5mg metoprolol

B. Give 500mcg digoxin

C. Give a fluid bolus

D. Give magnesium

E. Urgent cardiology referral

Q2. What drug would you use for rate control in a patient with fast AF and cor pulmonale secondary to COPD?

A. Verapamil

B. Digoxin

C. Metoprolol

D. Ramipril

E. Amiodarone

Q3. What is the definitive investigation in a patient who presents with decompensated right sided heart failure who has a background of AF on warfarin? The INR has been subtherapeutic for the past two weeks.

A. D-dimer

B. ECHO

C. ABG

D. ECG

E. CTPA

Q4. A patient is admitted with acute urinary retention. They are noted to be in AF with a ventricular rate of 108, but are clinically asymptomatic. How would you proceed?

A. Start amiodarone

B. Treat underlying electrolyte abnormalities and observe

C. Start digoxin

D. Anticoagulate with warfarin

E. Give IV metoprolol

Q5. You are called to review a patient. They are sweating, complaining of chest pain and are in fast AF. The ECG looks ischaemic. How would you proceed?

A. Start ACS treatment

B. Give adenosine

C. IV metoprolol

D. Seek senior help

E. Give amiodarone

Answers

1. Answer. E.

The patient has fast AF with haemodynamic compromise. Additional drug therapy could drop the BP further and lead to cardiac arrest. The patient needs to be urgently referred to cardiology for cardioversion.

2. Answer. B.

Whilst a ß-blocker could be used with caution, most clinicians would recommend digoxin in this setting (heart failure + lung disease). Verapamil will depress myocardial contractility and amiodarone should not be used first line. Ramipril is not a rate controlling drug.

3. Answer. E.

This patient is at high risk of pulmonary embolism and has presented with decompensated right heart failure. Whilst options A-D will all support a diagnosis of PE, only CTPA (or VQ scan) will confirm it.

NEW ONSET ATRIAL FIBRILLATION

DE Harding, SD Rosen

4. Answer. B.

This is rate-controlled, asymptomatic AF without evidence of compromise. It has been triggered by urinary retention and likely electrolyte disturbance. The patient should be observed, initially anticoagulated with LMWH and oral bisoprolol can be considered for rate control.

5. Answer. C/D.

This patient should be managed with senior support. They require rapid rate control with an IV ß-blocker. They may benefit from ACS treatment, but only if the troponin is elevated. Adenosine is not used to rate control AF and amiodarone is not first line in this setting.

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COCAINE-ASSOCIATED MYOCARDIAL INFARCTION

S Rayner, SJ Leslie

Abstract

Objective

To discuss the diagnosis, investigation and management of cocaine-associated myocardial infarction with an illustrative case.

Methods

A 47 year old man presenting with central chest pain 1 hour after snorting cocaine, with ECG changes consistent with an ST elevation myocardial infarction and significant 12 hour troponin rise.

Results

Diagnostic coronary angiogram demonstrated a filling defect in the proximal left anterior descending artery (LAD) and coronary intravascular ultrasound revealed minimal proximal LAD disease with associated thrombus.

Conclusion

Subtle but significant differences exist between a non cocaine-associated myocardial infarction and those caused by cocaine and therefore a thorough recreational drug history essential to guide optimal management.

Case History

A 47-year-old male smoker presented to a remote rural general hospital with a sudden onset of central chest pain with no radiation. This occurred 1 hour after snorting 'half a line' of cocaine (approximately 35mg). His past medical history included previous illicit intra-venous heroin use (now on a methadone programme), hepatitis C infection and a previous deep vein thrombosis.

On admission his ECG was normal (Figure 1). However, due to the nature of his pain which was typical for acute coronary syndrome (ACS) he was treated with aspirin 300mg and clopidogrel 300mg as per the local ACS algorithm.

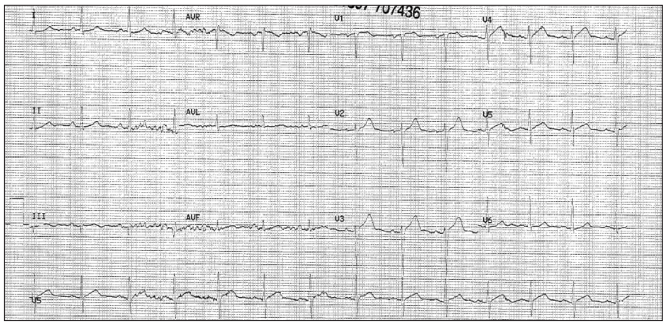

Figure 1 – Admission ECG

His subsequent ECG showed 1-2mm ST elevation in leads V1-3, consistent with an anterior ST segment elevation myocardial infarction (STEMI) (Figure 2) although this was not thought to reach 'thrombolysable criteria'. His 12-hour troponin I was 37,461ng/L and he was transferred to the regional percutaneous coronary intervention (PCI) centre for further investigations and treatment.

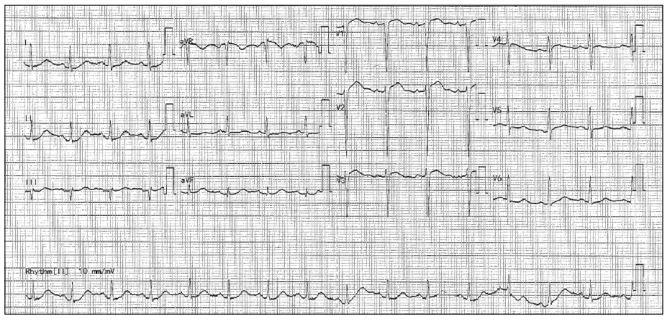

Figure 2 – 12 hour ECG showing ST elevation leads V1-V3

On arrival at the PCI centre he underwent immediate diagnostic coronary angiogram, this demonstrated normal coronary blood flow in all 3 major epicardial coronary arteries but a filling defect in the mid left anterior descending (Figure 3).

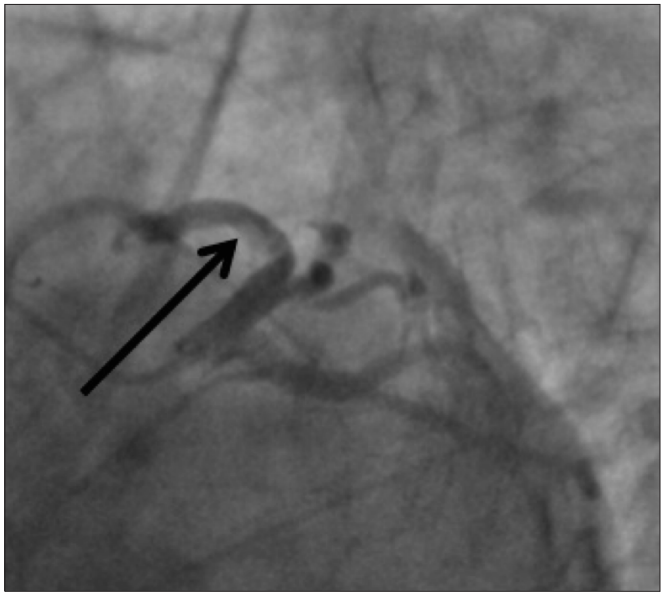

Figure 3 – LAO caudal view of coronary arteries with thrombus in mid left anterior descending artery (arrow)

COCAINE-ASSOCIATED MYOCARDIAL INFARCTION

S Rayner, SJ Leslie

Coronary intravascular ultrasound revealed mild atherosclerotic disease in the mid LAD with associated thrombus, but no obvious dissection or plaque rupture. Therefore he did not have a coronary stent but was treated medically overnight with an intravenous antiplatelet GPIIb/IIIa inhibitor (tirofiban).

An echocardiogram the following day demonstrated normal valve function but moderate left ventricular (LV) impairment. He subsequently underwent exercise tolerance testing following BRUCE protocol with no ECG changes or chest pain (test stopped due to leg pain).

He was discharged after 4 days and has remained well 9 weeks since discharge. His discharge medication included ticagrelor 90mg twice daily and rivaroxiban 20mg once daily as long term antiplatelet and anticoagulation for myocardial infarction and deep vein thrombosis. He was also started on lisinopril 5mg, bisoprolol 2.5mg to treat the LV dysfunction and atorvastatin 80mg due to the presence of mild coronary disease and STEMI presentation.

Discussion

Cocaine comes from the leaves of the Erythroxylum coca plant from the Andes Mountain region of South America (1) and in 1880 it was found to have local anaesthetic properties (2), which continue to hold a small role in modern day ENT practice (3).

Coca has a long history of recreational use amongst the Amara Indians of Peru who chewed the leaves thus rarely suffering toxic effects (4). Due to increased ease of cocaine synthesis, and the potentially desirable effects of ingestion (1), misuse is now commonplace in the Western world (5), leading to a concurrent increase in complications. Cocaine use was associated with 2247 hospital discharges in the UK in 2010/11(6) and 25% of non-fatal myocardial infarctions (MIs) in patients aged 18-45 years old (7).

The primary mechanism of action of cocaine is to block monoamine neurotransmitter presynaptic reuptake, leading to increased noradrenaline (8). There are three proposed mechanisms of myocardial ischaemia; increased myocardial oxygen demand, vasoconstriction or spasm and coronary artery thrombosis (9).

Increased myocardial oxygen demand is caused by increased adrenergic activity in the heart leading to tachycardia and increased mean arterial pressure (10). This in turn increases myocardial oxygen requirement and reduces coronary artery blood flow thus putting the heart at risk of ischaemia and infarct (11) - this is most likely to be a causal mechanism in patients with pre-existing coronary artery disease.

Alpha-adrenergic stimulation also contributes to the second proposed mechanism of vasoconstriction and spasm (11), by leading to both coronary artery vasoconstriction (11) and small vessel spasm (12).

The third proposed mechanism is promoting thrombus formation, which is relevant in our case as thrombus in the proximal LAD was found. According to Virchow's triad of thrombosis, thrombosis is caused by stasis of blood flow, endothelial injury and hypercoaguability.

There is debate as to whether thrombosis occurs in cocaine use secondary to adrenergic effect causing spasm and disruption to blood flow or cocaine acting as a prothrombotic (13). A systematic review concluded it likely that cocaine has a prothrombotic effect, potentially due to increasing platelet aggregation and clotting factors (14).

The most common cardiovascular presentation secondary to cocaine use is myocardial ischaemia causing chest pain, with only 6-14% of cocaine-related chest pain actually resulting in MI (9, 15).

Management

Diagnosis

The diagnosis of cocaine-associated MI is the same as diagnosis of non cocaine-associated ACS, based upon ECG changes and serial serum markers (usually troponin) (9, 16). However as cocaine involvement can alter management, a comprehensive history is essential and toxicology assays of blood or urine may be appropriate (9, 16) if exposure needs confirmation.

Immediate management

The variety of proposed mechanisms of cocaine-associated myocardial ischaemia (13) poses a management challenge.

The AHA scientific statement states that 'patients with cocaine-associated chest pain, unstable angina or MI should be treated similarly to those with non cocaine-associated ACS, or possible ACS, with notable exceptions' (16), the notable exceptions referring to use of benzodiazepines and avoidance of use of B blockers acutely.

COCAINE-ASSOCIATED MYOCARDIAL INFARCTION

S Rayner, SJ Leslie

Antiplatelet and anti-thrombin agents have been poorly studied in cocaine-associated chest pain but given the proposed prothrombotic behaviour of cocaine there is theoretical benefit (16), thus antiplatelet use as per ACS management remain appropriate. In our case, an intravenous GPIIb/IIIa inhibitor (tirofiban) was used after coronary thrombus was identified.

As cocaine is prothrombotic, it poses the question as to whether thrombolysis should be considered in these patients if PCI is not imminently available (within 120 minutes (17). Unlike STEMIs caused by atherosclerotic disease, cocaine-associated MI have a range of potential mechanisms which may or may not involve thrombus formation leading to infarction. However, if evidence of myocardial ischaemia is present, and no contraindications, evidence shows that it appears to be safe to use in cocaine-associated MI although it is unclear if thrombolysis is an 'important therapeutic intervention' (18).

There is case study evidence demonstrating complications of thrombolysis in cocaine chest pain in the absence of myocardial ischaemia (19) therefore it is important that adequate evidence of ischaemia is present and to consider the risks for each patient and that standard definitions for STEMI are adhered to (i.e. clear ST elevation, posterior changes or new left bundle branch block).

In addition to usual ACS treatment, cocaine users should be provided with IV benzodiazepines as part of initial management (16). They are used to sedate patients as well as help to reduce blood pressure (20). For summary of acute management see Figure 4.

	Non-cocaine associated MI Management	Cocaine associated MI Management
Aspirin	Yes	Yes
Benzodiazepines	Not indicated	Yes
Second antiplatelet e.g. Clopidogrel	Yes	Yes
GTN	Yes	Yes
Beta-blockers	Yes	Avoid acutely
Thrombolysis - if no PCI available and meet criteria	Yes	Yes

Figure 4 – Summary of medical management in non-cocaine associated versus cocaine associated myocardial infarction (16).

Subsequent management

It is suggested that beta-blockers should not be used acutely in cocaine-associated MI, which differs to management of non cocaine-associated MI. This is due to concern about worsening exacerbating coronary artery vasospasm (16).

Beta-blockers in non cocaine-associated MI reduce mortality but as mortality associated to cocaine-associated MI is so low, the risk of initial beta-blocker use outweighs the benefit (16). However if there is evidence of LV dysfunction or dysrhythmia they can be initiated on discharge as occurred in our case.

After the initial observation period some form of stress testing may be appropriate, although where this was used in patients as an initial screen strategy in those without clear STEMI only 4% were shown to have positive results requiring angiography (16). Echocardiogram can be useful to demonstrate long term damage from ischaemia however in longer term cocaine users, LV hypertrophy may be present which can 'mask regional wall motion abnormalities' (16).

On discharge, it is appropriate to continue dual antiplatelet therapy, a statin if atherosclerosis is present and an ACE inhibitor as well as considering starting a beta-blocker if ventricular dysfunction is present (16). A summary of overall management including acute and discharge is included in Figure 5.

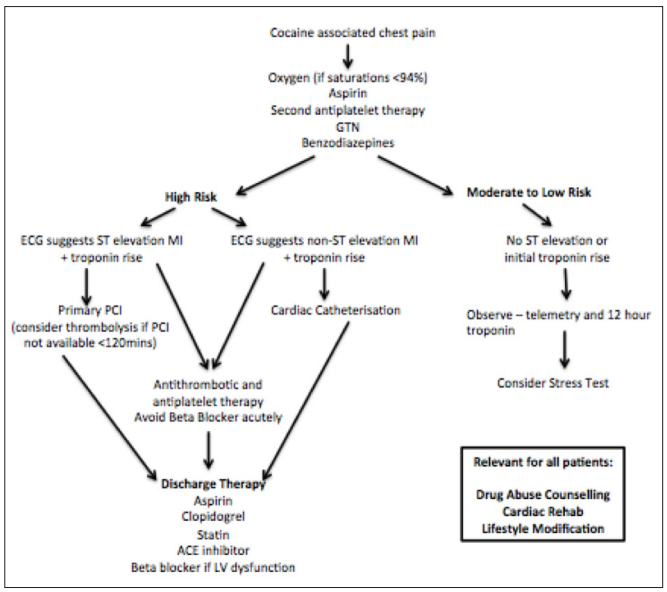

Figure 5 – Adapted from figure 'Therapeutic and diagnostic recommendations in cocaine-associated chest pain.' McCord J, Hani J, Hollander J. Management of Cocaine Associated Chest Pain and Myocardial Infarction. A scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Circulation 2008; 117: 1897-1907

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Other considerations

It is important to involve drug misuse support (16) when the patient is an inpatient and also on discharge to try to avoid the risk of future events. Formal referral to cardiac rehabilitation should be considered and addressing other risk factors such as smoking, obesity, and avoid sedentary behaviour in the usual manner.

Advice should be sought on legal issues regarding drug misuse although doctors have a pragmatic duty of confidentiality whilst being cognisant of wider issues such as driving and a duty of care to any dependents. Driving advice in the UK can be found on line on the DVLA website (21).

If the patient has children or other dependants it may be appropriate to involve social services. There will be local mechanisms for raising this issue with the appropriate services and if you have any doubt your defence union will be able to provide further guidance.

Conclusion

With increasing cocaine use in the UK, it is becoming increasingly important to recognise cocaine use in a cardiac history. Often people erroneously assume that because the patient if young that they cannot be suffering a MI. Particularly in the context of positive drug history or family history, having a low index of suspicion and performing repeat ECG and cardiac monitoring can help identify the patients in which MI is present and detect it early.

This case highlights the development of the clinical picture over time and therefore the importance of continued monitoring in on-going chest pain with risk factors. ACS treatment should be initiated early and use of benzodiazepines should be considered.

5 MCQs (Best of 5)

What medication should be used on admission in cocaine associated chest pain in addition to standard MI care?

- *Naloxone*
- *Diazepam*
- *Flumazenil*
- *Propranolol*
- *Ethanol*

What discharge medication is the most appropriate in a patient with cocaine associated ST elevation MI and preserved LV function?

- *Dual antiplatelet therapy*
- *Dual antiplatelet therapy, high dose statin, beta-blocker, ACE inhibitor*
- *Dual antiplatelet therapy, high dose statin*
- *Dual antiplatelet therapy, high dose statin, ACE inhibitor*
- *Dual antiplatelet therapy, high dose statin, beta-blocker*

What discharge medication is the most appropriate in a patient with a cocaine associated ST elevation MI and impaired LV function?

- *Dual antiplatelet therapy*
- *Dual antiplatelet therapy, high dose statin, beta-blocker, ACE inhibitor*
- *Dual antiplatelet therapy, high dose statin*
- *Dual antiplatelet therapy, high dose statin, ACE inhibitor*
- *Dual antiplatelet therapy, high dose statin, beta-blocker*

Which of the following is most true?

- *There are 2 proposed mechanisms of cocaine inducing cardiac ischaemia*
- *Cocaine associated MI are always due to thrombosis*
- *Cocaine associated MI are more likely to involve coronary spasm that non cocaine associated MI*
- *Cocaine associated chest pain usually has underlying ischaemia*
- *Cocaine associated MI only occur in chronic cocaine users*

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Which of the following is most true?

- *GTN is a good initial treatment for cocaine associated MI with ST elevation*
- *Cocaine associated MI does not need PCI*
- *Cocaine associated MI does not need thrombolysis*
- *In cocaine associated MI, thrombolysis should be considered in the absence of ST elevation*
- *In cocaine associated MI thrombolysis should always be given if ST elevation present and PCI cannot be done in less than 2 hours.*

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CARDIAC INVOLVEMENT IN ANDERSON-FABRY DISEASE IN A FEMALE PATIENT

EJ Kealaher, AH Bharucha, ZR Yousef

Abstract

Anderson-Fabry Disease is a rare X-linked disorder characterised by a deficiency in ∂-galactisodase A and resultant lysosomal accumulation of glycosphingolipids. It is a rare but important cause of cardiomyopathy and should be considered in patients with left ventricular hypertrophy (LVH) without an identifiable cause, as early diagnosis and treatment may alter prognosis.

There are significant gender differences in the natural history of Anderson Fabry Disease with later manifestations, lone cardiac involvement and myocardial fibrosis in the absence of LVH observed in female patients. These differences have important implications on investigation and management.

This clinical vignette seeks to illustrate some of the cardiac complications seen in female Anderson-Fabry Disease patients.

Case History

A 64 year old lady with known Anderson-Fabry disease (AFD) was admitted for assessment following an unwitnessed episode of cardiac syncope whilst at home. Physical examination was unremarkable and there were no features of cardio-respiratory compromise.

The patient was well known to cardiac services, having been identified as an AFD gene carrier during screening after her brother was diagnosed with AFD. Prior to formal diagnosis, she was already displaying clinical manifestations of the disease, namely features of gastrointestinal dysmotility, acroparasthesia and bilateral conductive hearing loss as a result of otosclerosis.

Previous investigations included an electrocardiogram (ECG), echocardiogram, coronary angiography and cardiac MRI. Her echocardiogram revealed features consistent with cardiac involvement particularly septal hypertrophy (Septal thickness 1.4cm), reduced tissue velocities in the basal septum and lateral walls and diastolic dysfunction (Figure 1).

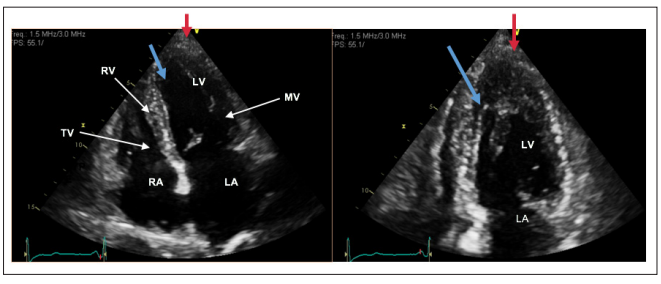

Figure I: Apical four chamber (left) and apical two chamber (right) echo views demonstrating septal (blue arrows)and apical hypertrophy (red arrows). Concentric Left Ventricular hypertrophy is a key feature in AFD. A subset of patients have an asymmetrical variant with septal thickening (as above) and posterior wall fibrotic thinning. (1,2)

Abbreviations: LA: Left Atrium, LV: Left Ventricle, RA: Right Atrium, RV: Right Ventricle, MV: Mitral Valve, TV: Tricuspid Valve

Previous coronary angiography, undertaken in the context of Non-ST Elevation Myocardial infarction (NSTEMI), had revealed unobstructed coronary arteries. The patient was already maintained on AFD Enzyme Replacement therapy (Replagal) on the basis of confirmed multi-organ involvement with AFD. Her only other medical background consisted of Chronic Obstructive Pulmonary Disease (COPD) and she was still smoking at the time of review. Her two sons were also confirmed to have AFD.

Her admission Electrocardiogram (ECG) revealed a short PR interval, global T wave inversion and QRS Voltages consistent with left ventricular hypertrophy (figure 2). A chest radiograph revealed changes consistent with COPD only. Blood biochemistry abnormalities included a Creatinine kinase of 318 and Troponin I of 0.3µg/L (Normal<0.03µg/L) which rose to 0.34µg/L at 8 hours (12hours from time of collapse). CT Head scan was normal.

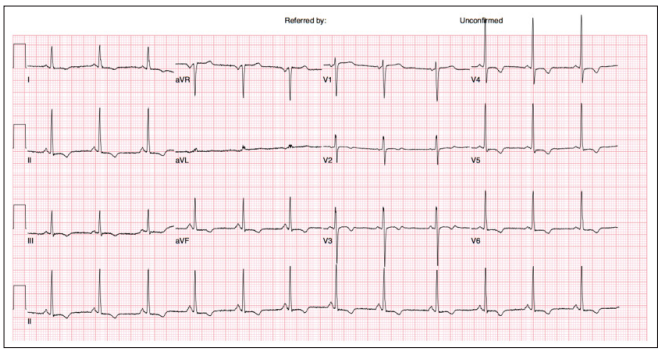

Figure II: Admission ECG

Demonstrating shortening of PR interval, diffuse T wave inversion and Voltage Criteria consistent with LVH. These features are consistent with the typical ECG changes encountered in AFD (1,11)

Whilst on the coronary care unit (CCU) she was noted to have multiple episodes of symptomatic non-sustained Ventricular Tachycardia and was therefore commenced on Amiodarone and Nebivolol. Subsequent coronary angiography revealed only mild three vessel disease. Cardiac MRI (figure 3) revealed mild concentric hypertrophy (12-13mm) and several defined areas of speckled delayed enhancement of myocardium, particularly inferolaterally and anteroseptally.

CARDIAC INVOLVEMENT IN ANDERSON-FABRY DISEASE IN A FEMALE PATIENT

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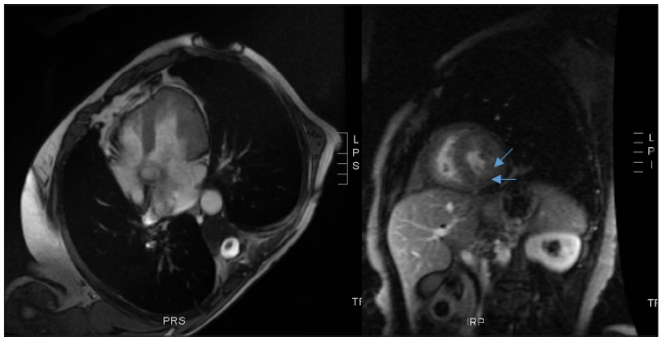

Figure III: Cardiac MRI revealed concentric LVH with septal thickening. There was delayed enhancement (arrowed) with speckling in the inferolateral and anteroseptal regions.

In view of the fact that this patient had symptomatic Ventricular Tachycardia and definitive areas of scar on Cardiac MRI, she underwent secondary prevention Implantable cardioverter defibrillator (ICD) implantation (Medtronic single chamber ICD with active fixation single coil right ventricular lead) and was discharged to long term outpatient follow up in which she has remained stable with no further arrhythmias.

Discussion

Anderson-Fabry Disease is an X-linked multi-system lysozymal storage disorder characterised by absent (males) or attenuated (females) production of ∂- galactisodase A (∂-GAL A). ∂-GAL A is responsible for the lysosomal breakdown of glycosphingolipids and its deficiency results in systemic lysosomal accumulation of globotriaosylceramide (1,2).

Lysosomal accumulation of globotriaosylceramide results in cell dysfunction triggering inflammation and fibrosis which manifests as progressive organ dysfunction (3). Among others, commonly affected organ systems include the heart, kidneys, skin and the nervous system producing a myriad of clinical manifestations.

Given the X-linked nature of the disease, women were initially considered only to be asymptomatic (phenotype negative) 'gene carriers', however, it is now recognised that heterozygous women, can develop clinical manifestations.

Furthermore, the natural history of the disease follows a different course in females. Indeed, as demonstrated in our patient, women are likely to develop relatively late organ dysfunction, typically in their thirties (approximately 10 years later than their male counterparts) and are also more likely to develop organ specific disease(1-4).

The diagnosis and management of AFD in female patients poses significant challenges. Enzyme activity is often low-normal in women owing to the X-linked nature of the disease, thus quantification of plasma ∂-galactisodase A activity, which is usually a first line test, can be equivocal. Many centres therefore advocate first line gene testing in females strongly suspected of having AFD (3,4).

Enzyme replacement therapy (ERT) has been shown to improve organ function and reduce morbidity in some studies, however the overall evidence base for ERT remains limited (5,6). Major treatment trials assessing ERT have predominantly focused on men and therefore application of treatment recommendations cannot be directly extrapolated to female patients. Treatment initiation and escalation depend on disease progression which displays gender variance thereby introducing significant uncertainty in management (2,6)

Cardiac involvement in AFD produces a plethora of manifestations with significant gender variance. Female AFD patients often have later manifestation of Left Ventricular Hypertrophy (LVH) usually presenting between the ages of 30-40 years, as seen in this case. In women with AFD, myocardial scarring may be present even in the absence of LVH thus cardiac MRI bears particular importance in female patients suspected of AFD. Finally, females are more likely to develop an isolated cardiac variant of AFD (1,2,6,7) The cardiac complications pertinent to our case are those of rhythm disturbance, ischaemia and diastolic heart failure.

Our patient has in fact had multiple attendances with NSTEMI in the context of mild coronary artery disease. AFD patients with cardiac involvement are prone to ischaemia emanating from increased myocardial oxygen demand resulting from LVH and microvascular disease (common in AFD patients) [1,4,7]. These patients have little scope for percutaneous coronary intervention and require optimal medical management with anti-platelets, anti-anginals and lifestyle modification. As such, our patient is maintained on lifelong aspirin and nebivolol as an anti-anginal agent.

Rhythm disturbance is a prominent feature of cardiac involvement in AFD. Indeed, arrhythmias occur in up to 47% of men and 27% of women (1) with cardiac involvement. Fibrotic scar produces a substrate for ventricular tachycardia (VT) in those with cardiac involvement and predisposes to sudden cardiac death. As in our patient, those with symptomatic VT and syncope or haemodynamic compromise have a class IA indication for secondary prevention ICD implantation (8-10)

The management of diastolic heart failure has a limited evidence base (9,10). A holistic approach is recommended, comprising of pharmacological and non-pharmacological interventions. Current European Society of Cardiology guidance suggests a limited role for diuretics, ACE inhibitors and beta blockers in diastolic heart failure. Non-pharmacological aspects of management include smoking cessation, cardiac rehabilitation programmes and strict control of primary cardiac risk factors such as hypertension and diabetes.

To summarise, Anderson-Fabry Disease is a rare but important cause of heart failure and should always be considered in those with LVH without another identifiable cause. Cardiac involvement in AFD produces a plethora of complications, three of which have been described in our patient. It is important to be aware of significant gender differences in the natural history of AFD as they have profound implications on diagnosis, management and prognosis.

CARDIAC INVOLVEMENT IN ANDERSON-FABRY DISEASE IN A FEMALE PATIENT

EJ Kealaher, AH Bharucha, ZR Yousef

Questions - Theme: Heart Failure

1. Which of the following commonly used agents for heart failure with reduced ejection fraction offer both prognostic and symptomatic benefit?

A. Digoxin

B. Furosemide

C. Hydralazine

D. Lisinopril

E. Metolazone

As the Foundation Doctor on call you are asked to review a 47 year old gentleman on the coronary care unit with increasing dyspnoea. He was admitted two days prior with decompensated heart failure on a background of severe ischaemic cardiomyopathy (estimated ejection fraction 15-20%).

On examination he appeared sweaty, clammy and breathless at rest. His blood pressure was recorded at 73/56mmHg, respiratory rate 25 breaths per minute and oxygen saturations 96% on 10 litres/min of oxygen. On examination coarse crepitations are audible to the mid-zones bilaterally with a Jugular venous pressure visible at the ear lobes.

2. Which of the following best describes the rhythm disturbance shown above?

A. Coarse Atrial Fibrillation

B. Monomorphic Ventricular Tachycardia

C. Polymorphic Ventricular Tachycardia

D. Wolf Parkinson White Syndrome Type A

E. Supraventricular Tachycardia (SVT) with aberrancy

3. Select the most appropriate treatment option:

A. Synchronised Direct Current Cardioversion

B. Intravenous Magnesium

C. Intravenous Lidocaine

D. Intravenous Amiodarone

E. Intravenous Metoprolol

4. Select the most effective intervention for prevention of sudden cardiac death in this patient:

A. Oral Amiodarone

B. Bisoprolol

C. Implantable Cardioverter Defibrillator

D. Biventricular Pacemaker

E. Left Ventricular assist device

5. Which of the following is the most common rhythm disturbance encountered in Heart Failure?

A) Monomorphic Ventricular Tachycardia

B) Torsades de Pointes

C) Complete Heart Block

D) Atrial Fibrillation

E) None of the above

Answers to Review Questions

1) D

Angiotensin Converting Enzyme inhibitors (ACEis) have been shown to reduce morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF) and are recommended to all patients in the absence of contraindications. The dose of ACEi should be up titrated to the maximum tolerable dose (9, 10). The other listed treatments provide no prognostic benefit to patients with HFrEF.

CARDIAC INVOLVEMENT IN ANDERSON-FABRY DISEASE IN A FEMALE PATIENT

EJ Kealaher, AH Bharucha, ZR Yousef

2) B

At a basic level, a regular broad complex tachycardia (QRS duration>120ms, usually >140ms) with ventricular complexes of uniform appearance and a rate of 120-250 beats per min would be consistent with monomorphic Ventricular Tachycardia (13)

3) A

The treatment of choice for any tachyarrhythmia associated with adverse features (shock, syncope, myocardial ischaemia or heart failure) is synchronised direct current cardioversion as per the Resuscitation council (UK) guidelines on peri-arrest arrhythmias(12)

4) C

A secondary prevention implantable Cardioverter defibrillator (ICD) is a class IA recommendation in patients who have recovered from ventricular arrhythmia causing haemodynamic instability and who are expected to survive >1 year with a good functional status. Anti-arrhythmic agents reduce the incidence of tachyarrhythmias and sudden death but do not reduce overall mortality and may in fact increase it (9, 10)

5) D

Atrial Fibrillation is the most commonly encountered arrhythmia in heart failure independent of left ventricular function (9)

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CARDIAC AMYLOID

J Langtree, RFG Simpson, ARJ Mitchell

Abstract

Amyloidosis is a rare and poorly understood disease which is often diagnosed late, it is caused by extracellular deposition of amyloid between one or more of the body's tissues or organs. AL amyloidosis is the most common type of systemic amyloidosis involving the heart, with an estimated annual incidence in the UK of 6 to 10 cases per million.

Clinical presentation is poorly specific and the most common symptom is shortness of breath, myocardial involvement leads to a progressive restrictive cardiomyopathy and subsequent heart failure. Definitive diagnosis relies on identifying Congo red-positive amyloid deposits within the involved site. Treatment requires a two-fold approach, management of cardiac symptoms and complications, and chemotherapy to suppress the underlying disease. We present a case of AL cardiac amyloid secondary to lambda light chain myeloma, and medical review of the condition.

Abbreviations

AL amyloid: Amyloidosis made from light chains, ATTR amyloid: Transthyretin-related amyloidosis, BNP: Brain natriuretic peptide, CMR: Cardiac magnetic resonance, Echo: Echocardiogram, ECG: Electrocardiogram, ICD: Implantable cardiac defibrillator, ILR: Implantable loop recorder, NT-proBNP: N-terminal pro b-type natriuretic peptide, SAP scan: Serum amyloid P component scan, SCD: Sudden cardiac death

Introduction

Amyloidosis is a rare group of conditions caused by extracellular deposition of amyloid between one or more of the body's tissues or organs. Cardiac amyloid results from deposition of amyloid within the myocardium. We felt amyloidosis was a rare and poorly understood disease which is repeatedly missed or diagnosed late, it is often not taught well at medical school and may not be encountered in a doctors formative years. We present a case of AL cardiac amyloid secondary to lambda light chain myeloma, and provide key clinical features, investigation findings, management and prognosis.

Case Report

A previously fit and active 41-year-old male was referred to the Emergency Department by his General Practitioner with a two month history of progressive shortness of breath on exertion. There were no other cardiorespiratory symptoms to note and systemically he was well. On physical examination he appeared well, his blood pressure 133/73, heart rate 83 beats/min, a loud second heart sound was heard over the left sternal edge, no murmurs and clear lung fields.

Jugular venous pressure was not elevated, and there was no hepatomegaly or peripheral oedema. Electrocardiogram (ECG) revealed sinus rhythm with first degree atrioventricular block, right bundle branch block, right axis deviation, T wave inversion in leads V3-6, III, and Q wave in lead I, Fig 1. Chest radiography was clear with no evidence of cardiomegaly. Routine blood tests including troponin were within normal limits however NT-proBNP was elevated at 2450pg/ml. No acute cause for his shortness of breath was identified and he was discharged home and referred for outpatient cardiology assessment.

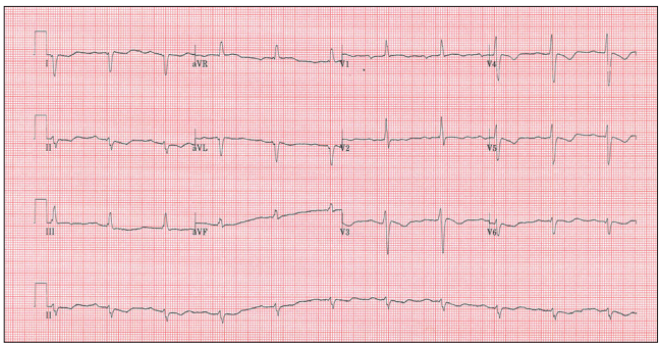


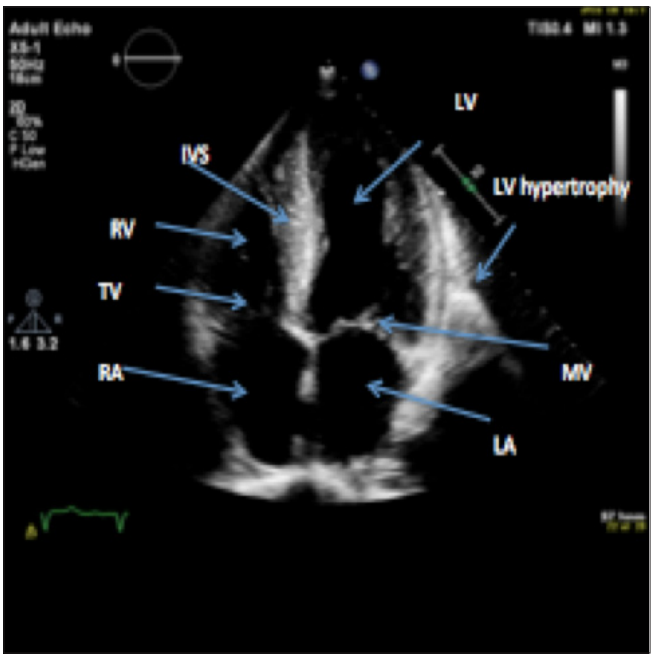
Figure 1: The patients ECG on admission. This shows sinus rhythm, with first degree atrioventricular block, a right bundle branch block, right axis deviation, T wave inversion in leads V3 to V6, lead III and a Q wave in lead I.

Prior to cardiology review the patient represented to the Emergency Department with pleuritic chest pain. CT Pulmonary Angiogram ruled out pulmonary embolism and aortic dissection, there was signs of early fluid overload and multiple osteolytic lesions in the right clavicle, left 2nd and 8th ribs and T2, T11 vertebral bodies. The diagnosis of possible myeloma was raised.

The outpatient review by a cardiologist included an echocardiogram (Echo) showing moderate left ventricular hypertrophy particularly affecting the septal wall with a granular sparkling myocardium, Fig 2. There was mild biventricular failure and evidence of focal wall motion abnormalities.

CARDIAC AMYLOID

J Langtree, RFG Simpson, ARJ Mitchell



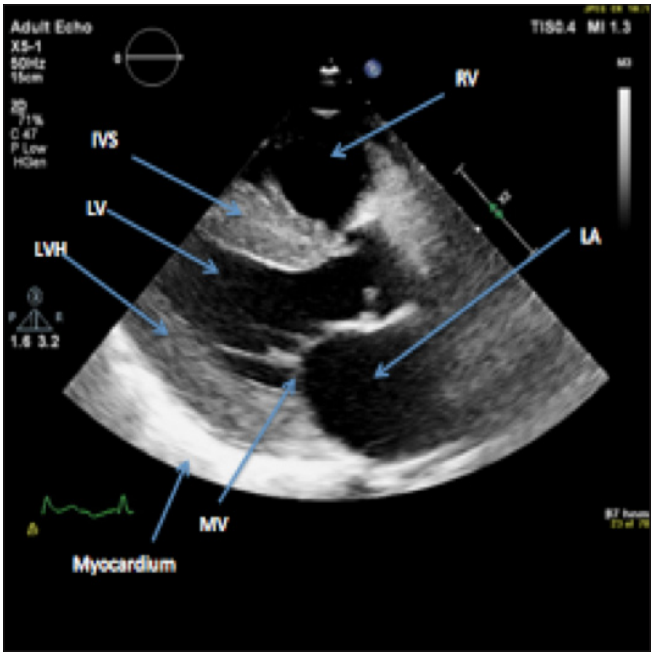


Figure 2: Echo images of the patient's heart. The image on the left is an apical 4-chamber view and a parasternal long axis view on the right. Note the thickened septum and concentric left ventricular hypertrophy. The myocardium has a characteristic granular sparkling appearance. LV= Left ventricle, IVS= interventricualr septum, RV= Right ventricle, TV= Tricuspid valve, RA=Right atrium, LA=Left atrium, MV= Mitral valve.

Urine analysis was positive for Bence Jones with free lambda light chains seen by immunofixation. There was a total urine protein of only 0.34g/l ruling out nephrotic syndrome. Serum free lambda light chain was raised at 539mg/l (range<26.3mg/l) with a skewed serum kappa:lambda ratio of 0.02 (range 0.26-1.65).

Bone marrow biopsy demonstrated apple green bifringence with Congo Red staining, suggestive of marrow-based amyloid deposition. Abdominal fat biopsy and serum amyloid P component scanning confirmed AL cardiac amyloid secondary to lambda light chain myeloma with no extra cardiac or visceral involvement.

A Bortezomib-Linalidomide-Dexamethasone based chemotherapy regimen was started with regular titration of furosemide against clinical symptoms of heart failure. There was a good response to therapy with a reduction in serum free light chains.

One month into chemotherapy (three months post initial presentation) the patient complained of further worsening of breathlessness on exertion. ECG revealed atrial flutter, 24 hour ambulatory ECG showed an average ventricular response of 77beats/min with no significant bradycardia, pauses or ventricular arrhythmias. He was treated with Apixaban, Spironolactone and Furosemide was switched to Bumetanide.

Shortly after he had an episode of syncope requiring admission to hospital, overnight monitoring revealed no arrhythmias and a Implantable Loop Recorder (ILR) was inserted. Two days following ILR insertion he had a further episode of syncope and interrogation of the device revealed a monomorphic ventricular tachycardia at a rate of 300bpm. The patient was admitted to hospital and loaded on amiodarone, unfortunately he suffered an episode of ventricular fibrillation and subsequent cardiac arrest requiring emergency cardioversion, Fig 3. The following day a dual chamber Implantable Cardiac Defibrillator (ICD) was inserted.

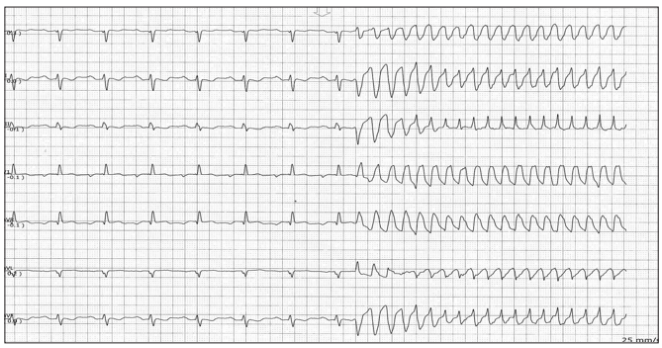


Figure 3: ECG showing onset of ventricular fibrillation leading to cardiac arrest.

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The patient is currently nine months post initial presentation and he is responding well to chemotherapy. Since insertion of his ICD he has had two episodes of ventricular tachycardia which have both self terminated. Cardiac biomarkers continue to improve and cardiac function is stable.

What is Amyloidosis?

Amyloid is made from the breakdown of normal and abnormal proteins that are then folded into insoluble Ð-pleated sheets, known as amyloid fibrils. More than 30 proteins have been shown to form amyloid fibrils. Amyloidosis is the disease that develops from the extracellular deposition of amyloid between one or more of the body's tissues or organs impeding the way they work.

Five different types of amyloidosis have been described; AL, familial, senile systemic, secondary and haemodialysis associated amyloidosis. The five types all have a different underlying aetiology and are derived from different precursor proteins. Diagnosing and identifying the specific type and cause of amyloid is extremely important as each disease affects different organs, and has varying treatments and prognosis.

Cardiac amyloid results from the deposition of amyloid within the heart. Amyloid deposits can be massive and replace substantial amounts of cardiac tissue leading to stiffening of the heart muscle and a characteristic restrictive cardiomyopathy.

AL Amyloidosis

AL amyloidosis is the most common type affecting the heart. AL stands for Amyloidosis made from Light chains, where the building blocks of the amyloid fibril are made from immunoglobulin light chain protein. AL amyloidosis is an acquired disease of the bone marrow.

It is the result of a plasma cell dyscrasia where approximately 5-10% of bone marrow plasma cells do not function properly (1), leading to overproduction of light chains. Light chains are able to circulate in the blood and deposit as amyloid in various body tissues including the heart. The most common forms of plasma cell dyscrasia leading to AL amyloidosis are multiple myeloma, B cell lymphoma and Waldenstroms macroglobulinemia (2).

AL amyloidosis accounts for 85% of all newly diagnosed cases of amyloid, generally the number of plasma cells, the degree of clonality and extent of marrow infiltration is proportionate to survival (3). It may advance quickly therefore early diagnosis and treatment is crucial. Patients with cardiac involvement at initial presentation carry the worst prognosis.

Epidemiology

AL amyloidosis has an annual incidence of 6 to 10 cases per million population in the UK, half of whom will have significant cardiac involvement (4). Two thirds of AL patients are men and average age at diagnosis is 65 years (5).

Clinical Features

Amyloid proteins can deposit themselves in all organs apart from the central nervous system and the clinical presentation will depend on the affected organ system and the type of amyloid protein. Approximately 90% of patients with AL amyloidosis have cardiac involvement and 50% of those have evidence of diastolic heart failure at presentation (6).

Affected myocardium is firm, rubbery and non compliant which leads to a restrictive cardiomyopathy, characterised by progressive diastolic failure and subsequent biventricular dysfunction. Affected individuals commonly present with non-specific symptoms of lethargy and decreased exercise tolerance, they may have signs of right-sided heart failure including an elevated JVP, peripheral oedema and ascites. Conduction disorders are seen due to infiltration of the sinoatrial and atrioventricular nodes, and the bundle branches.

Syncope and sudden cardiac death is usually due to electromechanical dissociation or bradycardia rather than ventricular arrhythmia. Rarely angina occurs due to amyloid deposition within the myocardial microvasculature. Atrial thrombus is common even before the onset of atrial fibrillation and may first present as embolic disease. Less than 5% of patients with AL amyloidosis have isolated cardiac involvement (7) and possible signs of systemic disease include nephrotic syndrome, autonomic neuropathy, soft tissue infiltration and cachexia.

Investigations and Diagnosis

Cardiac amyloidosis is a rare disease and the diagnosis is often overlooked, made late or missed. It is important for the diagnosing physician to have a high index of suspicion in any patient presenting with a restrictive cardiomyopathy and signs of cardiac failure. Nevertheless there are some features seen in basic cardiac tests that can help to make the diagnosis.

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Electrocardiography

Characteristic ECG features include low QRS voltages (<5mm in height) in the limb leads and poor R wave progression in the chest leads, and is seen in up to 50% of patients (8). These findings coupled with increased wall thickness on echocardiogram should raise suspicion of cardiac amyloid, since left ventricular hypertrophy due to other causes shows high QRS voltages. Voltage criteria for left ventricular hypertrophy occasionally occurs, usually as a result of another coexisting unrelated condition for example hypertension.

Other common ECG findings include conduction abnormalities; first-degree atrioventricular block (21%), non-specific intraventricular conduction delay (16%), second- or third-degree atrioventricular block (3%), atrial fibrillation/flutter (20%) and ventricular tachycardia (5%) (9). Holter monitoring reveals subclinical arrhythmias in >75% of cardiac AL patients (10).

Echocardiography

Ultrasound abnormalities in advanced disease are distinctive and include non-dilated concentric bi-ventricular thickening, valvular infiltration, and bi-atrial enlargement. A septum thickness of >15mm in diastole is a sign of advanced disease and median survival is 6 months if left untreated (11).

The myocardial texture is often described as "granular sparkling". This appearance whilst inexact has a sensitivity of up to 87%, and specificity of 81%. In the context of increased atrial thickness the specificity can reach up to 100% (12). In early amyloid disease the first detectable abnormality is a gradual deterioration of diastolic dysfunction that worsens as cardiac infiltration progresses.

Diastolic dysfunction is often detectable prior to the onset of cardiac symptoms. Systolic function is maintained until late into the disease, and as the ventricles do not dilate stroke volume is significantly reduced. Transoesophageal echo has been shown to detect atrial thrombus in up to a third of AL amyloid patients and may help to guide decisions on anticoagulation (13).

Cardiac Biomarkers

Cardiac biomarkers; troponin T and I, brain natriuretic peptide (BNP) and its N-terminal fraction (NT-proBNP) are reliable prognostic markers in AL amyloidosis. An abnormally elevated NT-proBNP (cutoff >152pmol/L) carries a higher mortality rate of 72% vs. 7.6% per year (14). Raised troponin is also associated with increased mortality. Scoring systems based on combining the serum levels of NT-proBNP and troponin T are used to risk-stratify patients at diagnosis.

Cardiac Magnetic Resonance Imaging (CMR)

Like echo, CMR can provide functional and morphological evaluation of the heart but also has the advantage of myocardial tissue characterisation. Myocardial tissue in advance cardiac amyloid has an unusual pattern of global, subendocardial late gadolinium enhancement, however enhancement can be atypical and patchy in early disease and the sensitivity of detecting early disease is not yet known.

Radionuclide Imaging

Serum amyloid P component (SAP) is a protein found in small quantities in the bloodstream of everyone. SAP binds strongly to amyloid fibrils, and is always found in the amyloid deposits. SAP scanning is a nuclear imaging technique that allows visceral amyloid deposits in the liver, kidneys, spleen, adrenal glands and bones to be imaged in a specific and quantitative manner.

Until recently SAP scanning has not been able to adequately image moving or hollow organs such as the heart or gut, however various case reports have indicated that scanning using a diphosphonate bone seeking radionuclide tracer such as 99mTc-DPD may be useful in detecting cardiac amyloid.

Tissue biopsy

The gold standard for diagnosing cardiac amyloid is endomyocardial biopsy. The easiest tissue to biopsy is usually abdominal fat, when positive the sample will demonstrates apple-green birefringence when viewed under a polarising microscope. Abdominal fat biopsy is positive for amyloid deposits in >70% of patients with AL amyloidosis, if diagnosis is not confirmed, endomyocardial sampling is safe and almost 100% sensitive (15).

Treatment

Management of amyloid requires input from a specialised centre, in the UK this is the National Amyloidosis Centre based at the Royal Free hospital in London. Generally treatment requires a two-fold approach, management of cardiac-related symptoms and treatment to suppress the underlying disease.

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Supportive Treatment

Standard therapy for heart failure may be poorly tolerated in cardiac amyloid and can lead to harm. There is little evidence to support the use of ACE inhibitors or angiotensin receptor blockers, even small doses may lead to profound hypotension due to coexisting autonomic neuropathy. The restrictive physiology of cardiac amyloid means maintaining an adequate cardiac output is especially dependent on heart rate. Rate limiting medications such as beta-blockers, calcium channel blockers and digoxin should be used with extreme caution.

Digoxin is bound extracellularly by amyloid fibrils and is relatively contraindicated due to potential hypersensitivity and toxicity. Amiodarone should be used as first-line therapy in patients with arrhythmia. There is a higher incidence of atrial thrombi seen even in patients with normal sinus rhythm (16). Anticoagulation with warfarin or a novel oral anticoagulant is recommended in the presence of atrial fibrillation irrespective of CHA2DS2-VASc score.

Fluid retention can be profound and high dose diuretics remain the mainstay of therapy. Patients should be educated and encouraged to monitor their salt/water intake and weight, whilst being supported by a heart failure team. Large resistant pleural effusions usually indicate pleural involvement, and may necessitate regular pleurodesis.

Conduction abnormalities may require permanent pacemaker insertion and indications for device therapy remain within current standard guidelines. Implantable cardiac defibrillator therapy may not prevent sudden cardiac death (SCD) as it is usually due to bradyarrhythmia and electromechanical dissociation, rather than ventricular arrhythmia. Furthermore current guidelines do not advocate ICD insertion for primary prevention of SCD in patients with a life expectancy of <1 year (17).

Specific Treatment

Definitive treatment of AL amyloidosis focuses on suppressing the responsible plasma cell dyscrasia and stopping the production of amyloid forming light chains. The most common chemotherapeutic agents used are melphalan, lenalidomide and/or bortezomib, usually in combination with high-dose dexamethasone and depending on the degree of heart failure autologous stem cell transplant.

Unfortunately the advanced nature of cardiac disease at the time of diagnosis renders many patients unfit for high dose chemotherapy and an ejection fraction of <40% is considered to be a contraindication. Treatment with dexamethasone can result in significant fluid retention and it should be introduced at a relatively low dose.

The goal of therapy is to achieve an adequate haematological response, which is measured by the amount of free light chains within the blood. Haematological response may be seen before any definite improvement in clinical symptoms. Routine assessment of serum NT-proBNP and troponin is also recommended. Levels may fall before any significant improvement is seen on echocardiography, a fall in levels suggests a favorable outcome (18).

Prognosis

Prognosis in AL amyloidosis is poor, survival depends on haematological response to therapy and the extension and severity of organ involvement. Median survival is 13 months without treatment, which can be extended to 17 months with cyclical melphalan and prednisolone therapy (19). 10 year survival rate is only 5% (20).

Cardiac involvement is a major determinant of prognosis, and median survival is 6 months from the onset of congestive cardiac failure (21). Syncope, degree of left ventricular wall thickness, presence of right ventricular dilatation and elevated levels of troponin T and I at diagnosis are all prognostic indicators associated with significantly shorter median survival times (22).

Conclusion

Cardiac amyloidosis is a poorly understood condition by both junior and senior physicians, it is often diagnosed late which may have a detrimental affect on a patient's prognosis. Diagnosis can be challenging mainly due to a wide variety of presenting symptoms that are often insidious in onset. This case highlights some of the key investigation findings which may help raise suspicion of cardiac amyloid.

Early imaging of the heart to detect cardiac involvement is important as complications can occur, including heart failure with restrictive cardiomyopathy, conduction disturbance, and malignant arrhythmias. Management of heart failure is mainly supportive and traditional medical therapies are often detrimental. Device therapy for the prevention of arrhythmia and SCD may not always be beneficial. Chemotherapy is used to treat the underlying disease process but overall prognosis remains poor.

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MEDICATION-RELATED OSTEONECROSIS OF THE JAW MRONJ - A REVIEW AND CASE REPORT

O Ni Choileain, Y Shammaa, C Williams, J Downie

Abstract

Osteonecrosis of the jaws is an uncommon but potentially serious side effect of treatment with anti-resorptive or anti-angiogenic therapy. Bisphosphonate-related osteonecrosis (BRONJ) of the jaws has been a recognised condition since 2003. In 2014, the AAOMS recommended changing the term to medicationrelated osteonecrosis of the jaw (MRONJ) to incorporate the growing number of cases associated with other anti-resorptive and anti-angiogenic therapies[1]. The following is an update on the recent literature, and a case report detailing a patient on oral alendronic acid who developed Stage 3 MRONJ, extending to her left orbit. Due to her significant co-morbidities, treatment had to be radically altered to be entirely conservative.

Case Definition

Patients who have all of the following criteria can be considered to have MRONJ:

1. Current or previous treatment with anti-resorptive or anti-angiogenic drugs.

2. Exposed bone, or bone that can be probed through an intra-oral or extra-oral fistula in the maxillofacial region, for more than eight weeks.

3. No history of radiotherapy, or obvious metastatic disease to the jaws[1].

Associated Medications

Oral bisphosphonates are most commonly prescribed for the treatment and prevention [2] of osteoporosis, and also for the treatment of osteopaenia [3], Paget's disease of the bone [3] and osteogenesis imperfecta [4]. Intravenous bisphosphonates are primarily used for the treatment of bone disease associated with malignancy [6-11], multiple myeloma [11-13], and severe forms of osteogenesis imperfecta. IV bisphosphonates can also be used for the management of osteoporosis in either a once yearly (zolendronate) or three monthly (ibandronate) infusion.

RANK ligand inhibitor (denosumab) is an anti-resorptive agent used to reduce the risk of fractures in osteoporotic patients, and is also effective in reducing skeletal related events related to bony metastasis [1].

Newer novel anti-angiogenesis agents have also been linked to cases of MRONJ. These drugs are used as part of the management of gastrointestinal carcinomas, renal cell carcinomas, neuroendocrine tumours and other conditions [1].

Drug name	*Type*	*Primary indication*	*Route of administration*
Antiresorptive			
Alendronate	Bisphosphonate	Osteoporosis	Oral
Risendronate	Bisphosphonate	Osteoporosis	Oral
Ibandronate	Bisphosphonate	Osteoporosis	Oral + IV
Pamidronate	Bisphosphonate	Bone Metastases	IV
Zolendronate	Bisphosphonate	Bone Metastases Osteoporosis	IV
Denosumab	RANK Ligand Inhibitor	Bone Metastases Osteoporosis	Subcutaneous
Anti-angiogenesis			
Sunitinib	Tyrosine kinase inhibitor	Gastrointestinal stromal tumour, renal cell carcinoma, pancreatic neuroendocrine tumour	Oral
Sorafenib	Tyrosine kinase inhibitor	Hepatocellular carcinoma, renal cell carcinoma	Oral
Bevacizumab	Humanised monoclonal antibody	Non-squamous non-small cell lung carcinoma, metastatic renal cell carcinoma, metastatic colorectal carcinoma, glioblastoma	IV
Sirolimus	Mammalian target of rapamycin pathway	Organ rejection in renal transplant	Oral

Table 1: Drugs associated with MRONJ [1]

Pathophysiology

Though the condition has been described and reported for over ten years, much debate surrounds the actual pathophysiology of the condition. As MRONJ is a form of avascular necrosis, it is thought that the primary mechanism is the long-term over-suppression of bone resorption and remodelling [1]. However, the process is likely multi-factorial, also involving inhibition of angiogenesis, soft tissue toxicity or infection and inflammation [13-19].

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Risk Factors

The risk of developing MRONJ can be grouped according to therapeutic indications. The reported risk of developing MRONJ in cancer patients ranges from 0.7-6.7% [21,22]. The risk for patients with osteoporosis is 100 times less than cancer patients [23]. In general, the risk of developing MRONJ is higher for drugs administered parenterally in comparison to oral medications [1]. The duration of medication therapy is a significant risk factor, regardless of indication for therapy [1]. Dentoalveolar surgery, most commonly tooth extraction, has been reported as the precipitating event in up to 69% of cases and is considered a significant risk factor [24].

Drug Related Factors	Therapeutic indication	Risk patients with malignancy > patients osteoporosis/ostepenia
	Duration	
Local Factors	Dentoalveolar surgery	Extractions, implant placement, periapical surgery, periodontal surgery involving osseous injury
	Anatomical structures	Mandible: lingual tori, mylohyoid ridge. Maxilla: palatal tori. Denture use
Systemic Factors	Systemic conditions	Obesity, diabetes, renal dialysis, corticosteroid therapy, tobacco use
	Concomitant oral disease	Inflammatory dental disease e.g. periodontal disease, dental abscess.
	Demographics	Age, Sex (F>M)
Genetics	Genetic polymorphism	Single nucleotide polymorphism located within the gene associated with bone turnover, collagen formation or certain metabolic diseases.

Table 2: Risk Factors [1]

Presentation

The main presenting feature of MRONJ is necrotic, exposed bone in the oral and maxillofacial region but clinical features can include pain, swelling, erythema, purulent exudate, parasthesia and sinus tract formation. Severe cases can present with extra-oral fistulae, oro-antral communications and pathological fractures [1]. Bone samples can be sent for histopathological analysis to confirm diagnosis and rule out bony malignancy or metastasis.

Case Report

A 70 year old female patient was referred by her General Dental Practitioner to the OMFS department of Forth Valley Royal Hospital with exposed bone in the left maxilla and associated soft tissue infection. She had not undergone recent dental extractions, however did have a poorlyfitting upper acrylic partial denture. She had been prescribed oral alendronic acid for the management of osteoporosis for the six years previously. Her other medical diagnoses included multiple sclerosis, hypertension, osteoporosis with previous vertebral fractures and trigeminal neuralgia.

A CT scan showed an extensive lesion involving the left maxilla, extending posteriorly into the pterygopalatine fossa. Biopsies of both hard and soft tissue were carried out which ruled out malignancy, and confirmed the diagnosis of MRONJ.

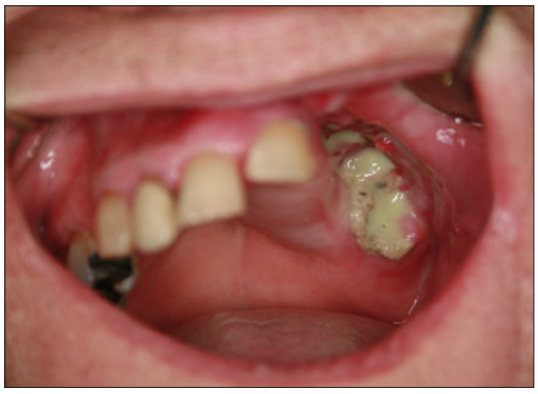

Fig 1. Exposed bone with soft tissue infection and purulent discharge evident.

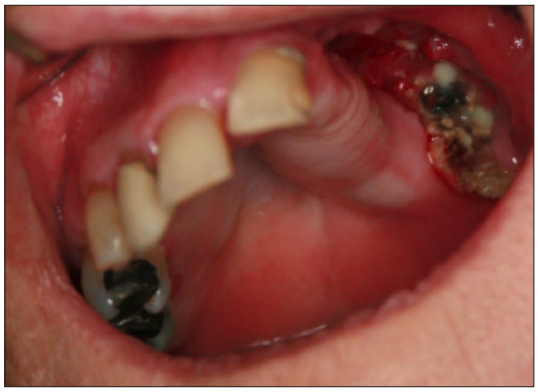

Fig 2. Bony defect after irrigation.

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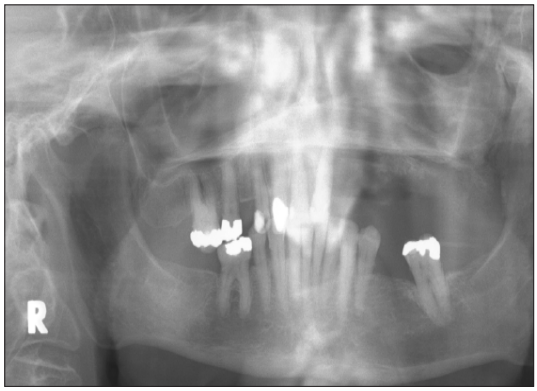

Fig 3. Dental panoramic radiograph showing loss of bony architecture in the left maxilla.

Initial management was to control the associated soft tissue infection with topical and oral anti-microbial agents, namely 0.2% chlorhexidine rinse, and her partial denture was relined. Mobile bony sequestrae were removed. She attended for regular visits and an emphasis was placed on maintaining excellent oral hygiene.

Maintaining a sufficient level of oral hygiene was a significant challenge due to the patient's poor mobility and dexterity and so, daily irrigation was originally performed by carers. Progressive debridement and removal of necrotic bone lead to the development of an oro-antral communication over the course of several months.

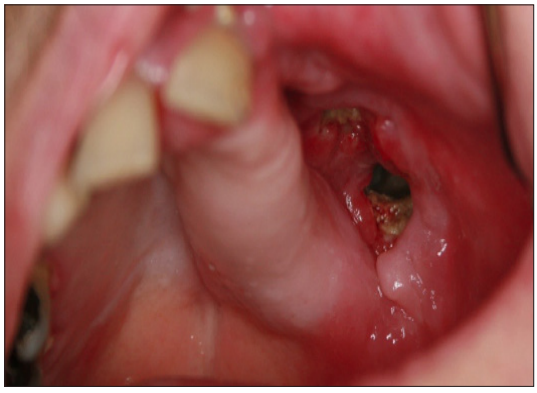

Fig 4. Development of oro-antral fistula left maxilla.

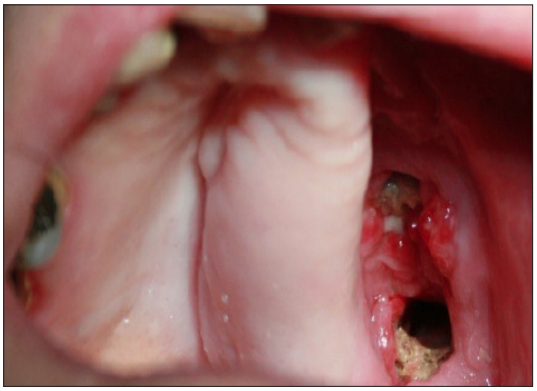

Fig 5. Development of oro-antral fistula left maxilla.

Fifteen months after original referral the patient developed an abscess associated with the upper right canine tooth. Her remaining upper front teeth, 321Ð1, were found to have severe mobility secondary to periodontal disease. The osteonecrosis had spread across the midline, and was now affecting the right maxilla.The remaining upper anterior teeth were extracted as per local protocol, using an atraumatic technique and with oral antibiotic (co-amoxiclav) prophylaxis

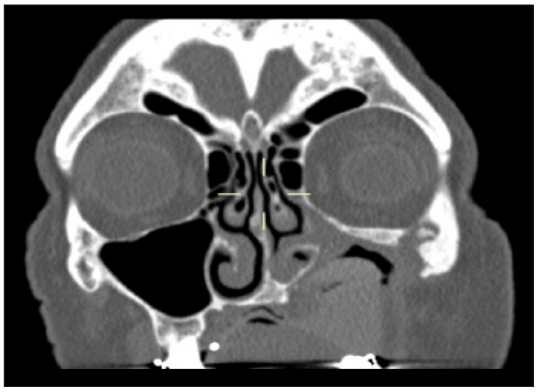

Fig 6. CT scan showing obliteration of the left maxilla, left maxillary sinus and extension left orbital floor.

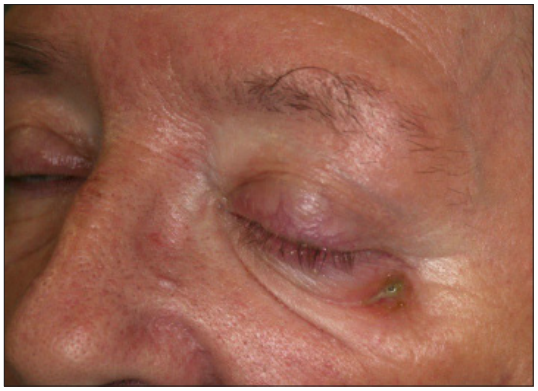

Fig 7. Extra-oral fistula draining below left eye.

MEDICATION-RELATED OSTEONECROSIS OF THE JAW MRONJ - A REVIEW AND CASE REPORT

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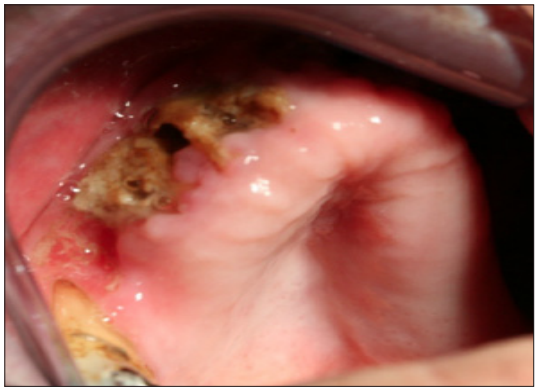

Fig 8. MRONJ affecting right maxilla post dental extractions.

Three months after the extractions, the patient presented with left maxillary and peri-orbital cellulitis . The osteonecrosis had significantly increased in severity, affecting the left maxilla, extending to the left orbital floor. There was a discharging sinus in the left infraorbital region. Due to the patients' significant co- morbidites, she was deemed to be a significant anaesthetic risk, and unsuitable for aggressive resection.
After admission as an in-patient for four weeks of antibiotic (co-amoxiclav) therapy, removal of exposed necrotic bone and twice-daily irrigation of the cavity in her maxilla, mucosalizaiton of the defect was eventually achieved. At this stage, oral bisphosphonate therapy was ceased.

Due to the patients' significant co:

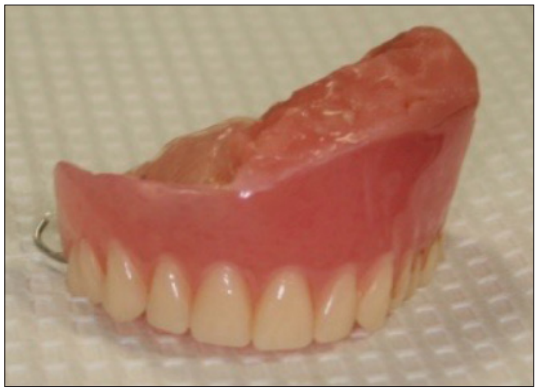

Fig 9. Obturator prosthesis.

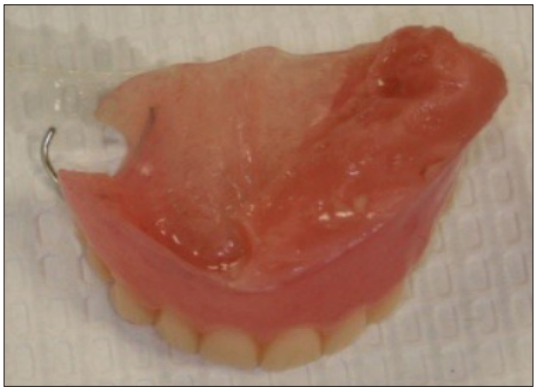

Fig 10. Obturator prosthesis.

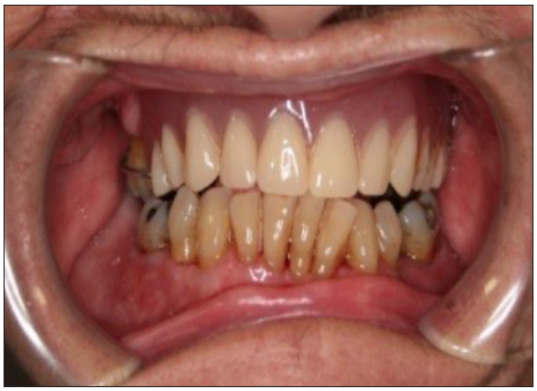

Fig 11. Obturator prosthesis

The defect was eventually reconstructed with an obturator by our colleagues in the Public Dental Service. Her carers perform twice-daily irrigation of the cavity, and she remains under regular review with both the OMFS service and a dental hygienist in the Public Dental Service. She has had a good result, remaining symptom-free and with aesthetics and function restored with the obturator prosthesis.

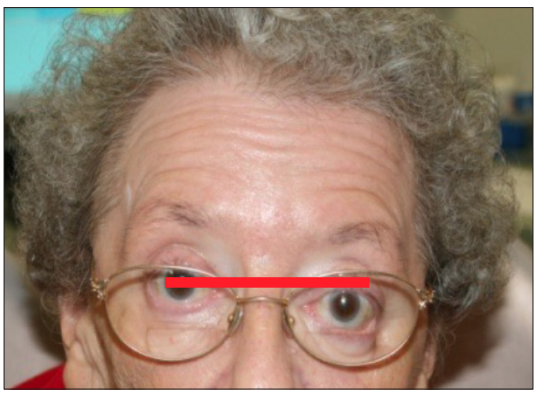

Fig 12. Enopthalmus of left eye and resolution of extra-oral sinus.

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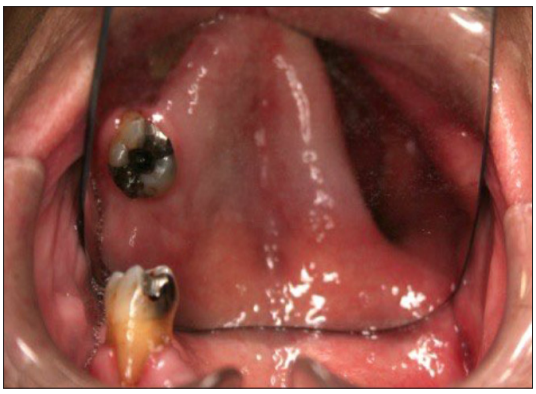

Fig 13. Mucosalisation of defect.

Discussion

The treatment of MRONJ represents a clinical challenge, and adversely affects patient quality of life. The case was a particular challenge, for both the extent of the lesion and the patient's significant co-morbidites which made radical surgical resection impossible. It also demonstrates how severe the condition can become, even in a patient on oral bisphosphonate.

Current approaches are to manage patients with as minimal intervention as possible, and treatment is based on AAOMS disease staging (see table 3). Patients with extensive disease can benefit from resection, in combination with antibiotic therapy, which may offer long- term palliation with resolution of acute infection and pain.

This case met the criteria for Stage 3 in both the anatomical extension into the sinus and orbital floor, and the degree or soft tissue infection and resultant extra-oral fistula. Unfortunately, the patient's systemic condition rendered radical surgical resection unsafe. However, a good result was achieved with conservative management, although attending for weekly wound irrigation was a significant burden to the patient. The use of obturator prothesis is most common in head and neck oncology patients, but was used to good effect to rehabilitate this patient.

Cessation of drug therapy is associated with alleviation, and quicker resolution, of symptoms. However, if used for the control of bone metastasis, discontinuation may result in recurrence of bone pain or a worsening of disease status in patients treated with anti-angiogenic therapies. Therefore, cessation of drug therapy should be considered on a case by case basis [27].

Recently, authors have advocated a move toward resection of all necrotic bone, with primary closure of mucosa even in early disease stages. This approach is associated with higher complete cure rates and a lower burden for wound management and follow up [25, 26, 28]. There is also research into the efficacy of newer, adjunct therapies such as pentoxifylline, teriparatide, medical ozone gel, hyperbaric oxygen therapy and low level laser therapy [28-32].

Conclusion

It is important that all the potentially serious side effects of antiresorptive and anti-angiogenic therapies are recognised. Prescribers of these drugs should consider referral for dental assessment to evaluate risk for developing MRONJ and initiate dental treatment before drug therapy. Good communication between general practitioners, dentists, oncologists, haematologists and above all with patients is key to successfully managing this condition.

MRONJ Staging	Presentation	Treatment Stratgies
At risk		No treatment indicated Patient education
Stage 0	Patients with no clinical evidence of necrotic bone, but present with non-specific symptoms or clinical and radiographic findings.	Systemic management, including the use of pain medication and antibiotics
Stage 1	Exposed and necrotic bone in patients who are asymptomatic and have no evidence of infection.	Antibacterial mouth rinse Clinical follow-up on a quarterly basis Patient education and review of indications for continued bisphosphonate therapy
Stage 2	Exposed and necrotic bone in patients with pain and infection evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage.	Symptomatic treatment with oral antibiotics Oral antibacterial mouth rinse Pain control Debridement to relieve soft tissue irritation and infection control
Stage 3	Exposed and necrotic bone in patients with pain, infection, and one or more of the following: • sequestrum • exposed necrotic bone extending beyond the region of alveolar bone, i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla • pathologic fracture • extra-oral fistula • oral antral/oral nasal communication • osteolysis extending to the inferior border of the mandible or sinus floor	Antibacterial mouth rinse Antibiotic therapy and pain control Surgical debridement/ resection for longer term palliation of infection and pain

Table 3. AAOMS Staging and treatment guidelines [1]

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Self Assessment Questions

1. Which of the following are symptoms of MRONJ?

A. Odontalgia with no dental cause

B. Sinus pain, with associated inflammation and thickening of sinus wall

C. Fistulae in the gingivae which can be probed to exposed bone

D. Loose teeth not linked with periodontal disease

E. All of the above

2. Which drug is associated with the highest risk of developing MRONJ?

A. Alendronic acid

B. Zolendronate

C. Sirolimus

D. Pamidronate

E. Ibandronate

Answers

1. Answer - E all of the above

All of the above are symptoms of early MRONJ - AAOMS stage 0 or 1. Many patients present in early disease with pain free areas of exposed bone, which gave failed to heal after a dental extraction.

2. Answer - B Zolendronate

IV zolendronate is associate with the highest incidence of MRONJ (1.15%). This is due to the drug potency and high dosing regime to treat skeletal events associated with metastases, commonly for patients with breast cancer.

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COMPLICATIONS IN HEAD & NECK INFECTIONS: SEPSIS & AIRWAY OBSTRUCTION

A Henry, A Cronin, JA McCaul

Abstract

We describe a case of sepsis and acute airway compromise secondary to an obstructed and infected submandibular salivary gland. A 42 year old man presented with a two-day history of mild neck pain, painful swallowing and general malaise. Examination suggested submandibular gland obstruction with secondary infection.

Despite initial conservative management of intravenous antibiotics and fluids, the patient rapidly deteriorated and developed acute airway compromise necessitating urgent endotracheal intubation, drainage of the affected gland and a three-day admission to the intensive care unit, before making a complete recovery. This case highlights the need for vigilance and prompt recognition and management of sepsis and airway compromise in all cases of infection involving the head and neck.

Case Presentation

A 42-year-old man self-presented to the accident and emergency department with a two-day history of diffuse right-sided neck pain, progressively painful swallowing (odynophagia) and general malaise. There was no history of recent illnesses, foreign travel, trauma, dental pain or treatment. There was no history of 'mealtime syndrome', which describes the classic symptoms of major salivary obstruction manifested by pain and swelling of the involved gland during eating (1).

On examination, he was tachycardic (heart rate 115), mildly pyrexic (37.8°C) and hypertensive (161/96). Blood oxygen saturations were normal on air (98%) and respiratory rate was 16. He had a tender well-defined 4 by 5 centimeter right-sided submandibular mass which was bimanually palpable and consistent with the submandibular gland. The right side floor of mouth was firm and very slightly raised and in keeping with an enlarged submandibular gland. He did not have trismus. Pus was easily expressed from Wharton's duct and was sampled for culture and sensitivity. Results of selected routine blood tests on admission are shown in Table 1.

Total white blood cell count	12.4 x 10^9/L
C-reactive protein	80
Haemoglobin concentration	137 g/L

Table 1: Selected blood test results.

Initial treatment included broad-spectrum intravenous antibiotics (co-amoxiclav), analgesia and intravenous fluids. The patient's heart rate and temperature normalised quickly, but after a period of approximately five hours these parameters had once again deteriorated and on examination the swelling in the right neck was less well defined and the floor of mouth had become raised and bilaterally oedematous. The patient also developed difficulty swallowing (dysphagia).

An urgent non-contrast computed tomograph of the neck was arranged and revealed oedema involving the lateral pharynx and base of tongue with considerable reduction of the supraglottic airway (Figure 1). A large stone (sialolith) was visible at the distal end of Wharton's duct (Figure 2) which was grossly distended (Figure 3.)

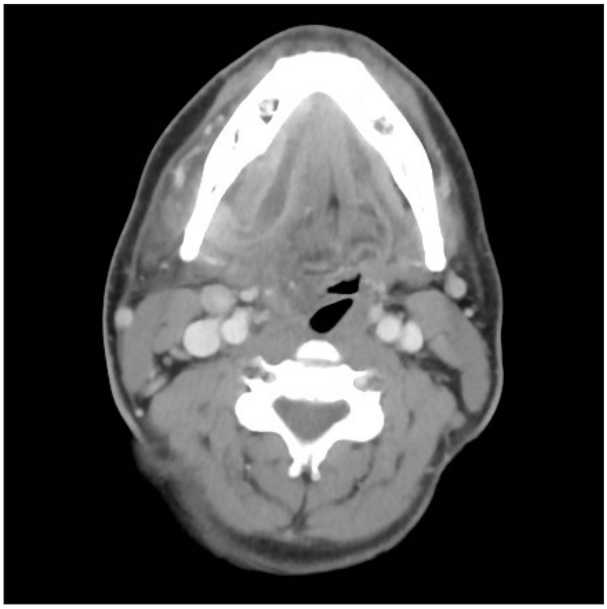

Figure 1. Axial CT image displaying significant reduction of the supraglottic airway due to oedema of the right lateral pharynx and base of tongue.

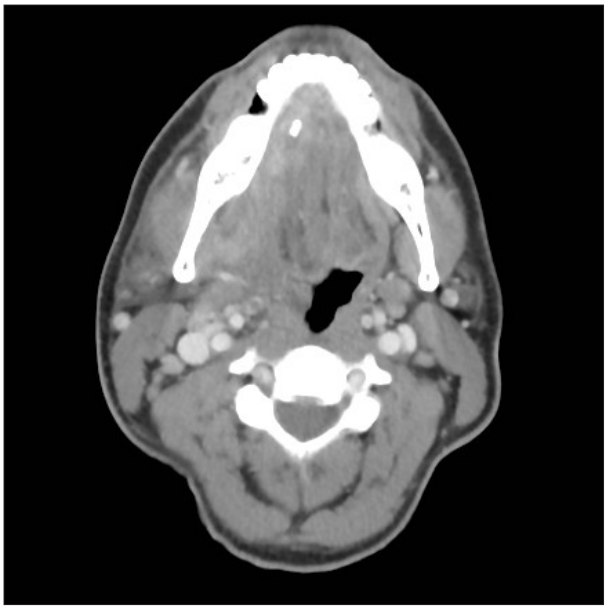

Figure 2. Large sialolith evident at the distal end of Wharton's Duct on axial imaging.

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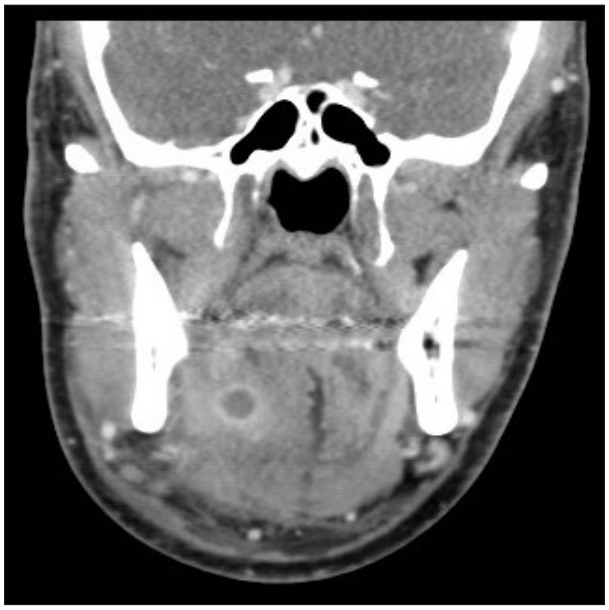

Figure 3. Grossly dilated right-side Wharton's Duct on sagittal imaging.

As a result of airway compromise, the patient underwent urgent awake fibre-optic intubation and surgical exploration of the affected Wharton's duct (intra-oral sialithotomy). Exploration revealed a large stone impacted at the distal end of the duct which was surgically removed to allow drainage of a large amount of pus.

Post-operatively, the patient required continued endotracheal intubation for a period of approximately three days on the intensive care unit before the pharyngeal swelling had reduced sufficiently to allow safe extubation. Following extubation, the patient made an uneventful recovery and was discharged from hospital after a total of six days. Culture of pus swabs taken at admission and intra-operatively revealed streptococcus constellatus and alpha-haemolytic streptococcus which were sensitive to penicillin. He was discharged from follow-up after a period of two months with no further intervention.

Discussion

Two important areas highlighted by this case report are the management of the septic patient and identification and appropriate management of patients with deep neck space infections.

Sepsis

This patient was systemically unwell when admitted and met criteria for sepsis on the basis that there was an identifiable source of infection and two positive SIRS criteria (heart rate and white cell count) as listed in Table 2. From this point of view, this patient was treated appropriately by way of rapid provision of intravenous broad-spectrum antibiotics and intravenous fluids.

Criterion	Positive Result
Temperature	< 36°C or > 38°C
Heart rate	> 90 / minute
Respiratory rate	> 20 / minute
White cell count	< 4 or > 12 x 10^9/L

Table 2: Systemic Inflammatory Response Syndrome (SIRS) criteria.

However, the definition of sepsis has recently been redefined by The Sepsis Definitions Task Force as 'life-threatening organ dysfunction caused by a dysregulated host response to infection' (2). In this most recent definition, organ dysfunction is identified by an acute change in Sequential Organ Failure Assessment Score (SOFA Score) of two or more points (2,3) as a result of infection, rather than by the previously used SIRS criteria.

The SOFA score (3) grades dysfunction in six categories; respiratory, coagulation, liver, cardiovascular, central nervous system and renal. This is a relatively complicated scoring system, so a new bedside clinical score termed quickSOFA2 (Table 3) has been developed to identify adult patients with suspected infection who are likely to have poor outcomes (2).

Criterion	Positive Result
Respiratory rate	≥ 22 / minute
Altered mentation	Any Glasgow Coma Scale score < 15
Systolic blood pressure	≤ 100 mmHg

Table 3: Quick Sequential Organ Failure Assessment Score (qSOFA Score) (2)

A qSOFA Score of two or more suggests a high risk of poor outcome and these patients should be assessed for evidence of organ dysfunction, including lactate levels. However, standard management of suspected sepsis should be continued if there is clinical suspicion.

COMPLICATIONS IN HEAD & NECK INFECTIONS: SEPSIS & AIRWAY OBSTRUCTION

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Recognition of sepsis enables appropriate treatment to be provided immediately and effectively, aiming to reduce morbidity and length of hospital stay (4). It is interesting to note that this patient would not have met these new criteria and may have been undertreated. This highlights the need to use clinical acumen when interpreting guidelines and protocols, and in this case where there was discharging pus it was obvious that antibiotic therapy was required.

Deep Neck Space Infections

Inflammation and infection within the head and neck can present with specific clinical features and site-specific complications determined by the fascial layers and potential spaces of the neck. Fascial layers play a role in directing the spread of infection once it has become established (5).

Infection frequently spreads in a predictable pattern within the fascial spaces of the neck (6), allowing anticipation of potential complications and timely treatment. Deep neck space infections often present with fever, pain and swelling, but can also display odynophagia, dysphagia, trismus and a change in voice quality depending on the area affected (7).

The most common origin for deep neck space infections is odontogenic (dental) infections (6,8,9,10) with less common sources including the salivary glands, tonsils, foreign bodies and malignancy (10). Additionally, sepsis is known to be common in patients admitted with infection of odontogenic (dental) origin, with one study finding at least 61.2% of patients meeting criteria for sepsis (6). Clinical and radiological examination of the dentition could not account for the clinical signs and symptoms in this case, while the location of the mass in the right side of the neck was consistent with the submandibular gland. Involvement of the submandibular gland was confirmed by pus from Wharton's Duct.

Infection of the deep neck spaces may result in numerous life-threatening complications such as sepsis, airway compromise, internal jugular vein thrombosis, descending mediastinitis and disseminated intravascular coagulation. These complications account for the high mortality rate (1.6 to 40 percent) (8). This forty-two year old patient presented with mild pyrexia and tachycardia, and initially complained of some odynophagia and neck pain. The admitting team was perhaps falsely reassured by the patient's response to fluids, analgesia and antipyretics and it was not until review some time later that his deterioration was obvious.

Formation of a calculus (sialolith) in the salivary glands or ducts (sialolithiasis) accounts for up to 60% of cases of salivary gland obstruction, with the submandibular gland being affected in up to 90 per cent of cases. The mainstays of treatment for deep space infection in the neck are rehydration, analgesia and antibiotics and surgical drainage (7). This regime was followed for this case.

Interestingly, after removal of the obstructing sialolith, copious drainage via the duct was obtained. Although very frequently part of management of deep space neck infection, surgical drainage of the neck spaces was not deemed necessary at initial surgery in this case due to the extent of drainage via the submandibular duct. This proved to be a good decision for this patient as his condition improved over the following three days and further surgical intervention was not necessary.

Acute airway obstruction and sepsis are unusual sequelae of obstructive sialadenitis and result from direct spread of the infective process and inflammation from the gland into the deep neck space in patients who have not been treated earlier in the disease process. The role of corticosteroids in managing airway compromise and severity of the inflammatory response for cervicofacial infection remains controversial.

This area is the subject of ongoing research by the UK Maxillofacial Trainee Research Network (MTReC). Standard UK practice of this condition has not involved corticosteroids but some units do prescribe these agents (Mr R Morrison – personal communication). The network has recently completed a survey of UK practice and a snapshot audit of cases across UK units is planned to occur in the Autumn of 2016.

Prompt recognition of airway compromise with appropriate airway management, by way of an awake fibre-optic intubation, was crucial in managing this patient. An awake fibre optic intubation describes the process where an endotracheal tube is inserted under fibre optic guidance using only local anaesthetic spray and mild sedation, with the intention that the tone of the airway is maintained until such time it is secured and the patient can be safely placed under general anaesthetic.

This procedure is indicated where there is a risk of airway compromise or where direct intubation using a laryngoscope would be difficult due to distorted upper airway anatomy. In severe cases, a surgical airway may be required under local anaesthesia. This is a procedure which must be carried out under carefully controlled conditions in the operating theatre environment by senior airway trained surgical teams. In this case CT imaging was obtained to assess the presence of fluid collections (pus) within the neck fascial spaces.

In cases of recognized airway compromise, care must be taken in considering whether imaging is required, or whether the deteriorating airway requires expeditious surgical intervention without delay. Apart from the delay to definitive management, laying the patient in a supine position may also provoke further deterioration of an already compromised upper airway and this must therefore also be considered.

COMPLICATIONS IN HEAD & NECK INFECTIONS: SEPSIS & AIRWAY OBSTRUCTION

A Henry, A Cronin, JA McCaul

Conclusion

Infections affecting the head and neck can rapidly progress to produce sepsis as well as localised complications including airway compromise. This case highlights the need for vigilance and prompt recognition and management of these complications, with due attention to clinical features. Clinical guidelines help to guide management but cannot replace clinical acumen and involvement of seniors and those with experience in managing difficult airways is vital to ensure patient safety where infections affect areas of complex anatomy such as the head and neck.

Multiple Choice Questions

1. The most common origin for deep neck space infections is:

a) Tonsillar

b) Salivary glands

c) Odontogenic

d) Skin

2. Which of the following is not used as part of the quickSOFA scoring system?

a) Respiratory ≥ 22 / minute

b) GCS < 15

c) Temperature > 37.4

d) Systolic blood pressure < 100 mmHg

3. Mealtime syndrome is the result of:

a) Major salivary duct obstruction

b) Parasympathetic nervous system overdrive

c) Excess release of acetylcholine from the pre-synaptic nerves within the salivary glands

d) Pilocarpine overdose

4. An awake fibre optic intubation is indicated for:

a) Hypertensive patients

b) Patients with difficult airways

c) Where time is very limited

d) When a patient has an allergy to general anaesthetic

5. Which of the following is a valid SIRS criterion?

a) Temperature > 37.4°C

b) Heart rate > 100

c) Respiratory rate >20

d) Urea > 7

Answers

1. C.

The most common origin for deep neck space infections is from the teeth. The teeth must be examined clinically and radiologically (if possible) in all cases of deep neck infection to confirm or refute suspicion

2. C.

Temperature does not form part of the new quickSOFA scoring system to identify patients at increased risk of poor outcome from infection

3. A.

Mealtime syndrome describes the classic symptoms of major salivary obstruction manifested by pain and swelling of the involved gland during eating.

COMPLICATIONS IN HEAD & NECK INFECTIONS: SEPSIS & AIRWAY OBSTRUCTION

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4. B.

An awake fibre optic intubation is generally indicated when patients have difficult upper airway anatomy or there is a risk of airway compromise. It generally takes longer to perform than a standard intubation.

5. C.

Respiratory rate >20 / minute forms part of the SIRS criteria. This is one of the most sensitive and often one of the most poorly recorded SIRS criteria. Other SIRS criteria include temperature < 36°C or > 38°C, heart rate > 90 / minute and white cell count < 4 or > 12 x 109/L

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FREE FLAP RECONSTRUCTION IN ORAL CANCER: THREE CASE STUDIES

S Saxena, S Prabhu, M Patel

Abstract

Whilst foundation programme jobs in Head and Neck oncology are uncommon, foundation trainees can play a crucial role in coordinating the multidisciplinary care for these complex patients. Squamous cell carcinoma (SCC) of the oral cavity is the 14th most common cancer in the UK and the overall 5 year-survival is around 60%. Oral and Maxillofacial surgeons (OMFS) play a central role in the treatment of these patients.

In light of the debilitating effects of the disease coupled with the major surgical procedures they often undergo, input from the multidisciplinary healthcare team (MDT) is vital to ensure optimal patient recovery. We present our experience with three patients treated for oral cancer using free flap reconstruction. Each case highlights both the unique surgical techniques deployed by OMFS surgeons and also the important contributions of the MDT.

Sound clinical decision-making and patient safety are particularly pertinent in these often challenging scenarios, as are other elements crucial to a foundation doctor's practice, such as safe prescribing, infection control, nutrition and health promotion.

Background

Sqaumous cell carcinoma (SCC) of the head and neck is a term that describes a heterogeneous group of epithelial malignancies, which may arise from the oral cavity, pharynx, larynx, nasal cavity or paranasal sinuses. SCC specifically of the oral cavity is the 14th most common cancer in the UK and represents 2% of all new cancer cases (1).

Unfortunately, the incidence of oral cancer is increasing worldwide, having gone up by 51% between 1989 and 2006 in the UK (2). The most important risk factors for developing oral cancer are tobacco and alcohol consumption and infection with human papilloma virus (HPV) (3). Around two-thirds of patients present with disease already having spread to the regional lymph nodes and a total of 10% with distant metastases (4,5).

Non-SCC in the head and neck region is a more uncommon and distinct entity, examples including melanoma, salivary gland tumours and osteosarcomas.

Principles of Management

Regardless of aetiology or cancer type, the clinical care of the head and neck cancer patient is a complex and highly involving process. Multiple specialties are often involved as a part of the multidisciplinary healthcare team (MDT). Oral and Maxillofacial surgery (OMFS) lead the management of oral cancers. Additionally, radiologists, pathologists, medical oncologists, restorative dentists, dieticians, speech and language therapists (SALT) and clinical psychologists are heavily involved in the diagnostic and rehabilitation process.

All head and neck cancer patients are discussed at the MDT meeting. The disease is staged using the tumour/node/metastasis (TNM) system and treatment options are discussed and offered to the patient. A variety of factors will influence choice of treatment, which can be divided into surgical and non-surgical. Whilst surgery is the mainstay of treatment in oral cancer, radiotherapy (with or without chemotherapy) may also have a role in some cases. Important aspects of surgical management include resection of the primary tumour, neck surgery in the majority of cases (which has both a diagnostic and therapeutic role in the management of regional disease) and subsequent reconstruction to maintain quality of life.

The following cases in this article illustrate both the surgical and medical complexities of managing these patients. Specifically, the focus is on patients who have undergone free flap reconstruction. These are blocks of tissue composed of skin, subcutaneous tissue and (if needed) muscle and bone that are detached from their source (donor site) with their blood supply intact. These are then transferred to another location (recipient site) where the blood supply is re-established by anastomosing the arteries and veins using microsurgery. Free flaps have revolutionized the treatment of head and neck cancer but also require diligent MDT involvement postoperatively to ensure optimal patient recovery.

Case Study 1: The DCIA Flap

Mr A is a 49-year old gentleman who originally presented to a dental hospital after an episode of infection associated with his partially erupted lower right wisdom tooth. He smoked approximately six cigarettes per day and drank 16-18 units of alcohol per week. An ulcerating lesion was seen in his right lower retromolar region. He underwent an initial extraction of the wisdom tooth in addition to an incisional biopsy of the lesion, which was confirmed as an SCC of the oral cavity.

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A CT chest and neck showed no evidence of metastatic spread to the neck lymph nodes or lungs. The case was discussed at the MDT meeting and surgery was offered to the patient. The choice of flap was heavily influenced by the patient's co-morbidities; due to the presence of old bilateral calcaneal fractures, the use of a 'fibular free flap' to reconstruct his mandible could have potentially exacerbated the patient's baseline limitations in mobility. Therefore, the DCIA flap was deemed appropriate.

Before neck surgery, tumour excision and reconstruction, a tracheostomy was inserted for airway protection and in anticipation of oropharyngeal oedema. The patient then underwent a selective right neck dissection of the lymph nodes in the anatomical levels I-IV. These nodes were sent to histopathology to rule out regional spread. The SCC was then resected through a wide local excision (WLE), using a margin of 1cm, which also encompassed a segment of the mandible.

The next procedural step was to harvest the free flap, which was based on the deep circumflex iliac artery (DCIA). The right internal oblique muscle was dissected and the artery pedicle of DCIA was identified. An iliac crest osteotomy was also performed, which formed the bony component of the free flap. The iliac crest was secured to the recipient site using a reconstruction plate and screws and the soft tissue flap shaped appropriately to fill the defect left by the tumour excision. Microscopes were used to create an anastomosis between the donor and recipient vessels: the DCIA was connected to the right facial artery and the vein was anastomosed to the internal jugular vein.

Postoperatively, Mr A was transferred to ICU for close monitoring and tracheostomy care. The tracheostomy was removed six days later, which he tolerated well. During his recovery on the wards, pain control was required for his iliac crest donor site, which had initially been affecting his mobility. This improved gradually with a careful physiotherapy regime. A subsequent decision was made at follow-up MDT to begin consideration for radiotherapy +/- chemotherapy, as he was found to have histological evidence of metastatic disease in his lymph node samples taken during the surgery.

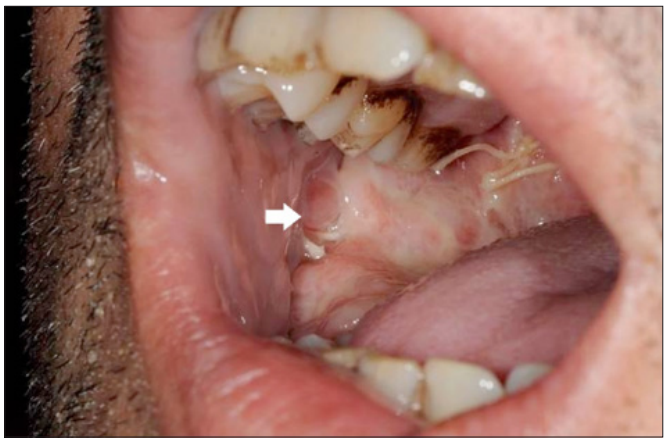

Figure 1: Flap appearance ten days after surgery. The internal oblique muscle of the DCIA flap (indicated by white arrow) is in the process of integration and mucosalization with the surrounding mucosal tissue.

Case Study 2: The Scapular Flap

Mr B is a 42-year old who presented with a one-year history of a right maxillary lesion and postnasal drip. On examination, he was found to have a 2 x 2.5cm bony hard swelling in the right upper buccal sulcus. He was a non-smoker and did not drink alcohol. CT initially suggested an osteogenic tumour and a biopsy showed features suggestive of an aggressive peri-osteal osteosarcoma.

A staging PET scan showed no evidence of distant disease. He was discussed at the Sarcoma MDT, which advised that he should undergo a neoadjuvant chemotherapy regime prior to surgery. This comprised of two cycles of 'MAP' chemotherapy (high-dose methotrexate, cisplatin and doxorubicin) under the medical oncology team.

To achieve clear margins of tumour resection, a right maxillectomy was performed with a 2cm margin, which included the overlying skin. The facial artery and vein were then identified and prepared for anastomosis. As this resection involved multiple tissue types ('composite'), the skin and bone needed to replace the defect required meticulous reconstruction in three dimensions. The scapular flap, which is classified as an 'osteocutaneous flap', allows for this and has the added benefit of leaving minimal donor site morbidity (6).

FREE FLAP RECONSTRUCTION IN ORAL CANCER: THREE CASE STUDIES

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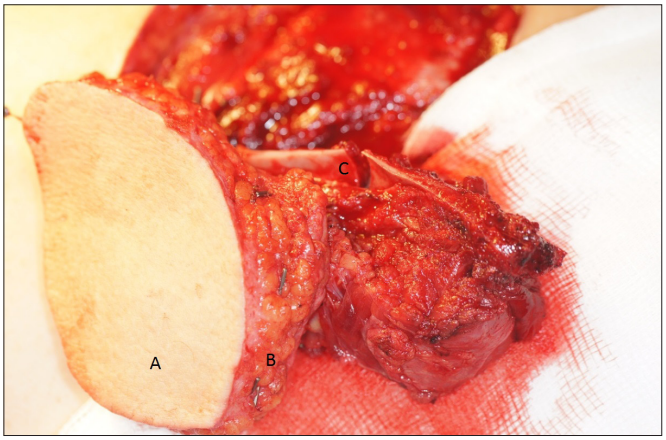

Figure 2: The composite scapular flap following harvest and prior to anastomosis. The skin paddle (A), subcutaneous tissue (B) and scapular bone (C) can be seen.

Both the soft tissue and osseous components of the left scapular free flap were dissected and shaped appropriately. The pedicle of the flap, the right lateral circumflex scapular artery, was then anastomosed to the superficial temporal artery and the circumflex scapular vein to the facial vein.

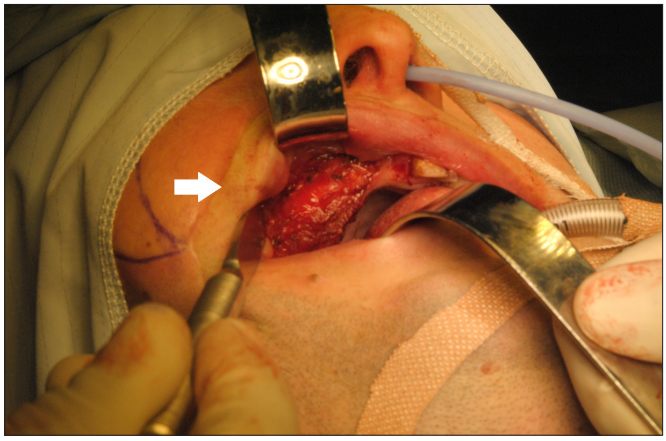

Figure 3: The scapular flap in place following anastomosis. Both the soft tissue (indicated by white arrow) and bony components of the free flap have replaced the initial site of the resected right maxilla.

Mr B progressed well postoperatively and regular physiotherapy to his left shoulder and arm enabled him to make a good recovery. Nutrition and oral intake was optimised with regular dietician and SALT reviews. He underwent further contouring of his free flap so that appropriate dentures could be made and fitted for his missing set of upper right teeth. He underwent two further cycles of MAP chemotherapy and recurrence was not found on follow-up.

Case Study 3: The Fibular Flap

Mrs C is a 64-year old lady who presented with a five-week history of an oral lesion in her right lower quadrant. She was a non-smoker. Initial incisional biopsy of the lesion had confirmed a SCC of the oral cavity. An MRI neck showed a 1cm area of hyperintensity at the site of the lesion, which was abutting her right mandible. No lymph node or distant disease was seen on MRI. Plan was made for surgical resection and reconstruction using a fibular flap, which is a typical choice in cases where a part of the mandible has been resected.

The patient underwent selective right neck dissection of levels I-IV. This was followed by a WLE of the oral SCC and a right segmental mandibulectomy. For reconstruction, the free flap was elevated on the left leg on a soft tissue paddle with associated fibular bone, all based on the peroneal artery. Finally, the peroneal vessels of the free flap were anastomosed to the recipient facial artery and internal jugular vein and the fibula was fixed to the mandible with a titanium plate.

Postoperatively and following a short stay on ITU, her diet was supervised by SALT who also encouraged jaw exercises to improve her mouth opening.

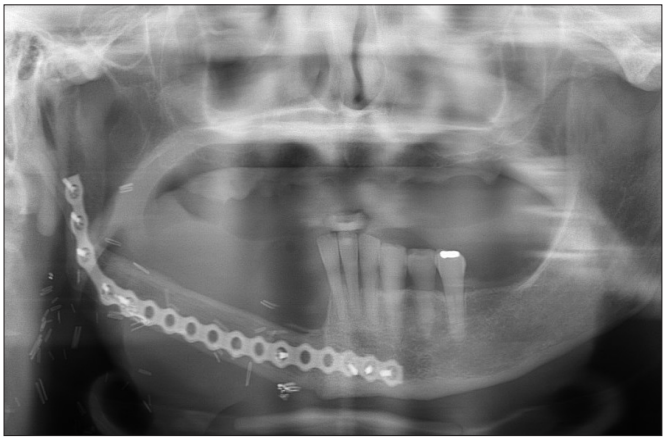

Figure 4: Post-operative orthopantomogram (OPG) x-ray view. The fibula bone can be seen in place of the resected right segment of the mandible and fixated with a titanium plate.

FREE FLAP RECONSTRUCTION IN ORAL CANCER: THREE CASE STUDIES

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Conclusions

Oral cancer is an especially debilitating disease, due to its effect on appearance, taste, speech, swallowing and psychological health. The overall 5-year survival for oral cancer is 60% (5), but identification at an early stage is associated with a 70-90% cure rate (7). The aim of treatment is to remove the cancer and also maintain quality of life. As well as understanding the central role of OMFS surgeons in treating these patients, foundation trainees should appreciate that the management of head and neck cancer patients provides an excellent framework for implementing effective and coordinated clinical care between many other healthcare professionals.

Test Yourself

Q1: Which of the following risk factors is most strongly associated with oral cancer?

A: Alcohol

B: Human papilloma virus

C: Smoking

D: Asbestos exposure

E: IV drug use

Q2: Which of the following clinical signs is most likely to indicate post-operative free flap failure?

A: Warm to touch

B: Capillary refill time of 2 seconds

C: Pink colour

D: An arterial waveform on the Doppler probe

E: Firm consistency

Q3: Which of the following is the medication used to treat acute alcohol withdrawal?

A: Pabrinex

B: Chlordiazepoxide

C: IV Dextrose

D: Haloperidol

E: Thiamine

Q4: Which artery is the fibular free flap based on?

A: Peroneal artery

B: Thoracodorsal artery

C: Deep circumflex iliac artery

D: Radial artery

E: Lateral femoral circumflex artery

Q5: Which of the following features would necessitate an urgent cancer pathway referral for suspected oral cancer?

A: Unexplained ulceration in the oral cavity lasting more than 3 weeks

B: A red/white patch in the oral cavity consistent with erythroplakia

C: Persistent and unexplained neck lump

D: A red/white patch in the oral cavity consistent with erythroleucoplakia

E: All of the above

Answers

Q1 – C

Whilst A, B and C are all recognized risk factors for developing oral cancer, smoking is considered the main avoidable risk factor. It is estimated that a total of 91% of oral cancer cases in the UK are linked to major lifestyle factors and smoking is attributed to 65% of oral cancer cases in the UK (1). Some environmental exposures, such as ionising radiation, are also linked to oral cancer.

Q2 – E

Postoperatively, it is crucial to monitor free flaps regularly for at least the first 72 hours, as most flap failures occur within this time frame. The flaps are generally checked hourly for the first 24 hours, during which time their clinical appearance is assessed. A Doppler probe may also be used to confirm patency of vessels by detecting blood flow.

The cause of failure is attributed to perfusion problems, namely arterial ischemia, venous congestion (the most common) or both. A flap that is firm in consistency may indicate congestion or an underlying haematoma. Both of these can compress the vascular pedicle of the flap, which can in turn further compromise both arterial perfusion and venous drainage.

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Q3 – B

Alcohol dependency is often seen in the oral cancer patient cohort. It is crucial to assess whether a particular patient is at risk of alcohol withdrawal, as this can manifest itself either pre or post-operatively and significantly impact the clinical outcome.

Chlordiazepoxide, a benzodiazepine, is the medication of choice to treat acute alcohol withdrawal. Pabrinex and Thiamine also have a role in the acute management, but mainly as a prophylaxis against the development of Wernicke's encephalopathy. IV dextrose should be avoided as it can precipitate Wernicke's.

Q4 – A

Good perfusion is the keystone to successful flap-based surgery. The surgeon must have a good knowledge of the bloody supply relating to the flap they intend to raise and especially of the primary arterial pedicle. After identification and careful dissection, the vessels must be prepared for anastomosis with the recipient site vessels.

Q5 – E

All of these features would necessitate urgent referral within 2 weeks for suspected oral cancer. It is important for foundation trainees and other non-specialists to also be aware of these features, as they may be identified as incidental findings in their own patients. For example, many patients with suspected oral cancer may initially be identified at a routine dental appointment (8).

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JUST TOOTHACHE?

H Kyte, M Virdi, N Mahon, G Walton

Abstract

Odontogenic tumours arise from tooth forming tissues and are exclusively treated by Maxillofacial surgeons. We report a case of an odontogenic tumour in a young girl. The diagnosis, investigations and surgical management of these tumours along with the multidisciplinary approach to post-operative oral rehabilitation are discussed.

Case report

A 22 year old lady was referred by her dentist with a cyst related to a left unerupted third molar tooth. She had a three month history of throbbing pain on the left side of the mandible. An orthopantomogram (OPG) radiograph revealed a large radiolucent area within the left side of the mandible related to an ectopic third molar. The initial working diagnosis was a dentigerous cyst which is a cyst that arises from the follicle of a developing tooth. Other possibilities could have been a keratocyst, periapical cyst, cementoblastoma or ameloblastoma.

On examination she had a diffuse hard swelling on the left side of the mandible which did not have a well-defined margin. Three months later the cyst was enucleated via an intra-oral approach (Figure 1). Risks of surgery included a mandibular fracture and numbness of the lip or tongue. Numbness may occur as the inferior alveolar nerve travels within the body of the mandible supplying sensation to the lower lip and the lingual nerve runs medially along the mandible supplying sensation to the tongue.

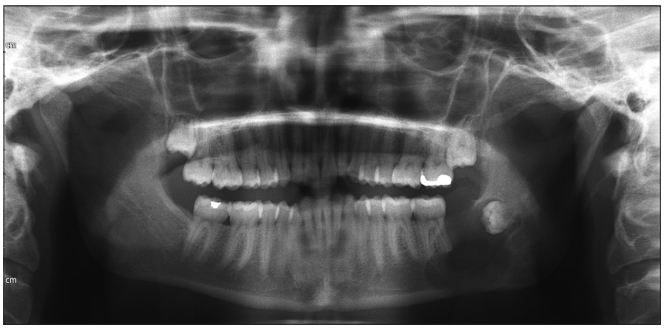

Figure 1: Post-operative OPG following initial enucleation of the suspected cyst which was later diagnosed as a unicytic ameloblastoma (March 2007).

The histology was atypical and an expert opinion was sought from an Oral Pathologist. The lesion was diagnosed as a unicystic ameloblastoma. This is a benign but locally invasive tumour of dental origin. It arises from ameloblasts, which are precursors of enamel forming cells. Her case was discussed the following week at the head and neck multidisciplinary meeting.

Treatment options include enucleation/curettage or local resection with a margin of bone or segmental resection. Whilst the former has produced good results the latter approach is more commonly adopted to ensure complete resection. Such a large resection necessitates the use of a vascularised bone graft to reconstruct the resultant defect.

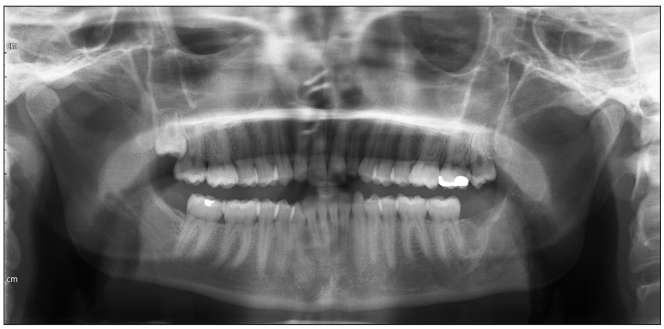

Figure 2: Post-operative OPG following second enucleation of the unicytic ameloblastoma (March 2009).

The options were discussed with the patient and her family. Unsurprisingly for an attractive 22 year old beautician, she was upset at such a radical approach to benign disease. She subsequently opted for enucleation of the cyst (Figure 2). There were two further operations to enucleate the cyst and remove the unerupted tooth. Monitoring consisted of six monthly reviews and regular OPGs but she soon failed to attend follow up appointments.

Seven years after her initial presentation she was referred back by her dentist with pain and a submandibular swelling. CT scans confirmed a large recurrence in the mandible (Figure 3). She had a resection of the mandible body and ramus and reconstruction with a fibula free flap (Figure 4). The surgery consisted of a left hemimandiblectomy, neck access to locate satisfactory neck vessels to anastomose to the fibula flap and a temporary tracheotomy to be placed for safe airway management.

JUST TOOTHACHE?

H Kyte, M Virdi, N Mahon, G Walton

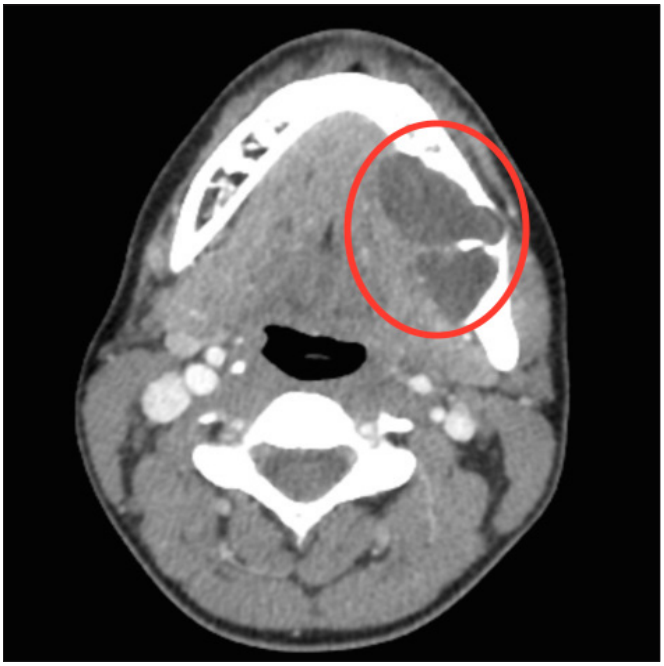

Figure 3: CT scan demonstrating recurrence of the ameloblastoma (in red) on the left side of the mandible. The lesion has breached both the buccal and lingual cortical plates of the mandible (September 2014).

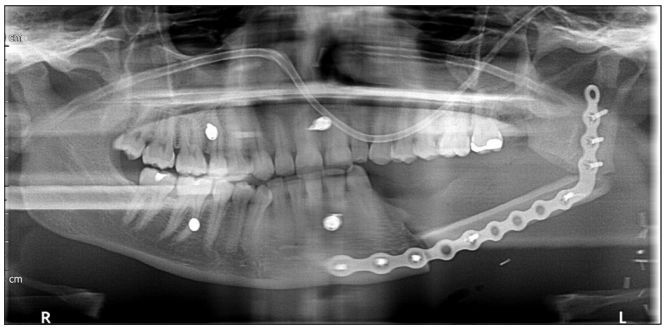

Figure 4: Post-operative OPG following segmental resection of the left side of the mandible with repair of the defect using reconstruction plate and fibula myo-osseus free flap (February 2015).

Discussion

There are three immediate post-operative concerns when monitoring patients who have had complex head and neck surgery with free flap reconstruction:

1. Airway complications

Such surgery results in extensive swelling and a temporary surgical tracheostomy is often required. When assessing the airway in the post-operative period one should be aware of imminent threats to the airway which include a dislodged or obstructed tracheal tube, neck haematomas, profound neck swelling, and subcutaneous emphysema. (1,2)

2. Donor site complications

Tight closure of the donor site may lead to severe complications such as compartment syndrome. A patient complaining of severe pain, paraesthesia should raise concern among clinicians to assess for compartment syndrome. Compartment pressures and perfusion of the limb should be evaluated. (3)

3. Free flap complications

The arterial supply or the venous drainage may be interrupted resulting in loss of viability and failure of the flap. Signs of a well perfused flap include a warm temperature, pink colour, capillary refill time 2-3 seconds, soft texture without skin changes e.g. blisters. Concerning signs would be a blue, white or cold flap with prolonged refill time. For most free flaps the arterial inflow can be monitored with a Doppler but this is difficult with intra-oral flaps.

Therefore monitoring is usually performed by inspection only and by experienced staff. Frequent flap monitoring should be performed every hour for the first 72 hours post-operatively, to assess viability of the flap and the need for urgent intervention if required (4).

Other complications include scarring of the leg and neck, numbness of the lip/tongue, asymmetry of the face, trismus and loss of multiple teeth in the area.

Due to the multifunctional qualities of the mouth, surgery in this area may affect a patient's breathing, eating, swallowing, chewing, speech and appearance. A multidisciplinary approach is adopted to provide the best possible oral rehabilitation. Speech and language therapists assess the patients swallowing in the early post-surgical period.

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They advise as to when the risk of aspiration is low enough to start introducing fluids followed by solids and wean off enteral-assisted feeding e.g. nasogastric (NG) tube or gastrostomy feeding from either a percutaneous endoscopic gastrostomy (PEG) or a radiologically inserted gastrostomy (RIG).

Dieticians address the patient's nutritional needs by advising appropriate feeds and replacing electrolytes as required. Physiotherapists perform chest physiotherapy in the early phase of treatment as these patients have undergone many hours under general anaesthesia and have increased secretions as a result of having a tracheal tube in situ. They then assess when the patient can weight bare.

A restorative dentist examines the patient and advises if the bone graft is sufficient for dental implants or if removal dentures are the only option. Emotional support is provided by head and neck specialist nurses.

Ameloblastomas

An ameloblastoma is a benign neoplastic odontogenic tumour which presents in the maxilla or the mandible. It represents 1% of all tumours found in the jaws (5). It originates principally from epithelium of the enamel organ which has not undergone differentiation to hard tissue (6). They are asymptomatic and slow growing, and can show no evidence of swelling (5). It was unusual for a 22 year old female to present with an ameloblastoma as peak incidence is usually seen in the third or fourth decades of life.

Ameloblastomas can be cclassified clinically into solid/multicystic, peripheral and unicystic. Unicystic ameloblastomas show radiological/gross features of mandibular cysts, however, histological examination shows typical ameloblastomatous epithelium lining of cavity with or without luminal/mural growth. They are the least aggressive type and respond favourably to conservative surgery (7).

Local recurrence rates of ameloblastomas have been seen to reach 90% (8) therefore their main modality of treatment is surgery with adequate surgical clearance. Literature shows that wide resections (margins of 1.5-2.0cm) reduces recurrence rates to 13-15% as it ensures all microcyts are removed (5).

This stresses the importance of long-term follow-up of these patients as recurrent lesions appear on average every 14-15 months. Some recurrences can appear up to 4-10 years later (9). The rate of recurrence is a crucial factor when planning treatment, however, consideration of the patient's morbidity and quality of life must be taken into account especially with ameloblastoma occurrence at a young age.

Fibula Free Flap

A free flap is a flap in which the donor vessels are completely divided, the tissue is transported to a recipient site, and the flap is revascularised by anastomosis of vessels in the recipient bed to the artery and vein(s) of the flap. The fibula free flap (FFF) is a free tissue transfer of fibula with its vascular pedicle. Its use has become integral in the management of extensive mandibular and maxillary reconstruction.

The technique has been refined to include a cutaneous portion for the closure of defects such as from those resulting from oral squamous cell carcinoma, osteoradionecrosis in addition to odontogenic cysts and tumours. There exist a variety of other suitable flaps which include the radial forearm flap and pectoralis major flap for use in head and neck reconstruction.

The FFF confers many advantages over other flaps. Firstly, the fibula is a substantial long bone (up to 26cm) in close proximity to the peroneal artery and venae that can thus be harvested as a long, single pedicle (10). Length is an important factor for reconstructing oral defects as the pedicle needs to be sufficiently long to reach the neck vessels without being under excessive tension. Secondly, the peroneal artery provides both endosteal and periosteal vascular supply allowing for multiple osteotomies and therefore accurate contouring to approximate the original shape of the mandible (10).

In addition, the vascular supply to the cutaneous region of FFF is also provided by the peroneal artery via the septocutaneous and musculocutaneous perforators. This allows for a cutaneous portion to be harvested although it is necessary to maintain the delicate perforators (10). In this case, the FFF was selected to minimise the aesthetic impact on the patient. The donor site is less conspicuous than radial or pectoralis donor sites and this was particularly relevant due to the young age of the patient.

Conclusion

The multidisciplinary management of such a case is very important with respect to the outcome of the patient particularly due such a radical approach to benign disease in a young girl. It demonstrates the successful application of a FFF for the reconstruction of a mandibular defect due to an ameloblastoma. It reminds all clinicians that thorough clinical investigation is extremely important in order to establish a definitive diagnosis and that pain occurring in the mouth can be more than just 'toothache'.

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Questions

1) What is the recurrence rate of ameloblastoma following surgical intervention?

a) <10%

b) 23-25%

c) 13-15%

d) >30%

e) 15-20%

2) Select the correct differential diagnoses of a bony swelling?

a) Lipoma & sebaceous cyst.

b) Odontogenic keratocyst & ameloblastoma.

c) Leukoplakia & pyogenic granuloma.

d) Dental abscess & fibrous polyp.

e) Pseudomonas candidiasis & odontogenic keratocyst.

3) Which of the following statements is correct with regards to the FFF?

a) The FFF is strictly an osseous flap.

b) The vascular supply to the FFF is from the radial artery.

c) The vascular supply to the FFF is only periosteal.

d) It is not possible to obtain multiple osteotomies from the FFF.

e) Post-operative complications of FFF include compartment syndrome, ischaemia and reduced ankle stability and function.

4) Which of the following statements would indicate failure of free flap?

a) White appearance with a positive Doppler signal.

b) Purple-blue appearance with a negative Doppler signal.

c) Pink appearance and warm to touch.

d) Pink appearance, warm to touch and positive Doppler signal.

e) Warm to touch with positive Doppler signal.

5) What is the histological origin of an ameloblatoma?

a) Enamel organ

b) Dental lamina

c) Hair follicle

d) Rests of Malassez

e) Wolffian duct

Answers

1) Answer: c.

Local recurrence rates of ameloblastomas have been seen to reach 90% when treated with curettage. Their main modality of treatment is surgery with adequate surgical clearance. Literature shows wide resections (margins of 1.5-2cm) reduces recurrence rates to 13-15% as it ensures all microcyts are removed.

2) Answer: b.

Odontogenic keratocysts are derived from remnants of the dental lamina. They are aggressive in nature and patients commonly present pain, soft tissue swelling, bony expansion and paraethesia of lip or teeth. Ameloblastomas are derived from the remnants of the enamel organ. They are slow growing benign tumours which cause bony expansion.

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3) Answer: e.

The peroneal artery provides both endosteal and periosteal vascular supply allowing for multiple osteotomies to be obtained from the FFF.

4) Answer: b.

A viable free flap should be well perfused and therefore is usually pink in colour although this is not always the case. In addition, the flap should be warm to touch and provide a positive Doppler signal.

5) Answer: a.

Ameloblastomas originate principally from epithelium of the enamel organ which has not undergone differentiation to hard tissue

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