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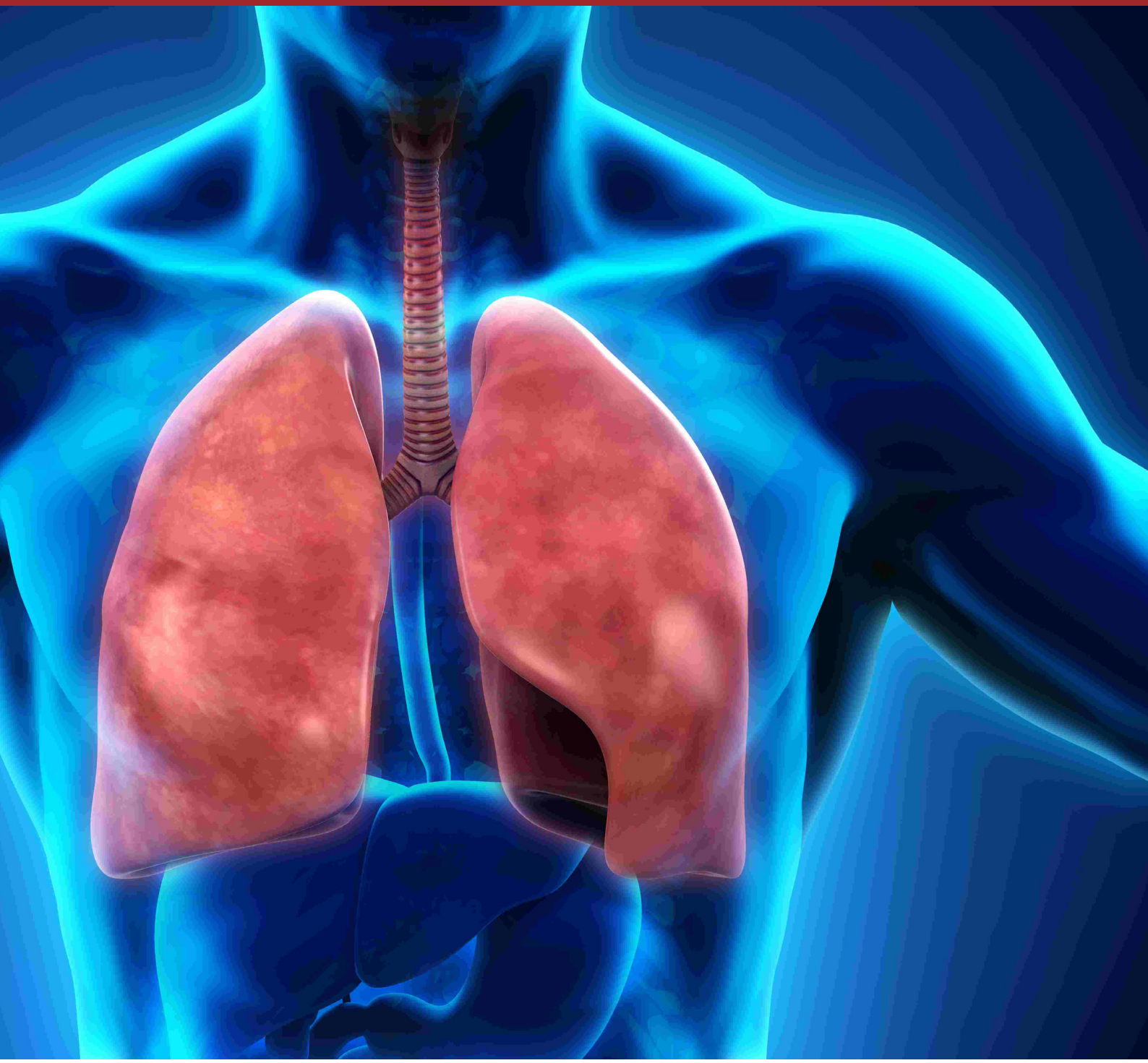

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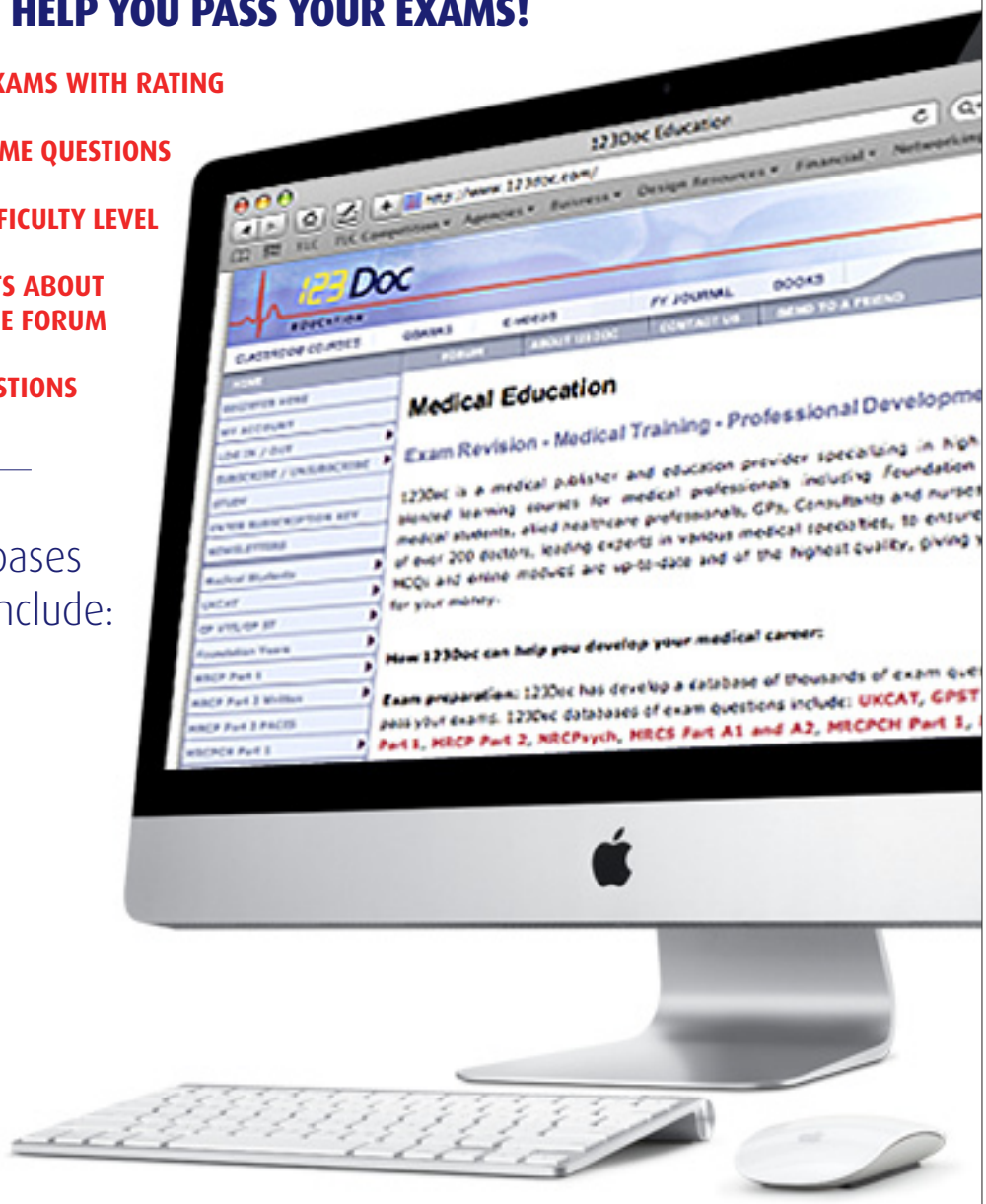

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Volume 10

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A RARE PRESENTATION OF LUNG CANCER COMPLICATED BY SEVERE SURGICAL EMPHYSEMA & BRONCHO-PLEURAL FISTULA

G Nocentini, K Pannu, DK Mukherjee

Abstract

Hydropneumothorax is a rare presentation of lung cancer.

This case report describes a patient with spontaneous hydropneumothorax found to be secondary to previously unknown lung cancer, complicated by broncho-pleural fistula (BPF) and severe surgical emphysema.

Diagnosis and management of the aforementioned complications are discussed, and most important learning points for Foundation Doctors are highlighted.

Case Presentation

A 93 years old man presented to the Emergency Department complaining of shortness of breath and reduced exercise tolerance. He was an ex-smoker with a 40 pack years smoking history and had a past medical history of chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and mild left ventricular failure (LVF).

On admission, his vitals showed respiratory rate 24/min, oxygen saturation 90% on room air, pulse rate 80/min, blood pressure 135/84 mmHg.

An ABG on air revealed Type I Respiratory Failure (pH 7.41, pO_2 8.44, pCO_2 5.96, HCO_3- 27.8, BE 2.7, Lactate 0.8). His target saturation range was set between 88% and 92% as he was deemed at risk of Type II Respiratory Failure due to COPD. An urgent chest X-ray (CXR) showed a left-sided hydropneumothorax (Fig. 1) and raised concerns of a possible mass in the left perihilar area. The hydropeumothorax was treated with a 12F chest drain inserted using the Seldinger technique and connected to underwater seal chest drainage system .

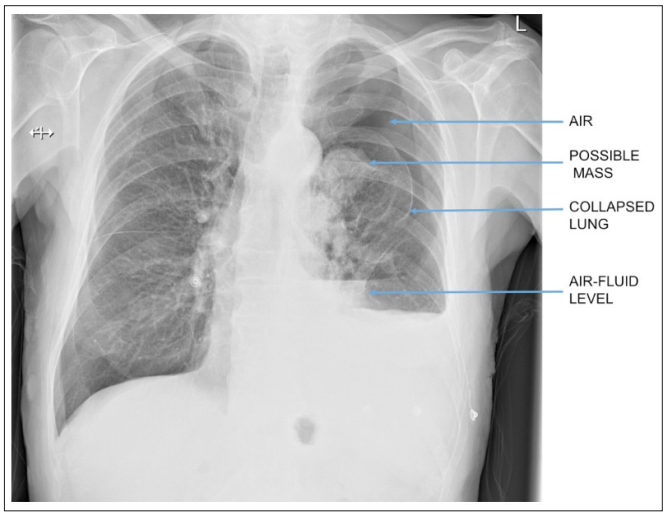

Fig. 1 – CXR on admission

The correct placement of chest drain was confirmed with a CXR and clinically the respiratory swing of the fluid column confirmed chest tube patency. Suction was started on the following day because of incomplete re-expansion of the lung on subsequent CXRs and as constant bubbling of the underwater seal suggested a persistent air leak.

To further evaluate the CXR findings, a CT Chest Abdomen Pelvis was performed and showed a 3 x 2.6 cm spiculated necrotic soft tissue mass in the apical segment of the left lower lobe (LLL) and a 2 x 2.8 cm soft tissue mass in the left upper lobe (LUL), with left chest wall surgical emphysema extending into the neck and mediastinum (Fig 2).

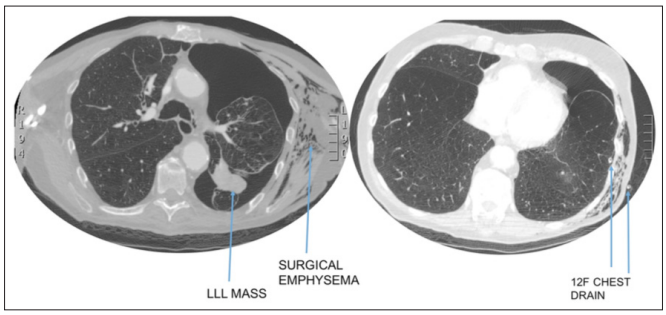

Fig. 2 - CT Chest showing the underlying cause for hydropneumothorax

Cytological analysis of the aspirated pleural fluid showed occasional isolated cells with dense cytoplasm and irregular pleomorphic nuclei with conspicious nucleoli. These features were felt to be consistent with an epitheloid malignancy. The case was discussed in the Lung Cancer MDT and in view of the patient's age, other comorbidities and a performance status of 2, a clinical diagnosis of lung cancer for best supportive care was made.

After four days, because of persistent bubbling of the chest drain, a repeat CXR was performed and this showed a worsening pneumothorax (Fig. 3). Potential causes of non-resolving pneumothorax were persistent air leak due to a broncho-pleural fistula, small 12 F chest drain size and inadvertent blockage of this small chest drain due to twisting or kinking.

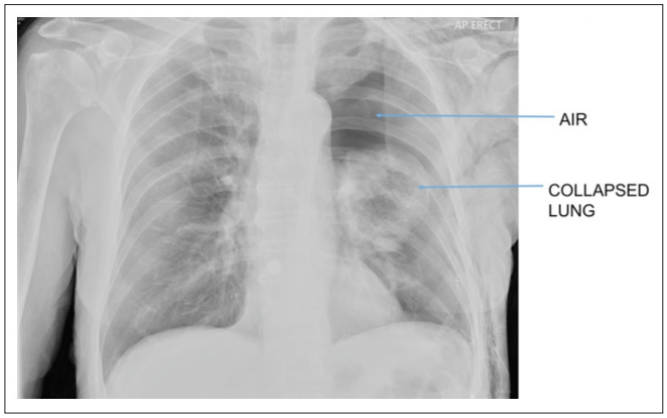

Fig. 3 – Worsening CXR after four days

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The 12F chest drain was therefore removed and a new 18F chest drain was inserted, with consequent improvement in lung re-expansion as seen on post insertion CXR (Fig. 4).

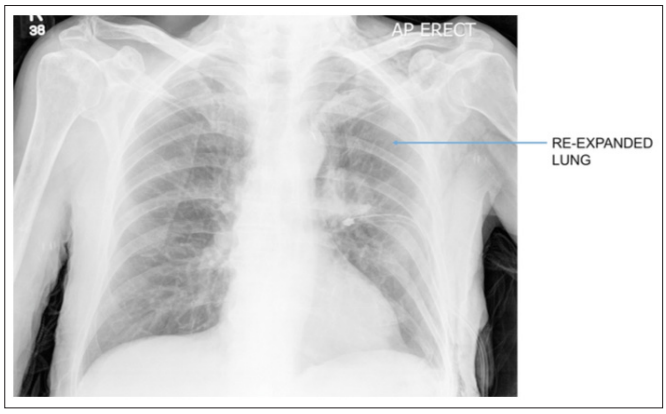

Fig. 4 – CXR after the insertion of 18F drain

Unfortunately, after a few days, the 18F chest drain fell out and another 18F chest drain had to be inserted. After two more days, following almost complete resolution of the pneumothorax, a chemical pleurodesis with talc was performed to prevent recurrence.

However, within 24 hours of attempted talc pleurodesis, the patient developed clinical signs of progressively worsening surgical emphysema and a new CT chest confirmed marked surgical emphysema and pneumomediastinum (Fig 5).

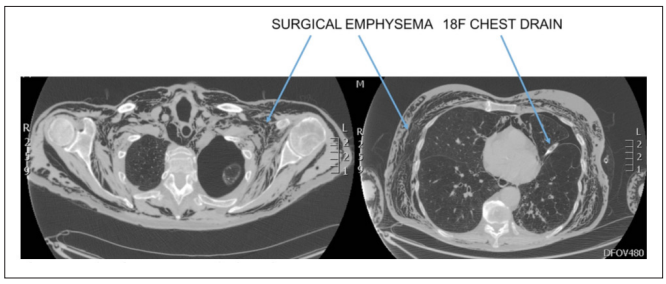

Fig. 5 - CT showing severe surgical emphysema

Because of the worsening clinical condition an emergency 28F surgical drain was inserted, following which the surgical emphysema gradually resolved and the patient slowly made a full recovery, without need for further intervention. Patient was finally discharged home with palliative care support in place.

Discussion

1. Hydropneumothorax

Hydropneumothorax is defined as presence of both air and fluid in the pleural space and is rarely the presenting manifestation of lung cancer. Among different types of lung cancers, it is more likely to be associated with Squamous Cell Carcinoma because of its tendency to erode the surrounding tissue (1-3). (Table 2).

Category	Examples
Iatrogenic	Post invasive procedures – e.g. biopsies
Cavitating lesions	TB S. Aureus Metastasis
Lung cancer	Mesothelioma Squamous Cell Carcinoma Adenocarcinoma – few cases reported
Boerhaave Syndrome (pneumomediastinum)	Spontaneous oesophageal rupture

Table 2 – Causes of Hydropneumothorax

2. Surgical Emphysema & Pneumomediastinum

One of the possible consequences of the pleural procedures performed to treat pneumothorax or hydropneumothorax, particularly when repeated several times, is that repeated pleural punctures result in multiple communications between the pleural cavity and the other layers of the thoracic wall, eventually causing surgical emphysema.

Surgical emphysema is caused by air tracking along the subcutaneous tissue planes; it is clincally detectable on palpation with a crackly "tissue paper" feeling under the fingers.

Pneumomediastinum is detected radiologically as lucent areas between the mediastinal visceral structures and tissue planes. Pneumomediastinum can occur following pneumothorax or oesophageal perforation.

Pathophysiological mechanism is explained by the Macklin effect, characterised by air spreading to the mediastinum along the bronchovascular sheaths after alveolar rupture(4).

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Clinically, patients can develop dysphonia and dysphagia as air dissects into the tissue planes of the neck.

In severe cases surgical emphysema can cause respiratory and cardiovascular compromise because of upper airway and jugular vein compression (5), and definitive airway management with tracheostomy may be necessary.

Boerhaave Syndrome must be considered in differential diagnosis of pneumomediastinum and subcutaneous emphysema (6) (Table 3). This occurs due to spontaneous rupture of the oesophagus, usually after intractable retching and vomiting, and patients present with severe chest pain.

SPONTANEOUS PNEUMOMEDIASTINUM	SECONDARY PNEUMOMEDIASTINUM		
	IATROGENIC	TRAUMATIC	NON TRAUMATIC
Tobacco use	Endoscopic procedures	Blunt injuries	Asthma
Recreational drug use	Intubation	Penetrating chest or abdominal injuries	COPD
- marijuana	Pleural cavity instrumentation		Bronchiectasis
- cocaine	Central lines insertion		ILDs
	Chest or Abdominal surgeries		Malignancy
			Boerhaave Syndrome
			Toxic fumes Inhalation
			Child birth

Table 3 – Causes of Pneumomediastinum.

3. Broncho-Pleural Fistula

BPF is defined as persistent air leak or failure of lung to re-inflate in spite of chest drainage for 24h. In our case non-resolution of the pneumothorax was due to a BPF probably located in the apical segment of the LLL; this prevented complete re-expansion of the lung and required a second and bigger drain after treatment failure with the first 12F chest drain. We felt that intermittent blockage of this small drain could have also played a role, as 12F chest drains are more prone to kinking and blockage.

We believe that large air leak because of the BPF and ineffective drain size forced the air into the subcutaneous tissue via the communications created by multiple pleural procedures, leading to worsening subcutaneous emphysema. Similar cases have been reported in literature, supporting the hypothesis that creating multiple communications between the atmosphere and the thorax cavity should be avoided (12).

When a BPF is suspected, it is pivotal to ensure that chest drain size is appropriate to match the air leak. Management of a BPF is particularly challenging; resolution may occur spontaneously by up-sizing the Seldinger chest drain and using high volume/low pressure suction or, ideally, inserting a surgical chest drain measuring at least 24F.

Persistent air leak may require bronchoscopic intervention with embolic agents use such as blood clots, gelatin, silicon rubber plugs, fibrin glue, metallic coils or stents (7,8).

Possible alternative treatments described in literature include transcutaneous BPF closure via a patent duct arteriosus (PDA) occluder (8), endobronchial sealing using GoreTex plugs (9) and fibrin sealant administration through a chest tube if endobronchial techniques fail (10). Large or recalcitrant BPFs require a surgical intervention for complete obliteration. This can be obtained with loco-regional muscular flaps, thoracoplasty, lung resection or stapling, pleural abrasion or decortication (11).

Conclusions

1. Lung cancer should be considered as the possible cause of a spontaneous hydropnuemothorax;

2. Multiple pleural procedures can increase the likelihood of surgical emphysema and possibly pneumomediastinum with potentially life-threatening consequences;

3. Chest drain should be secured to prevent drain fall out and need for reinsertion;

4. Tight dressing of the insertion site should be ensured to avoid atmospheric air from entering pleural space;

5. Non-resolution of a pneumothorax after 24 h with a bubbling chest drain is highly suggestive of a BPF.

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MCQs

1. The most common cause of hydropneumothorax is:

a. malignancy
b. trauma
c. invasive procedure
d. infection
e. COPD

2. Surgical emphysema:

a. is defined as presence of air in the subcutaneous tissue
b. indicates pulmonary emphysema secondary to surgical intervention
c. always requires surgical intervention to resolve
d. manifests at its worst within 12 hours after an invasive procedure
e. is more common in males

3. 12F chest drains:

a. are more likely to kink or block because of the small diameter
b. are only indicated for pneumothorax
c. don't require tight dressing because of the small diameter
d. must be removed within 24h after insertion
e. don't require ultrasound guidance to be inserted

4. Boerhaave Syndrome:

a. is an inherited disorder
b. occurs due to a lung abscess
c. is characterised by the spontaneous rupture of the oesophagus
d. is a paraneoplastic syndrome
e. usually resolves spontaneously

5. A broncho-pleural fistula

a. can only be caused by lobectomy
b. always requires surgical intervention
c. can be ruled out if not evident on a CT scan
d. is defined as persistent air leak or failure to reinflate the lung in spite of chest drainage for 24h
e. occurs more commonly in the right upper lobe

Answers

1. Answer: b

Traumatic injuries are the most common cause of hydropneumothorax, followed by invasive procedures. Hydropneumothorax can rarely be a presenting finding in lung cancer, particularly Squamous Cell Carcinoma.

2. Answer: a

Surgical emphysema can develop slowly after an invasive procedure and can worsen over days. It has no gender predilection and can resolve spontaneously.

3. Answer: a

12F chest drains can be used to resolve pneumothorax but also to drain pleural fluid; there is no specific indication for removal after 24 hours. The chest drain should always be inserted under ultrasound guidance as per BTS guidelines and a tight dressing should be applied to prevent surgical emphysema.

4. Answer: c

Boerhaave Syndrome is not a genetic or paraneoplastic condition. It occurs due to repeated episodes of retching and vomitting resulting in sudden oesophageal rupture. It can lead to pneumonediastinum, mediastinitis and sepsis secondary to the communication between the gastro-intestinal tract and the pleural cavity. Management includes volume resuscitation, broad spectrum antibiotics and prompt surgical intervention.

5. Answer: d

BPF can occur after a lobectomy and can often be undetectable on a CT scan. It doesn't have any lobar predilection. Spontaneous resolution is possible and surgical intervention is not always necessary.

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ARTERIAL BLOOD GAS (ABG) INTERPRETATION & OXYGEN ADMINISTRATION

PP Velu, PA Reid

Introduction

Knowledge of the safe use of Oxygen and methods to assess the adequacy of Oxygen therapy are essential for the Foundation Doctor. Arterial Blood Gas (ABG) analysis is considered the gold standard for the measurement of oxygenation (PaO_2 sufficient to prevent anaerobic metabolism), alveolar ventilation ($PaCO_2$), acid-base status (H+/pH) and allows the detection of possible Ventilation-Perfusion (V/Q) mismatch (using the Alveolar-arterial or 'A-a' gradient).

Case 1

A 74-year old man with known COPD presents with an infective exacerbation. Oxygen saturations (SpO_2) at presentation are 84% on room air. An ABG performed on an FiO_2 of 0.28 shows H+ 49, $PaCO_2$ 7.2, PaO_2 7.3, HCO_3 29. Normal values ABG analysis are represented in Table 1.

Parameter	Normal Values
PaO_2	12 – 15kPa
$PaCO_2$	4.4 – 6.1kPa
H^{+*}	36 – 44 nmol/l
HCO_3^-	21 – 27.5 nmol/l
Base Excess	-2 to +2 mmol/l

Table 1 – Normal values for ABG analysis

**Some ABG analysers present a pH value instead, normal values are 7.35 – 7.45*

How much Oxygen should you give and how?

Oxygen can be administered using Uncontrolled or Controlled methods of deliveriy (Table 2). Prior to performing an ABG, patients with risk factors for hypercapnoeic respiratory failure (COPD, morbid obesity, neuromuscular disorders, chest wall deformities) should have supplemental Oxygen aiming to achieve SpO_2 of 88-92% using a controlled oxygen delivery device 1. An initial FiO_2 of 0.28 using a 28% Venturi (Fixed-flow device) at 4L/min is recommended. Oxygenation should be reassessed according to the patient's clinical state (respiratory rate and effort) and SpO_2, 5 minutes after the initiation of Oxygen therapy (1).

	Uncontrolled (High-flow or Variable) **Oxygen therapy**	**Controlled** (Low-flow or Fixed) **Oxygen therapy**
Devices	Nasal Cannulae (FIGURE 1), Simple Face Masks, Non-rebreathe/Reservoir Mask (FIGURE 2)	Fixed-flow (Venturi) masks – Pure Oxygen delivered via a fixed jet which entrains surrounding air to achieve a desired concentration of Oxygen (FIGURE 3)
Indications	Supplemental Oxygen when there is no concern of hypercapnoeic respiratory failure secondary to excessive Oxygen administration	Supplemental Oxygen when ventilation is dependent on hypoxic drive
Examples of clinical presentations	Sepsis / Pneumonia Pulmonary Embolism Acute Pulmonary Oedema Exacerbation of Asthma	Exacerbations of COPD Deteriorations in stable ventilatory failure (Obesity hypoventilation syndrome, Neuromuscular disease)
Target saturations	94 – 98%	88 – 92%

Table 2 – Comparison of Uncontrolled and Controlled Oxygen Therapy (2)

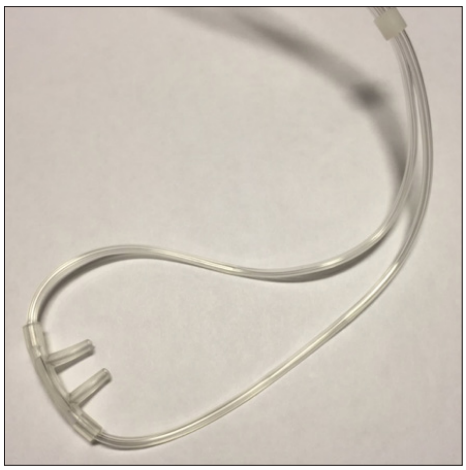

Figure 1 – Nasal Cannulae

Figure 2 – Non-rebreathe/Reservoir Mask; Also known as a Trauma Mask

Figure 3 – A selection of Venturi mask adaptors, each with pre-specified FiO_2 and flow-rate of Oxygen required to achieve FiO_2

ARTERIAL BLOOD GAS (ABG) INTERPRETATION & OXYGEN ADMINISTRATION

PP Velu, PA Reid

Do I need to perform an ABG?

ABG measurement is indicated in patients with exacerbations of COPD who are referred to hospital (1, 3). Some patients are susceptible to hypercapnoeic respiratory failure, even at SpO_2 of 88-92%. If the ABG does not show hypercapnoea, revise target saturations to 94 – 98% and re-check ABG in 30 to 60 minutes (1). ABG measurements should be repeated regularly according to response to treatment.

What does the ABG show?

A low PaO_2 with a high $PaCO_2$ suggests hypercapnoeic (or Type 2) respiratory failure with a respiratory acidosis. This is in contrast with purely hypoxic (or Type 1) respiratory failure where there is a normal or low $PaCO_2$ (suggesting a degree of hyperventilation to increase PaO_2 and 'blow-off' CO_2).

What is the appropriate management?

Initial treatment would be with oral Prednisolone (or IV Hydrocortisone) nebulised bronchodilators and antibiotics. Ensure nebulisers are driven with air and not Oxygen as excessive supplemental Oxygen may worsen hypercapnoeic respiratory failure. The gas being used to drive a nebuliser should always be specified in the prescription (1, 3).

An ABG repeated 2 hours later shows H+ 54, $PaCO_2$ 8.1, PaO_2 7.2, HCO_3- 31, suggesting progressive hypercapnoeic respiratory failure. Non-Invasive Ventilation (NIV) should now be considered following the maximal medical therapy for 1 to 2 hours 3. A review of contraindications (Table 3) is required before proceeding (4).

- **Pneumothorax**
- **Cardiorespiratory arrest**
- **Inability to protect airway**
- **Coma (GCS <8)**
- **Facial trauma or burns**
- **Inability to clear secretions**
- **Vomiting or haematemesis**
- **Confusion or agitation**
- **Severe hypoxaemia**

Table 3 – Contraindications for NIV in patients with Hypercapnoeic Respiratory Failure

Bi-level positive pressure ventilation ('BiPAP' is a trade name and is often used synonymously) has been shown to be efficacious in the management of Type 2 Respiratory Failure: reducing mortality and need for intubation whilst providing symptomatic relief. Bi-level aids ventilation using a higher inspiratory positive airway pressure (IPAP) than expiratory positive airway pressure (EPAP). The difference between IPAP and EPAP is defined as the 'Pressure Support' that is provided, aiding alveolar recruitment and ventilation (4, 5).

Provision for NIV varies according to clinical site and you should familiarise yourself with facilities available in your hospital. Ceiling of care should be determined prior to commencement of NIV should respiratory failure and clinical state not improve despite NIV. Any decision to proceed to NIV should thus be undertaken having consulted senior medical staff (including HDU/ICU) and with the patient themselves.

Case 2

A 42-year old lady who has recently been abroad presents with a 4-day history of worsening dyspnoea, minimally productive cough and general malaise. Observations at presentation: respiratory rate 28 breaths/minute, SpO_2 82%, heart rate 122 bpm, BP 98/65mmHg and Temperature 38.6^{0}C. Chest X-Ray reveals right basal consolidation.

How much Oxygen should we give and how?

The clinical picture is one of severe sepsis from a likely respiratory source. Given that she is still making respiratory effort, supplemental Oxygen should be given using a reservoir/non-rebreathe mask at 15L/min, aiming for target SpO_2 of 94 – 98% (1).

Do I need to perform an ABG?

Yes. In addition to parameters mentioned previously, some point-of-care ABG analysers also provide a measurement of lactate, which is part of the 'Sepsis Six' bundle and correlates with mortality in sepsis 6. An ABG on room air shows: H+ 54, $PaCO_2$ 2.4, PaO_2 7.1, HCO_3- 19.

What does the ABG show?

The ABG shows a metabolic acidosis (likely driven by lactate in the context of sepsis) and Type 1 respiratory failure. The low $PaCO_2$ in this case could be due to a degree of hyperventilation. Her SpO_2 only improves to 90% on 15L/min supplemental Oxygen via a reservoir/non-rebreathe mask and the patient remains tachypnoeic. A repeat ABG on 15L/min shows H+ 56, $PaCO_2$ 2.6, PaO_2 7.5, HCO_3- 18.

Does this patient need Intubated?

This patient is in Type 1 Respiratory Failure that is not responding to maximal supplemental oxygen that can be provided in the ward setting. Note that 15L/min oxygen via a reservoir mask only delivers an FiO_2 of approximately 0.8 and that the patient may require a higher FiO_2, or a similar FiO_2 with a degree of PEEP (positive end-expiratory pressure) to improve alveolar ventilation and oxygenation (5). Given the patient's prior level of functioning, lack of co-morbidities and age, she would be a candidate for intubation and mechanical ventilation and a conversation with Intensive Care should be had.

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CPAP or High-flow Oxygen via Nasal Cannulae (HFNC) is occasionally used as a means to improve oxygenation and avoid intubation in patients with Type 1 Respiratory Failure. The positive pressure generated with CPAP has been suggested to improve alveolar recruitment and oxygenation in severe pneumonia, resulting in a theoretical reduction in the need for intubation. However, no significant differences in mortality and length of hospitalisation have been demonstrated (5). HFNC may play a similar role to CPAP, however evidence suggests no difference in intubation rates when HFNC was compared to standard oxygen therapy and high-flow oxygen therapy but a significant difference in 90-day mortality in favour of HFNC (7).

These methods should not delay definitive management in patients who are candidates for intubation and mechanical ventilation. Thus, any decision to consider CPAP of HFNC to be made in collaboration with medical support from Intensive Care and preferably be undertaken in a Level 2 or 3 area (8).

Case 3

A 34-year old man is admitted with hypoxaemia from his GP surgery. He has a history of IV drug misuse and is on daily Methadone and Diazepam. He smokes 20 cigarettes per day and also reports smoking cannabis. He denies any symptoms. SpO_2 on room air is 88% with a respiratory rate of 10 breaths per minute. An ABG on room air shows H+ 45, $PaCO_2$ 9.1, $PaO2_2$ 7.2, HCO_3- 39.

What does the ABG show?

Hypercapnoeic (Type 2) respiratory failure. The high HCO_3- suggests a degree of chronic compensation but considering the borderling acidaemia on this ABG, one should always be wary that the patient is at risk of decompensated hypercapnoeic respiratory failure.

What is the underlying pathology?

The clue is in the history and low respiratory rate. The most likely explanation for the chronic hypercapnoeic respiratory failure in this case is respiratory depression (effectively ventilatory dysfunction) secondary to opiate or benzodiazepine use. Although the high HCO3- suggests a degree of chronicity, a primary respiratory cause for hypoxaemia still needs to be excluded. One way to do this would be by calculating the Alveolar-arterial (or A-a) gradient.

$$PIO_2 - [PaO_2 + PaCO_2/0.8]$$

PIO2 – Inspired PO2 (in kPa). When breathing Air (FiO2 =0.21), the PIO2 is 0.21 x (100 – 7) = approximately 20kPa; where 100kPa is the atmospheric pressure and 7kPa is the water vapour pressure as inspired air is humidified). Thus, when FiO2 = 0.28, PIO2 is approximately 23kPa.
PaO2 – Arterial PO2 (kPa)
PaCO2 – Arterial pCO2 (kPa)
0.8 – Respiratory coefficient

Figure 4 – Formula for the calculation of A-a gradient (2)

What is the A-a gradient?

The A-a gradient provides a measure of the difference between alveolar (A) and arterial (a) Oxygen concentration, or $PAO_2 - PaO_2$. The A-a gradient can help localise the cause of hypoxaemia to intra-pulmonary (A-a gradient increased), indicating V/Q mismatch of left-to right shunting or extra-pulmonary (A-a gradient normal) (2).

In normality, there is relative under-perfusion of the apices and over-perfusion of the bases. Thus, an A-a gradient of 1 – 2kPa is acceptable in a healthy, adult non-smoker. The A-a gradient increases with age, and an A-a gradient of 2 – 3 kPa is acceptable in the elderly.

Using the formula in Figure 4, the A-a gradient in Case 3 can be calculated as : 20 – [7.2 + 9.1/0.8] = 1.4kPa, which is normal, suggesting the problem is extra-pulmonary or purely ventilatory.

What is the appropriate management?

The patient should be observed to ensure that SaO_2 does not fall below 88 – 92%, respiratory rate does not fall further and that acidosis does not worsen. Should these occur, cautious Oxygen therapy and a trial a Naloxone would be indicated. Naloxone is a reversible, short-acting opiate antagonist and may reverse the effects of opiate excess briefly to improve ventilation and improve acidosis. Seek senior support.

Conclusion

An ABG is an essential investigation in the assessment and diagnosis of patients with respiratory disease. As with any other investigation, practice of interpreting results will consolidate your knowledge and demonstrate its utility in clinical practice.

Multiple-Choice Questions

1. Calculate the A-a gradient for the patient in Case 2, based on her ABG on room air at presentation and the formula in Figure 4: H+ 54, $PaCO_2$ 2.4, PaO_2 7.1, HCO_3- 19

A. 2kPa
B. 3kPa
C. 6kPa
D. 10kPa
E. 12kPa

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2. Which of the following conditions is most likely to cause hypoxemia with a normal A-a gradient?

A. Pulmonary embolism
B. Obstructive Sleep Apnoea Hypoapnoea Syndrome (OSAHS)
C. Eisenmenger syndrome
D. Pulmonary oedema
E. Idiopathic Pulmonary Fibrosis

3. Which of the following statements regarding supplementary Oxygen therapy is true?

A. Patients with suspected myocardial infarction should be given supplemental Oxygen, aiming for target SpO_2 of 100%
B. Supplemental Oxygen delivered via a Non-rebreathe mask at 15L/min generates an FiO_2 of 1.0
C. All patients with COPD should receive supplementary Oxygen, aiming for target SpO_2 of 88-92%
D. Nasal cannulae can deliver supplementary Oxygen to a maximum flow rate of 4L/min
E. The FiO_2 generated by a Venturi mask can be titrated by altering the Oxygen flow rate (L/min)

4. A 48-year old lady is referred to hospital with an exacerbation of COPD. She has a history of eczema, allergic rhinitis and smokes 5 cigarattes per day. On examination, she is noted to have widespread wheeze. Bloods are unremarkable except for an eosinophilia and a Chest X-ray is normal. Respiratory rate is 28 breaths per minute. ABG on 15L/min Oxygen via a Non-rebreathe mask at presentation: H+ 49, $PaCO_2$ 6.6, PaO_2 7.9, and HCO_3 27. She has been treated with oral Prednisolone and Nebulisers. What is the appropriate next step in her management?

A. Continue with back-to-back nebulisers until 1 hour from presentation
B. Urgent transfer to the Respiratory ward for Bi-level positive pressure ventilation
C. Urgent referral to Critical Care for initiation of High-flow nasal cannulae
D. Urgent referral to Critical Care for consideration of intubation and mechanical ventilation
E. Give IV Doxapram

5. A 72-year old lady with a history of COPD who is on long-term domiciliary Oxygen (2L/min for at least 15 hours per day) is referred to hospital with a suspected exacerbation of COPD. She arrives via ambulance and an ABG on arrival on an FiO_2 of 0.35 shows H+ 56, $PaCO_2$ 8.2, PaO_2 9.2, HCO_3 32. What would you do about her Oxygen therapy?

A. 15L/min Oxygen via a non-rebreathe mask
B. Increase to 40% via Venturi (FiO_2 0.4)
C. Increase to 60% via Venturi (FiO_2 0.6)
D. Urgent transfer to Respiratory ward for commencement of Bi-level positive pressure ventilation
E. Reduce to 24% via Venturi (FiO_2 0.24)

MCQ Answers & Teaching Notes

Question 1: Answer: D

The A-a gradient for the initial ABG from Case 2: 20 – [7.1 + 2.4/0.8] = 9.9kPa (rounded up to 10kPa). The A-a gradient is >2kPa, which would suggest an intra-pulmonary cause for hypoxaemia, which would be consistent with pneumonia causing V/Q mismatch.

Question 2: Answer: B

The A-a gradient is elevated in conditions where there is a V/Q mismatch (Pulmonary embolism, Pulmonary oedema) and reduced diffusion capacity (Idiopathic Pulmonary Fibrosis).

Eisenmenger syndrome is the development of right-to-left shunting of blood in patients with long-standing left-to-right shunts that lead to pulmonary hypertension (most commonly due to ventricular septal defects, atrial septal defects and patent ductus arteriosus). Right-to-left shunts are another cause of elevated A-a gradient. OSAHS is predominantly a problem of ventilation and can lead to chronic hypercapnoeic respiratory failure but is not often associated with an elevated A-a gradient.

Question 3: Answer: D

Patients with suspected myocardial infarction or acute coronary syndrome often do not require supplemental Oxygen and if required, Oxygen should be titrated to target SpO_2 of 94 – 98% as there is concern that excessive Oxygen therapy could lead to further myocyte damage (1).

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Supplemental Oxygen delivered via a Non-rebreathe mask at 15L/min generates an FiO_2 of approximately 0.8. Some patients with mild COPD may not be at risk of developing hypercapnoeic respiratory failure and others may require target saturations <88% to ensure they do not develop hypercapnoeic failure. Target SaO_2 of 88 – 92% are a guide, but this should always be confirmed using an ABG. A Venturi mask generates a fixed FiO_2 at a pre-specified flow-rate of Oxygen and titration should be done by switching masks.

Question 4: Answer: D

Be cautious of labels. Although this patient has been referred into hospital with a provisional diagnosis of 'Exacerbation of COPD', the history of atopy, relatively minimal smoking history and eosinophilia point towards an underlying diagnosis of Asthma. The ABG shows hypercapnoeic respiratory failure, which in a patient with an exacerbation of asthma would qualify them as having 'near-fatal asthma'.

The immediate priority here would be a referral to Intensive Care for consideration of intubation and mechanical ventilation. Treatment with nebulised bronchodilators should be continued and consideration should be given to the use of IV Magnesium Sulphate and IV Aminophylline. Doxapram is a respiratory stimulant that can be used in the manangement of hypercapnoeic respiratory failure (commonly secondary to COPD) when a patient is not a candidate for Bi-level positive pressure ventilation.

Question 5: Answer: E

The ABG on arrival suggests a degree of Hypercapnoeic respiratory failure and subtle Oxygen toxicity. Given that she is on Long-term domiciliary Oxygen, she is not likely to require target SpO_2 of more than 88 – 92% and she may have had supranormal Oxygen saturations as a result of supplemental Oxygen on her way into hospital.

The appropriate management in this scenario would be to reduce the FiO_2 to 0.28, aiming for target SaO_2 of 88 – 92% and repeat an ABG in 30 to 60 minutes. She will also need treated for her exacerbation of COPD with nebulisers, steroids and antibiotics (if an infective exacerbation is suspected). Should maximal medical therapy and controlled Oxygen not improve her acidosis, consideration should be given to Bi-level positive pressure ventilation.

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ABSTRACT FOR ASBESTOS RELATED LUNG DISEASES

J Ibrahim, A Ali, I Hussain

Introduction

Asbestos related lung diseases are the disorders of lung and pleura caused by exposure to asbestos fibres. Asbestos related diseases include non-malignant disorders such as pleural plaques, diffuse pleural thickening, asbestosis, benign pleural effusion and malignant conditions such as mesothelioma and lung cancer. They are occupational diseases in majority of cases since asbestos was widely used in the past in many industries. In this article we review a case of malignant pleural mesothelioma followed by discussion on asbestos related lung diseases and compensation available.

Case History

A 84 year old gentleman who was a lifelong non-smoker presented with an 8 week history of progressive shortness of breath on exertion, right sided non-pleuritic chest pain which was described as a dull ache and a chronic cough. He denied any haemoptysis, weight loss or voice change; his appetite was stable.

His past medical history included: type 2 diabetes mellitus and hypercholesterolaemia. His WHO performance status was 2 (ambulatory and capable of all selfcare but unable to carry out any work activities, up and about more than 50% of waking hours), due to shortness of breath. He was a retired floor tiler with previous significant chrysotile asbestos exposure between 1954 and 1980.

Examination revealed evidence of a right sided pleural effusion. There was no evidence of finger clubbing or cervical lymphadenopathy, the rest of the clinical examination was unremarkable and the pain could not be elicited on palpation. Chest radiograph (Fig 1) demonstrated a right sided pleural effusion and computerised tomography (CT) scan (Fig 2) confirmed the presence of a pleural effusion in addition to widespread irregular nodular pleural thickening.

A pleural biopsy was performed via Video Assisted Medical Thoracoscopy (VATS) and this yielded a diagnosis of desmoplastic malignant mesothelioma. He was initially considered for palliative chemotherapy, but unfortunately his condition deteriorated significantly and was managed with supportive care. He died 4 months after presentation with palliative care support, which included pain control and management of his breathlessness.

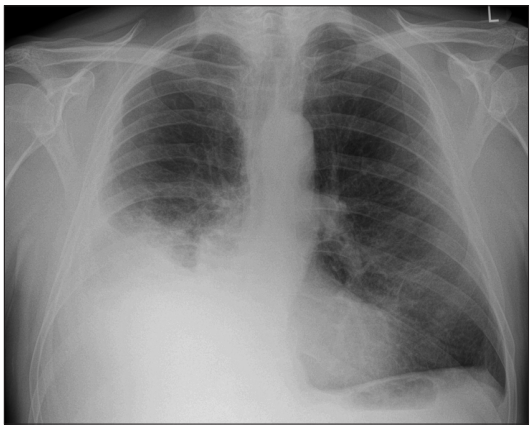

Figure 1

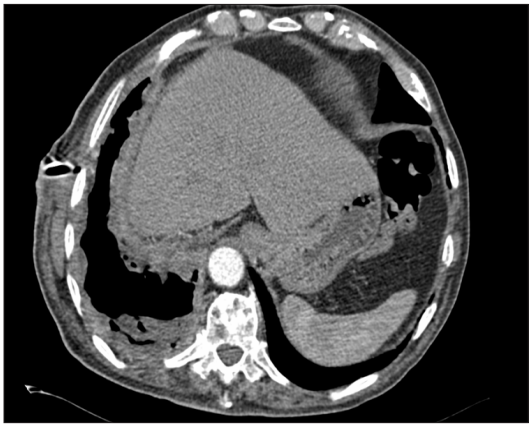

Figure 2

Discussion

Inhalation of asbestos fibres can lead to variety of respiratory diseases from benign to malignant. Asbestos was commonly used in the past in a variety of industries, including ship building and construction. Exposure occurred via variety of occupational and non/para occupational settings. Occupations commonly associated with asbestos exposure include: asbestos mining, construction, plumbing (installing heating insulation) and ship building. More recently, other occupations, such as school teachers (due to asbestos exposure from old school buildings) have started to develop asbestos related lung diseases.

Asbestos fibres are divided into two categories based on their shape: chrysotile, has long serpentine fibres that have the appearance of long, curly strands; whereas amphibole fibres (crocidolite, amosite, tremolite) have the appearance of long, straight, rod-like structures. Chrysotile fibres accounted for over 90 percent of the asbestos in commercial use and is generally considered less toxic than the amphibole fibres.

Benign Conditions

Asbestos exposure can lead to a host of benign pathologies including: pleural plaques, benign asbestos pleural effusion, diffuse pleural thickening and asbestosis. We will discuss pathophysiology, incidence and complications of each phenomenon in greater detail.

1) Pleural Plaques

The commonest manifestation of an exposure to asbestos is the development of pleural plaques, these are well circumscribed areas of hyaline fibrosis of the parietal pleura and visceral pleura (1). Pleural plaques are considered a benign entity and merely signify previous asbestos exposure. Pleural plaques can occur with relatively low level expsoure and usually appear 12 to 20 years after asbestos exposure (2). Pleural plaques are almost asymptomatic and are found as incidental findings on plain chest radiograph or CT scan of thorax. They are usually symmetrical, bilateral and are found in up to 50% of asbestos exposed workers.

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The British Thoracic Society (BTS) acknowledges the anxiety and stress occasionally caused by the existence of pleural plaques in patients with prior asbestos exposure. It is of paramount importance to explain to patients the distinction between pleural plaques and other asbestos related lung diseases; pleural plaques indicate asbestos exposure, but malignancy does not arise from the plaques themselves. There are no specific treatments for pleural plaques and repeat chest radiographs are not warranted in the absence of sinister symptoms (1). Following a House of Lords ruling, pleural plaques are not compensable. (1)

2) Benign Asbestos Pleural Effusion (BAPE)

Benign Asbestos Pleural Effusion (BAPE) was first described in 1964 as an exudative (high protein content) pleural effusion in the presence of previous asbestos exposure and the absence of an alternative cause for the effusion 4. The effusions tend to be haemorrhagic in nature and usually resolve following pleural aspiration (4,5). Patients with BAPE tend to be asymptomatic and clinical signs include dull percussion note and reduced air entry at the side of the effusion (5). BAPE can only be diagnosed with reasonable confidence after thorough investigations and a prolonged period of follow up. Investigations for this benign condition include: diagnostic/ therapeutic aspiration of effusion, CT Thorax and thoracoscopy (4).

3) Diffuse Pleural Thickening (DPT)

DPT is defined as extensive fibrosis of the visceral pleura with 'unilateral or bilateral diffuse pleural thickening with obliteration of the costophrenic angle(s)' due to working with or handling of asbestos (6). DPT may co-exist with other asbestos-related pleural diseases including pleural plaques and it is occasionally predated by BAPE. The pathophysiology of DPT is thought be secondary to the formation of a fibrinous intrapleural matrix as a consequence of asbestos exposure. (7)

DPT is considered dose related and clinical signs include dyspnoea and chest pain. Distinguishing DPT from pleural plaques may prove difficult on a conventional chest radiograph; lack of calcification and ill-defined costophrenic angle(s) obliteration points towards DPT rather than pleural plaques. (8). High resolution CT scan is more sensitive and specific than a plain chest radiograph.

Furthermore, magnetic resonance imaging (MRI) and/or a positron emission tomography (PET) scan can aid in distinguishing between DPT and malignant mesothelioma due to increased uptake of tracer. DPT can lead to a restrictive picture on spirometry and in the rare cases, can cause ventilatory failure. There are no specific treatments for DPT and the management is supportive by controlling symptoms such as breathlessness with opiates.

4) Asbestosis

Asbestosis is pneumoconiosis caused by inhalation of asbestos fibres. This condition is dose related, and a significant asbestos exposure is required. It is an inflammatory and fibrotic process affecting the pulmonary parenchymal cells. The most widely held theory for pathophysiology of asbestosis is that the fibres exert a direct toxic effect that leads to the release of inflammatory mediators including oxygen radicals, cytokines and growth factors. (9)

Most patients with asbestosis are asymptomatic and the latency period is 20 to 30 years. Dyspnoea on exertion is the commonest presentation of asbestosis followed by dry cough. Physical examination often reveals bi-basal end inspiratory crackles and as the disease progresses finger clubbing, peripheral and/or central cyanosis may develop. (9)

A detailed history of asbestos exposure and reasonable latent period is crucial for a diagnosis of asbestosis. Plain chest radiograph may show other asbestos related changes such as pleural plaques and bilateral small opacities with predilection to the lower lobes, though the middle and upper lobes may be involved. (10) HRCT is more sensitive and specific than plain chest radiograph.

Typical HRCT findings include intralobular interstitial thickening, interlobularseptal thickening and sub-pleural reticulations; In advanced disease, ground glass opacities and honeycombing may be present. (9) Full pulmonary function tests classically show a restrictive impairment with reduced lung volumes and gas transfer factor (DLCO) (10). Histological confirmation is reserved for the rare cases where diagnostic doubt remains and this can be achieved via VATS(2).

The mainstay of treatment of asbestosis is supportive with emphasis on prevention of further exposure, smoking cessation and provision of pneumococcal and influenza vaccination. In progressive disease, palliative measures may be appropriate (i.e.: oxygen therapy for respiratory failure, diuretics for right heart failure and opioids for chest pain). (10)

Malignant Conditions

1) Malignant Pleural Mesothelioma (MPM)

MPM is a rare and highly aggressive tumour. Asbestos exposure is the only risk factor. Its incidence is 1.25/100,000. Prognosis remains poor with median survival of 8 - 14 months. (12) There are three main histological types (epithelioid, sarcomatous and mixed) with 60% being epithelioid.

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Aetiology

· Occupational exposure to asbestos fibres – This accounts for up to 85% of cases of mesothelioma. Hence it's classification as an occupational lung disease. The mean latency of MPM after exposure to asbestos is 40 years accounting for diagnostic difficulty. (13) Among commercially used fibres, crocidolite and amosite have highest carcinogenic pleural potency.

· Para occupational exposures – In household contacts of asbestos workers, mainly because of domestic exposure via clothes used at work.

· Environmental mesotheliomas – These are either linked to: a) ''natural'' exposure in areas of the world where asbestos (generally tremolite) exists as a geological component of the soil (Turkey, Corsica, Cyprus and New Caledonia) b) where it is often used for white-washing walls of houses, c) neighbourhood exposures in people living close to asbestos mines or factories. (13)

Diagnosis

It is essential to use a combination of history, examination, radiology and pathology to reach a diagnosis of malignant mesothelioma (Figure 3).

Clinical Features

The clinical manifestations of MPM are usually nonspecific and insidious and should not be used alone as diagnostic criteria. Patients usually present with advanced disease with symptoms of chest pain, and/or dyspnoea. Physical examination may reveal signs of a unilateral pleural effusion.

Investigations

· Chest radiograph: unilateral pleural effusion, pleural thickening or a mass.

· CT Thorax: features of asbestos exposure such as pleural plaques, pleural thickening or lung fibrosis. Diffuse or nodular pleural thickening, especially on the mediastinal pleural surface, are suggestive of MPM, however CT alone is not diagnostic.

· Pleural aspiration: initial diagnostic investigation; although able to identify mesothelial cells on immunocytochemistry, it may be difficult to distinguish malignant from reactive cells.

· Pleural Biopsy: pleural tissue can be obtained for diagnosis either via ultrasound guided percutaneous fine needle biopsy, thoracoscopy or surgical biopsy.

Fine Needle biopsy for diagnosis of MPM has a low sensitivity (30%). (13) In the presence of pleural fluid, thoracoscopy should be preferred for diagnostic investigation, allowing complete visual examination of the pleura and adequate pleural biopsy samples for a tissue diagnosis. This provides a diagnosis of MPM in >90% of cases. (13)

After drainage of pleural effusion, talc pleurodesis can be performed to prevent recurrence of effusion.

· PET: May be useful in differentiating benign from malignant lesions and to assess lymph node status.

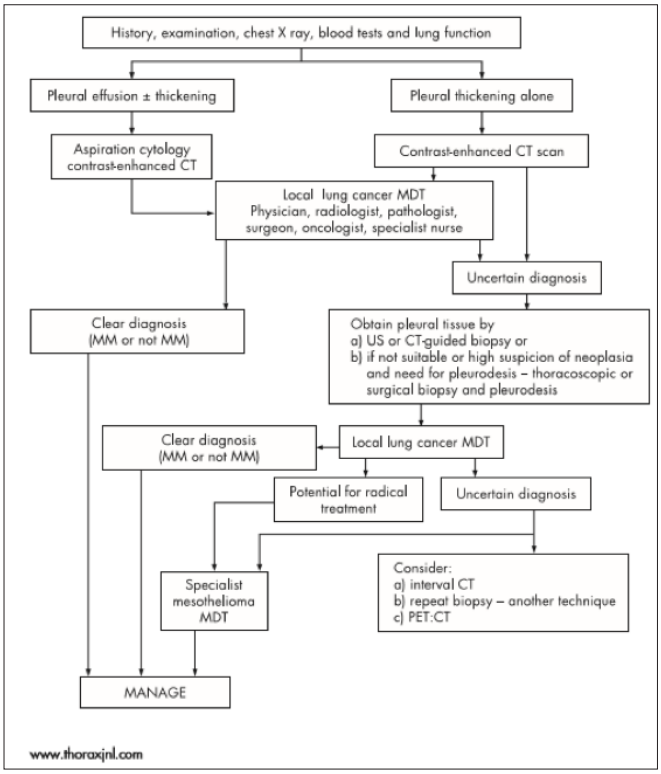

Figure 3

Management

a) Multi-disciplinary team (MDT)

All cases of suspected MPM should be discussed at a MDT, often this is the lung cancer MDT, though some regions have specialist mesothelioma MDTs. The MDT should include surgeons, physicians, specialist nurses, radiologists, oncologists and palliative care specialists. All treatment decisions will take into account: patient wishes, performance status and stage of disease.

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b) Surgery (13)

The role of surgery in MPM is uncertain. Curative treatment is considered only in epithelioid tumours and in clinical trial setting.

2 types of surgery

- Extra pleural pneumonectomy,
- Debulking surgery.

c) Radiotherapy

Radiotherapy is very rarely used for curative intent or as an adjunct to surgery. But it is more commonly used for palliative pain control. Prophylactic radiotherapy can also be used to prevent the risk of tumour seeding from scars produced from biopsy or pleural drainage. PIT (Prophylactic Irradiation of Tracts) is an on-going Phase III Randomised Trial looking at the benefit of radiotherapy in patients with MPM following invasive chest wall intervention. (14,15)

d) Chemotherapy

All patients with mesothelioma and WHO performance status of 0-2 should be considered for palliative chemotherapy. First line combination chemotherapy includes Cisplatin with Pemetrexed or raltitrexed. Sarcomatoid and mixed subtypes have worse outcomes compared with epitheliod mesothelioma.(16)

e) Management of pleural effusion

Early and successful talc pleurodesis is the key to symptom control and prevention of trapped lung, where the lung does not re-expand after the drainage of the pleural effusion. This can be achieved via Intercostal drain or thoracoscopy. Indwelling Pleural Catheter (IPC) can be considered if pleurodesis fails or in case of trapped lung. (15)

f) Supportive care

Given the poor prognosis of mesothelioma, most patients require early referral to palliative care team, for help in pain and breathlessness management.

2) Bronchogenic carcinoma:

Both small cell and non-small cell lung cancers are associated with asbestos exposure. The increased risk of lung cancer associated with asbestos is greatly magnified by coexisting exposure to tobacco smoke. Relative risk (RR) of lung cancer is increased to 59 in smokers with asbestos exposure as compared to RR of 6 in non-smokers with asbestos exposure (10).

3) Other Malignancies

These include cancers of the larynx, oropharynx, kidney, oesophagus, and biliary system. (17)

Compensation for asbestos related diseases

Patients with the following asbestos related diseases can claim compensation from the government (Department for Work and Pensions) provided that they were not self-employed when their exposure occurred: (11)

1. Diffuse Pleural Thickening

2. Asbestosis

3. Lung cancer in association with other asbestos-related diseases

4. Mesothelioma

Pleural plaques on it is own does not warrant compensation in England and Wales. The degree of patient's disability and the age of disease onset are taken into account. Patients must initiate their claims within three years of diagnosis and their next of kin are allowed to claim on their behalf within 6 months posthumously. Furthermore, patients can also claim for compensation directly from their employer's insurer through Civil Law, even if the employer is now out of existence. (2,11)

MCQs

Q1: Which of the following statements is correct regarding pleural plaques?

a) Pleural plaques are one of the commonest manifestations of asbestos exposure.

b) Patients with pleural plaques are eligible for compensation in England and Wales.

c) There is enough evidence to suggest that pleural plaques are pre-malignant.

d) Pleural plaques develop one to two years after asbestos exposure.

e) Pleural plaques are usually asymmetrical and commoner on the right hemithorax.

ABSTRACT FOR ASBESTOS RELATED LUNG DISEASES

J Ibrahim, A Ali, I Hussain

Q2: The following statements are correct for asbestosis except:

a) The commonest presentation of asbestosis is a pleuritic type chest pain.

b) Finger clubbing and central cyanosis are one of the early manifestations of asbestosis.

c) Plain chest radiograph is more sensitive and specific than HRCT.

d) Pleurectomy is the gold standard treatment for asbestosis.

e) Characteristic full lung function test finding in asbestosis is restrictive impairment with reduced lung volume and DLCO.

Q3: which of the following statements is correct regarding Malignant mesothelioma:

a) A common malignancy with good prognosis.

b) Usually secondary to cigarette smoking.

c) Thoracoscopy (medical or VATS) has higher sensitivity than fine needle biopsies in diagnosing malignant pleural effusions.

d) Patients with malignant mesothelioma are not eligible for compensation.

e) Indwelling Pleural Catheters (IPC) are contraindicated in malignant mesothelioma.

Q4: All of the following are indications for compensation except:

a) Diffuse pleural thickening.

b) Pleural Plaques.

c) Asbestosis.

d) Lung cancer in association with other asbestos related diseases.

e) Mesothelioma.

Q5: All of the following are true regarding management of mesothelioma except:

a) Surgery is always considered as first line treatment.

b) Radiotherapy is more commonly used in the palliative setting.

c) Patients with WHO performance status 0-2 are considered for chemotherapy.

d) Patients with recurrent effusion are considered for talc pleurodesis.

e) Palliative team referral should occur early in the management of mesothelioma.

Answers

Q1: a) Pleural plaques are one of the commonest manifestations of asbestos exposure.

Q2: e) Characteristic full lung function test finding in asbestosis is restrictive impairment with reduced lung volume and DLCO.

Q3: c) Thoracoscopy (medical or VATS) has higher sensitivity than fine needle biopsies in diagnosing malignant pleural effusions.

Q4: b) Pleural Plaques.

Q5: a) Surgery is always considered as first line treatment.

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ABSTRACT FOR ASBESTOS RELATED LUNG DISEASES

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BRONCHOPULMONARY ASPERGILLOSIS

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Abstract

Broncho pulmonary aspergillosis is a clinical syndrome of distinct clinical entities caused by aspergillus species commonly aspergillus fumigatus. The clinical manifestations of BPA are variable and depend on the underlying lung disease and immune status of the patient. The BPA clinical entities include allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, chronic necrotizing aspergillosis (CNA) or invasive pulmonary aspergillosis (IPA).

Clinical features of BPA are variable and depend on the particular clinical entity of the disease and the associated underlying pulmonary disease. Some common symptoms include malaise, cough, wheeze, recurrent chest infections and haemoptysis which may be life threatening. BPA is generally a progressive disease that causes significant structural and functional damage to the lungs. It consequently carries substantial morbidity and mortality risk. Early and accurate diagnosis is vital so treatment can be initiated in a timely manner which can be effective and rewarding.

Case History

A sixty years old lady of Pakistani origin presented to the chest clinic with poor asthma control and frequent exacerbations requiring oral corticosteroids (OCS) and antibiotics treatment. She was treated for pulmonary tuberculosis 35 years ago. She was on symbicort turbohaler (200/6 µg) two inhalations twice daily and salbutamol inhaler for asthma treatment.

She had received 6 courses of OCS and antibiotics in the preceding 12 months for severe exacerbations of asthma. Chest auscultation revealed scattered polyphonic ronchi and basal crepitations. There was proximal bilateral patchy pulmonary shadowing in both upper zones and the lower right lower zone on the chest X-ray. (Figure 1). Results of blood investigations and lung function are presented in table 1, and a demonstration of the CT scan of thorax in figure 2.

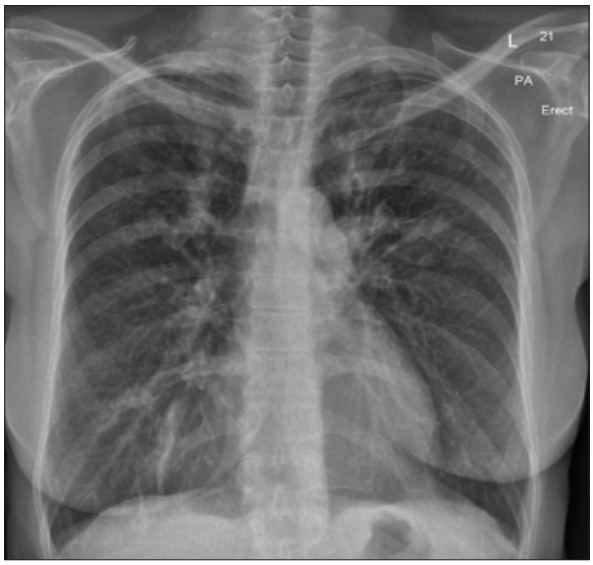

Figure 1: Chest X-ray showing increased peribronchial markings in the hilar, both upper and the right lower zone.

Investigation	Results
White Cell Counts	12.5 x10^9/L (4.00 - 11.00)
Peripheral blood eosinophils	3.14 x10^9/L (0.04 - 0.44)
Total serum immunoglobulin E (IgE)	176 kU/L (0.0 – 200)
Specific IgE to House Dust Mite (SIgE HDM)	7.82 kUA/L (0.00—0.34)
Specific IgE to aspergillus (SIgEAspergillus)	0.82 kUA/L (0.00—0.34)
Specific IgG to aspergillus (SIgGAspergillus)	160 mgA/L (0.00—34.99)
FEV1	1.59L (78% of predicted)
FVC	2.21L (92% of predicted)
FEV1/FVC ratio	72 (93% of predicted)

Table1: Blood results and lung function tests.

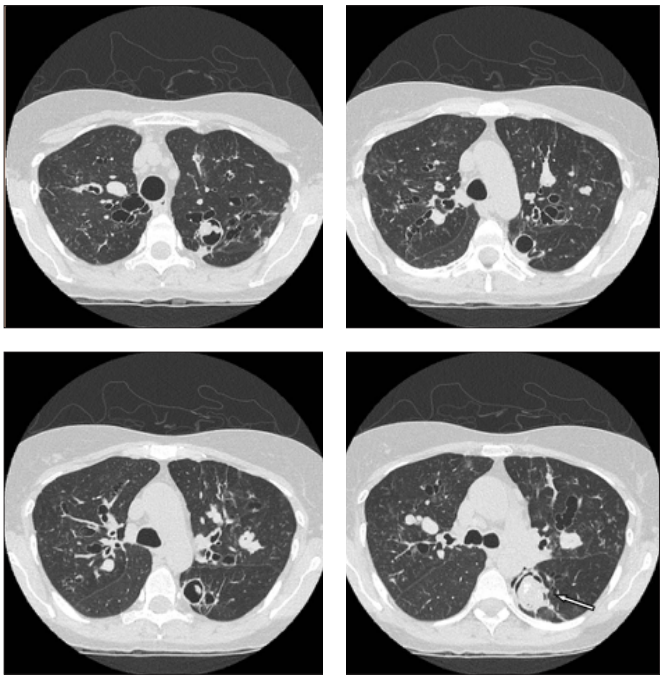

Figure 2: CT scan of thorax demonstrating significant varicose bronchiectasis in both lung fields, alongside areas of mucus plugging and acute bronchiolitis. An aspergilloma is seen in the left lower lobe (arrow).

The sputum mycology and mycobacteriology cultures were negative. Consequently, on the basis of the typical radiological changes, peripheral blood eosinophilia and positive specific IgE/IgG to aspergillus, a diagnosis of ABPA with aspergilloma was made. Her asthma treatment was escalated to symbicort 200/6 SMART (2 inhalations twice daily and up to 8 extra inhalations as required).

In addition, due to history of frequent severe exacerbations, she was commenced on oral itraconazole 200mg twice daily, initially for six months, (with a view to extend to minimum of 18 months of therapy). When she was reviewed in clinic two months later, she experienced improvement in her asthma symptoms and no further exacerbations.

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Introduction

Bronchopulmonary aspergillosis is a group of specific pulmonary disorders caused by aspergillus species of which a.fumigatus is commonly responsible for most of the cases. Patients usually present with one or a combination of the following clinical entities:

1) Allergic bronchopulmonary aspergillosis (ABPA)

2) Aspergilloma

3) Chronic necrotising aspergillosis (CNA)

4) Invasive pulmonary aspergillosis (IPA)

Aspergillus fungal spores are ubiquitous and are readily present in indoor atmospheric environment. Aspergillus spores inhalation in a normal lung is harmless, however the presence of an underlying pulmonary disease and/or compromised immune status increase the risk of BPA development.

Figure 3: ABPA (Allergic bronchopulmonary aspergillosis), CAN (chronic necrotising aspergillosis), IPA (Invasive pulmonary aspergillosis). (Diagram modified from reference 3)

Allergic bronchopulmonary aspergillosis (ABPA)

ABPA is a complex hypersensitivity related disease caused by aspergillus species, commonly a. fumigatus. It frequently occurs in patients with asthma and cystic fibrosis (CF).

Pathophysiology of ABPA

The pathophysiology of ABPA has not been entirely elucidated. It generally presents as a complication of persistent asthma and CF. Inhaled conidia of aspergillus fumigatus germinate in the airways and release exoproteases and other products that breach the respiratory epithelium and activate the immune response.

This response includes combinations of aspergillus-specific IgE mediated type I hypersensitivity reaction, specific IgG mediated type III reaction and abnormal T-cell immune responses to aspergillus. Aspergillus specific CD4 +T helper lymphocytes type 2 (Th2) seems to play central role in orchestrating this immune response. ABPA is characterised by marked airway and systemic eosinophilia and elevated specific immunoglobulins (Ig) G, A and E to aspergillus as well as profound increase in "interleukin 4 (IL4) driven" non-specific total serum IgE.

Histological features of ABPA include bronchial impaction by mucus, eosinophilic pneumonia, and bronchocentric granulomatosis. Septate hyphae with acute branching may be seen in the mucus-filled bronchial lumen but fungi do not invade the mucosa.

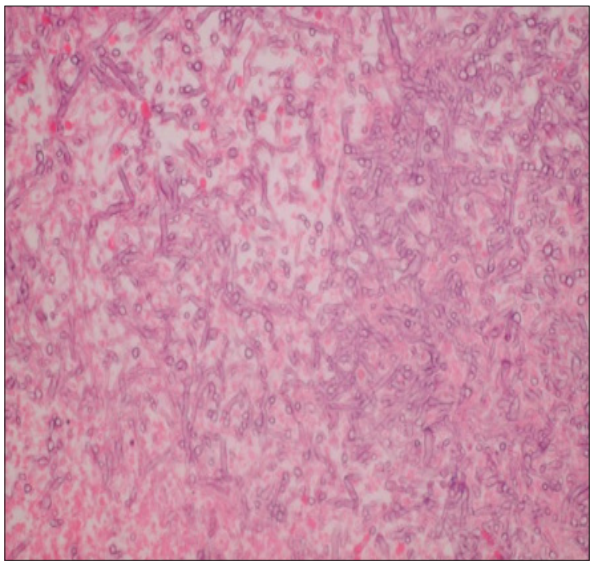

Figure 4: Branching fungal hyphae.

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Clinical Features

ABPA is usually suspected on the basis of clinical history, findings from clinical examination and confirmed by radiological and serological investigations. The presenting features of ABPA include recurrent episodic wheeze, productive cough of sputum containing characteristic brownish plugs, recurrent lower respiratory tract infections, fever, malaise and pleuritic chest pain. Occasionally patients may present with haemoptysis.

Investigations

Blood and radiological investigations play important role to confirm the diagnosis. Bloods tests usually reveal peripheral blood eosinophilia and positive serology for aspergillus in the form of raised specific serum IgE & IgG levels and positive skin prick test to aspergillus.

Radiologically, the chest X-ray may be normal. During acute exacerbations, fleeting pulmonary infiltrates are characteristically seen in upper zones and central locations. Transient linear opacities due to atelectasis caused by mucus impaction are also common findings. There may also be band-like opacities extending from hilum and ending in rounded distal margins (gloved finger sign). The ring sign is also a feature seen due to mucus filled bronchi enface next to pulmonary blood vessel. This usually represents bronchiectasis.

High resolution computerised tomography (HRCT) scan of chest usually shows central bronchiectasis predominantly in upper lobes (figure 5). Fibrosis may be present in later stages.

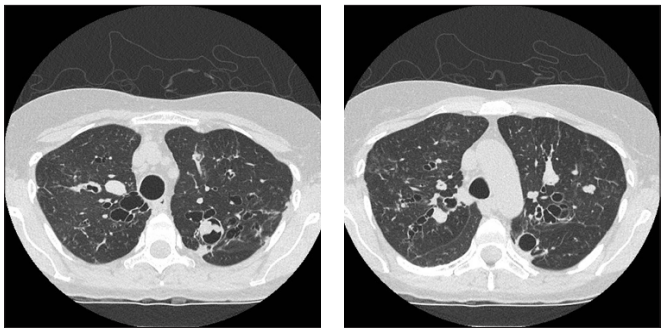

Figure 5: HRCT in ABPA showing central bronchiectasis and mucus impaction .

Diagnosis & Treatment

Diagnosis of ABPA is made with combination of clinical findings and various investigation described above. There is no single diagnostic test for ABPA, nor there a universally accepted set criteria. However diagnostic criteria for ABPA, initially described by Rosenberg in 1977 and later revised by Greenberger in 1991 have been established which are listed in table 2:

Major Diagnostic Criteria for ABPA

Asthma
Immediate skin reactivity to aspergillus
Positive serum presipitins to aspergillus fumigatus
Increased serum IgE and IgG to a. fumigatus
Total serum IgE>1000 ng/mL or >471 IU/ mL
Current or previous pulmonary infiltrates
Central bronchiectasis
Peripheral eosinophilia (>500/mm³)

Table 2: The allergic bronchopulmonary aspergillosis diagnostic criteria (Greenberger 1991)

Patients with ABPA can also be subdivided into two main groups, of ABPA with central bronchiectasis (ABPA-CB) and ABPA without central bronchiectasis (ABPA-S, sometimes referred to as sero-positive ABPA) (table 3).

Minimum diagnostic criteria for ABPA-CB	Minimum diagnostic criteria for ABPA-S
• Asthma	• Asthma
• Skin reactivity to aspergillus	• Skin reactivity to aspergillus
• Total serum IgE>1000 ng/ml or > 471 IU/ml	• Total serum IgE>1000 ng/ml or > 471 IU/ml
• Raised serum IgE& IgG antibodies to aspergillus	• Raised serum IgE& IgG antibodies to aspergillus
• Central bronchiectasis	• Pulmonary infiltrates

Table 3 Abbreviations: ABPA-CB; allergic bronchopulmonary aspergillosis with central bronchiectasis, ABPA-S; allergic bronchopulmonary aspergillosis-seropositive.

The clinical course of ABPA can be divided into five stages details of which are beyond the scope of this article but are briefly summarised below.

Stage I

This is the initial acute presentation with asthma, high total and aspergillus specific serum IgE and IgG antibodies, blood eosinophilia and Pulmonary infiltrates on chest x-ray.

Stage II

The remission stage in which total serum IgE levels may fall with absent blood eosinophilia and clear chest X-ray but IgG antibodies to aspergillus may remain elevated.

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Stage III

The exacerbation stage which is similar to stage I and occurring in patients who are known to have ABPA.

Stage IV

This is the corticosteroid dependent stage where patients require regular systemic corticosteroids for control of asthma symptoms and exacerbations. Frequently these patients have radiological changes of central bronchiectasis and elevated total serum IgE.

Stage V

This is fibrotic stage of the disease characterized by established bronchiectasis and fibrosis which is irreversible. Blood eosinophils and serum IgE may be low or high.

Treatment

Main focus in treatment of ABPA is to reduce inflammation and the frequency of exacerbations to minimise the disease progression and avoid irreversible damage.

Corticosteroids

Are the mainstay treatment which suppress the inflammatory response to aspergillus but do not eradicate the organism. Corticosteroids work by relieving the bronchospasm, reducing eosinophilia and IgE levels and resolving radiographic changes. Usually Prednisolone at a dose of 0.5mg/kg/day for two weeks with gradual tapering is recommended.

There is no consensus on total duration of the treatment, which will depend on the patient's clinical condition and treatment response. Serum total and specific IgE levels can be measured to monitor disease activity at 6-8 weeks interval for one year to assess response.

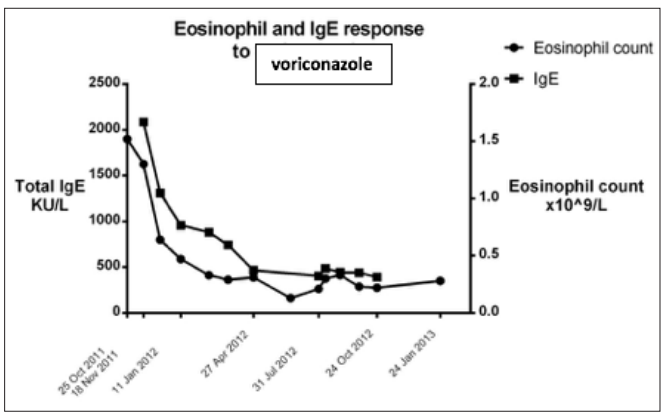

Figure 6: Illustration of good response to antifungal treatment with significant reduction in total IgE and blood eosinophils counts (the patient was treated by voriconazole 200mg twice a day from October 2011 to January 2013).

Inhaled corticosteroids often help relieving asthma symptoms but there is no evidence to suggest that they prevent progression of disease.

Antifungals (Azoles)

Are commonly and increasingly being used for treatment of ABPA as they help in weaning from corticosteroids and improving clinical and radiological aspects of the disease. Two randomised control trials, one retrospective cohort study and a small prospective study have demonstrated additional benefit of itraconazole in treatment of ABPA when combined with corticosteroids.

The largest randomised, double-blind and placebo-control trial by Steven (2000) of itraconazole 200mg twice a day for 16 weeks in patients on maintenance corticosteroids treatment, demonstrated 46% response rate (response was defined by at least 50% reduction in the baseline corticosteroids dose, at least 25% reduction in total serum IgE levels and one of the following: 25% improvement in lung function or exercise tolerance, or partial or complete resolution of radiographic changes).

It is important to monitor the patient's liver function whilst on Itraconazole. Voriconazole and posaconazole are potential alternatives in the event of intolerance or lack of response to itraconazole treatment. However they are much more expensive than itraconazole (Chishimba 2012). The Infectious Disease Society of America (IDSA) 2008 guidelines for the management of ABPA recommended a combination therapy of corticosteroids and itraconazole. Other potential treatments include nebulised amphotericin B and anti-IgE therapy (omalizumab).

Aspergilloma

Aspergilloma is a fungus ball which primarily consists of fungal hyphae, mucus, fibrin and tissue debris, developing in pulmonary cavities. It is one of the most common forms of aspergillus related lung diseases where a. fumigatus yet again being the main culprit though some other species like zygomycetes and fusarium may also cause fungal ball formation.

Risk Factors

The commonest and most important risk factor for aspergilloma development is presence of pre-existing cavity within the lungs, where 15-20% of cavities of > 2cm in diameter develop aspergilloma. The aetiologies of such cavities include tuberculosis, bronchiectasis, sarcoidosis, bronchial cysts, chronic obstructive pulmonary disease, bullous disease, ankylosing spondylitis and cavitating tumours.

Clinical Features

Most of these patients are usually asymptomatic and it is found incidentally on routine imaging when not suspected otherwise. When symptomatic, haemoptysis is common feature which can be life threatening. (with variable mortality rate from 2% to 15%). Other features are cough, fever and dyspnoea.

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The severity of the underlying lung disease, immunosuppression, recurrent large volume haemoptysis, increasing number of lesions and HIV are all associated with poor outcome in aspergilloma.

Diagnosis

Diagnosis of aspergilloma is based on clinical, radiological, serological and or microbiological evidence. It is usually located in upper lobes.

The chest X-Ray usually reveals a mass in pre-existing cavity with a rim of air around it (Halo sign). CT scan of the chest is more accurate in determining size and position of aspergilloma and is useful in cases when there is no visible aspergilloma on CXR (as in our patient above).

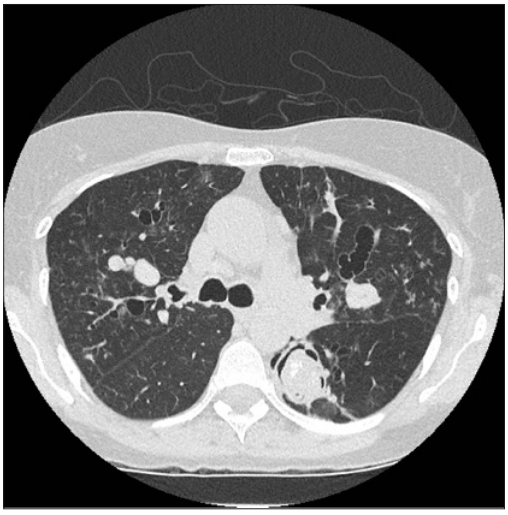

Figure 7: Aspergilloma with rim of air "Halo Sign".

Careful consideration should be given to important differentials such as Wegener's granulomatosis, neoplasm, abscess and hydatid cyst. Aspergilloma can also coexist with any other aspergillus diseases, often in the form of ABPA. Sputum cultures can be positive for aspergillus and serology tests usually show elevated aspergillus specific IgG antibodies.

Treatment

Unfortunately there is no definite consensus on treatment of aspergilloma and usually close observation is recommended when the patient is asymptomatic. However symptomatic patients may benefit from oral itraconazole treatment which can improve symptoms and radiological changes. Due to disease chronicity, several weeks may elapse before any benefit can be observed.

There are reports that resistance to itraconazole may be more common in aspergilloma in which case treatment with other azoles such as voriconazole and posaconazole may be considered. Patients presenting with large haemoptysis should be considered for bronchial artery embolization. However, recurrence of haemoptysis is common due to development of collateral supply. Surgical resection is a treatment option in patients with good performance status and lung functions. Less proven treatment options include inhaled, intracavitary or endobronchial instillation of antifungals.

Chronic necrotizing aspergillosis (CNA)

It is also referred to as semi-invasive or subacute invasive aspergillosis. It is usually caused by aspergillus fumigatus which leads to a slowly progressive, invasive and infectious process that leads to cavity formation.

The risk factors for CNA include elderly patients, middle aged patients with underlying lung disease such as pulmonary tuberculosis, bronchiectasis, pneumoconiosis, chronic obstructive pulmonary disease and CF. Systemic illness that can cause immunosuppression such as diabetes mellitus, and patients receiving long term immunosuppression for other diseases (e.g. connective tissue disease) are also at risk for developing CNA.

Invasive pulmonary aspergillosis (IPA)

Invasive pulmonary aspergillosis (IPA) is an aggressive form of aspergillus related pulmonary disease with high mortality. Fortunately, it is rare though the incidence is increasing due to the increasing use of chemotherapy and other immunosuppressive agents. Common risk factors for IPA include cytotoxic drugs, haematological malignancies, transplantation (especially haematopoietic stem cell transplantation), prolonged neutropenia and prolonged use of steroids.

Detailed description of IPA is beyond the scope of this article.

Conclusion.

Aspergillus related lung diseases are common and manifest as a spectrum of specific clinical illnesses which primarily depend on patient's immune status and pre-existing lung disease. ABPA and aspergilloma are the two commonest patterns often seen in patients with asthma and cavitary lung disease respectively.

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Prompt clinical evaluation should be undertaken in symptomatic individuals in order to achieve early diagnosis and initiation of specific therapy in a timely manner. Corticosteroids and azole class of anti-fungal (itraconazole, voriconazole or posaconazole) are the mainstay treatment in ABPA. Patients with symptomatic aspergillomas should be considered for anti-fungal treatment and bronchial artery embolization in the event of significant haemoptysis.

Whilst on treatment, disease activity can be monitored by serial measurements of serum total and specific IgE levels and peripheral blood eosinophils, usually every 6—8 weeks, along with monitoring of liver function tests to look for other potential side effects of the treatment. Chronic necrotizing aspergillosis (CNA) and invasive pulmonary aspergillosis (IPA) are relatively less common and usually affect immunocompromised patients. These constitute the invasive forms of pulmonary aspergillosis that generally carry poor prognosis.

Learning Points

- *Aspergillus is a common cause of pulmonary illnesses especially in certain risk groups.*
- *Clinical suspicion should be high in "at risk" patients (see risk factors)*
- *Deteriorating control of asthma in previously well controlled cases should alarm clinicians of possibility of allergic bronchopulmonary aspergillosis.*
- *Once the diagnosis of ABPA is confirmed, appropriate treatment should be started as soon as possible in order to prevent progression of the disease.*
- *Referral to a specialist clinic should be considered at an early stage.*

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CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: AN UNDERDIAGNOSED, BUT LIFE THREATENING COMPLICATION OF PULMONARY EMBOLISM

P Venkatappa, M Bhattacharya, A Kavidasan, R Randhawa, H Eliis, Y Odedina, E Mekonnen

Abstract

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is a rare, life-threatening medical condition caused by chronic obstruction of major pulmonary arteries. As a result, patients develop various degrees of pulmonary hypertension (PH). Left untreated, this leads to right ventricular failure and death.

CTEPH is a form of pulmonary hypertension (categorised by the World Health Organisation in Group Four) and has been reported as a long-term complication of pulmonary embolism (PE).

The symptoms experienced by CTEPH patients are similar to those of other more common respiratory diseases and to those of other types of pulmonary hypertension. As these symptoms are nonspecific, CTEPH is underdiagnosed and often misdiagnosed.

This article reports the case of a lady who presented with a long history of progressive dyspnoea on exertion and subsequently diagnosed CTEPH.

Case History

A 77 year old lady was admitted to a District general hospital with progressive exertional breathlessness in December 2014 with a significant reduction in exercise tolerance. She did not report any other cardiorespiratory symptom of note. She was treated for provoked PE in February 2013 and had been persistently short of breath since then. She was an ex-smoker with a 10 pack year history and worked in a canteen. Her past medical history included systemic hypertension well controlled with anti-hypertensives.

Clinically, her oxygen saturation was 90% on 40% oxygen. She was haemodynamically stable and physical examination revealed bilateral pitting pedal edema.

On this admission her routine blood investigations and D-dimer were within normal limits. Chest radiography revealed prominent pulmonary vessels and ECG showed sinus tachycardia.

A CT chest with contrast demonstrated evidence of circumferential thickening of the main pulmonary artery, lobar branches, and the right middle and lower lobe segmental branches with peripheral pruning of vessels. This was in keeping with chronic thromboembolic disease.

An Echocardiogram was done which showed bi-atrial dilatation and mild Tricuspid regurgitation with estimated systolic pulmonary artery pressure (PASP) of 50 mm Hg. Her previous ECHO in February 2013 demonstrated an increase in PASP from 38 to 50mm Hg.

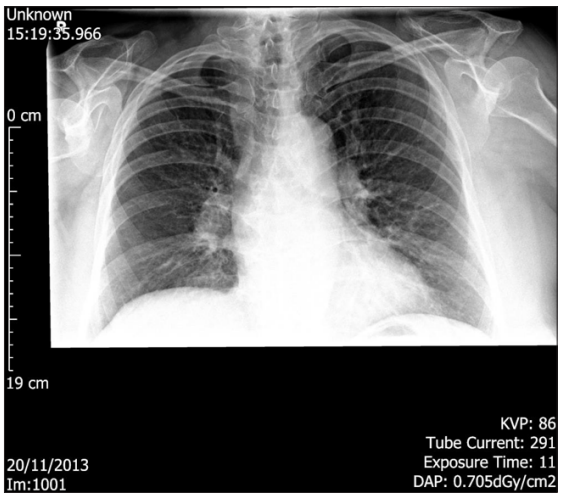

Figure 1: Chest Xray shows prominent central vessels with attenuated peripheries.

She was then referred for further investigation to the Pulmonary Hypertension specialist centre for the diagnostic evaluation of pulmonary hypertension on the background of chronic thromboembolic disease.

Right heart catheterisation revealed a right atrial pressure of 6 mm Hg, right ventricular systolic pressure (RVSP) of 47/18mm Hg, mean pulmonary artery pressure (mPAP) of 26 mm Hg, pulmonary vascular resistance (PVR) - 218 dynes·s·cm-5 and pulmonary capillary wedge pressure (PCWP)of 11 mm Hg.Pulmonary Angiogram was not perform due to difficulty with breath holding.

MR Pulmonary Angiography demonstrated extensive perfusion defects seen in the right mid and lower zones. It also demonstrated proximal amputation of the apical segment of the right upper lobe with web at the origin of the anterior segment and amputation of middle lobe and right lower lobe basal segmental vessels.

The overall impression was of proximal CTEPH with right sided predominance. The patient was discussed at the Surgical MDT for Pulmonary Thromboendartectomy and deemed technically operable, but she declined surgery.

She was discharged with long term oxygen therapy and lifelong anticoagulation. She continues to have regular follow up with the Pulmonary Hypertension team.

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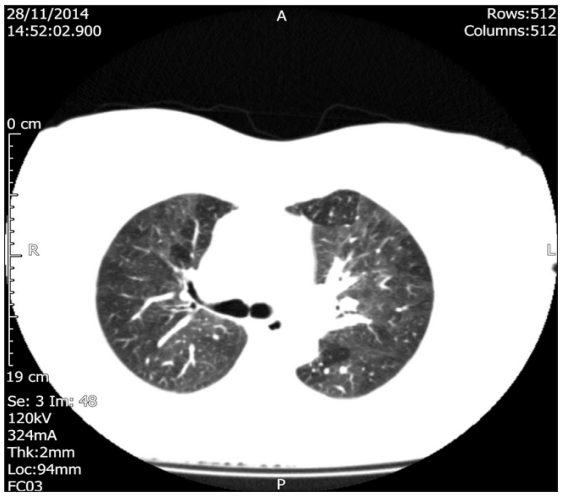
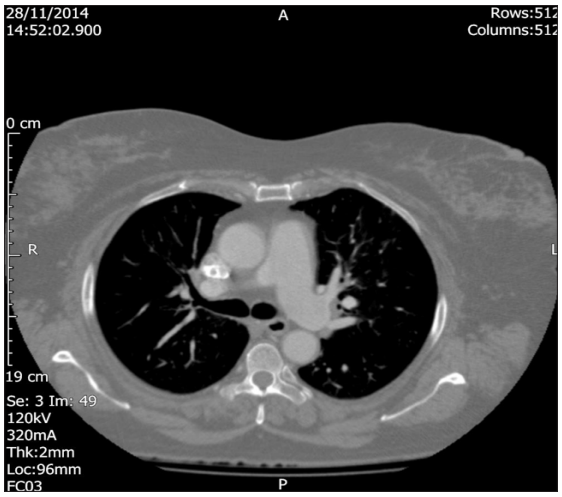
Figure 2: CT Thorax with contrast.



a) CT Thorax shows mosaic pattern of perfusion which reflects the inhomogeneity of lung perfusion associated with CTEPH.



b) CT Thorax shows circumferential soft tissue thickening of the wall of the main central pulmonary arteries and the lobar branches around both hila, particularly on the right side which is extending into the right middle and lower lobe segmental arterial branches.

Definition (1)

CTEPH is defined as a mean pulmonary arterial pressure ≥25 mmHg and pulmonary capillary wedge pressure ≤15 mm Hg in the presence of multiple chronic/organised occlusive thrombi/emboli in the elastic pulmonary arteries (main, lobar, segmental, sub segmental) after at least three months of effective anticoagulation.

Epidemiology

The rate of CTEPH in patients with previous PE was estimated at 4% in Europe and the US. In the UK, the prevalence of diagnosed CTEPH is 19.2 per million, equating to 1,169 cases in 2012–2013. Based on the prevalence of PE and population projections, CTEPH incidence will increase to >75000 cases in 2025.

Pathophysiology

CTEPH is a dual vascular disorder, with major vascular obliteration due to the fibrotic transformation of pulmonary arterial thrombi and a persistent vasoconstrictor response leading to a secondary small vessel arteriopathy.

Clinical characteristics

Clinical symptoms and signs are nonspecific or absent in early CTEPH, with signs of right heart failure only in advanced disease stages. Typically, a symptomatic thromboembolic event is followed by a "honeymoon period", characterised by the absence of symptoms.

Recurrent, unprovoked, or idiopathic PE
Large perfusion defects when PE was detected
Younger or older age when PE was detected
Pulmonary-artery systolic pressure >50 mm Hg at PE's first manifestation
Persistent PH evident when echocardiography is performed six months after acute PE was detected

Table 1: Common factors of CTEPH related to pulmonary embolism (PE)

Infected surgical cardiac shunts or pacemaker or defibrillator leads
Splenectomy
Chronic inflammatory disorders
Cancer
Thrombotic and genetic factors

Table 2: Medical conditions independent of PE, associated with increased risk of CTEPH.

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Diagnosis and Evaluation of CTEPH

Any patient with unexplained PH should be subjected to a CTEPH evaluation. Suspicion should be high, particularly when the patient presents with a history of previous VTE (Venous thromboembolism) and CTEPH should be ruled out in PE survivors with persistent dyspnoea and >15% persistent perfusion defects.

Echocardiography

Transthoracic echocardiography estimates pulmonary artery systolic pressure and establishes whether PH is present. Pulmonary-artery systolic pressure >50 mm Hg at PE's first manifestation is a high risk factor for CTEPH.

An echocardiogram should be performed six weeks after acute PE to screen for persistent PH that may predict the development of CTEPH.

Ventilation–Perfusion Scan

Ventilation–perfusion (V/Q) scan is the preferred and recommended screening test for chronic thromboembolic disease in patients with PH. A normal V/Q scan virtually rules out CTEPH.

A diagnosis of CTEPH may be confirmed by the presence of a mismatched wedge-shaped perfusion defects.

Computed Tomographic Angiography (CTA)

Diagnosis of CTEPH can be supported by characteristic findings on CT angiography. A mosaic pattern of perfusion on the CTA is virtually diagnostic of CTEPH

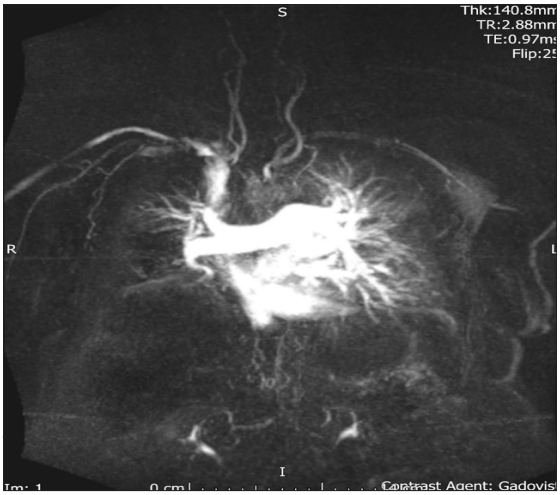

Figure 3: MR Angiography.

The MR Angiography shows blunt cut off in middle lobe and right lower lobe basal segmental vessels with extensive perfusion defects seen in the right mid and lower zone.

MR Angiography

Contrast-enhanced MR angiography (CEMRA) is an established alternative to CT. No ionizing radiation is involved, therefore the technique is ideally suited to young patients and those requiring serial assessments (e.g. for postoperative follow-up).

The typical findings of CTEPH (intraluminal webs and bands, vessel cutoffs, and organised central thrombus) are well demonstrated and can be seen in vessels to segmental level.

Pulmonary angiography

Pulmonary angiography is regarded as the gold-standard diagnostic tool in the work up for CTEPH. Through identifications of occlusions and intravascular webs, it confirms the diagnosis and gives an indication of operability.

Right Heart Catheterisation (RHC)

RHC confirms the diagnosis of CTEPH and has an additional importance of estimating the pulmonary vascular resistance which is the most important determinant of prognosis and the risk associated with surgery.

Treatment

All patients with CTEPH should receive lifelong anticoagulation with warfarin (target INR 2–3) to prevent recurrent thromboembolic events, but the regression of pulmonary hypertension due to anticoagulation therapy is unlikely.

Pulmonary Thromboendarterectomy (PTE) surgery is the only potentially curative treatment for CTEPH and it is the recommended first option for CTEPH patients.

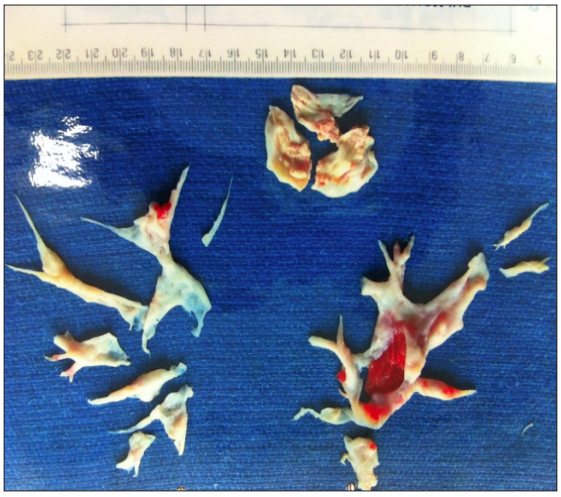

Figure 4: Pulmonary endarterectomy cast.

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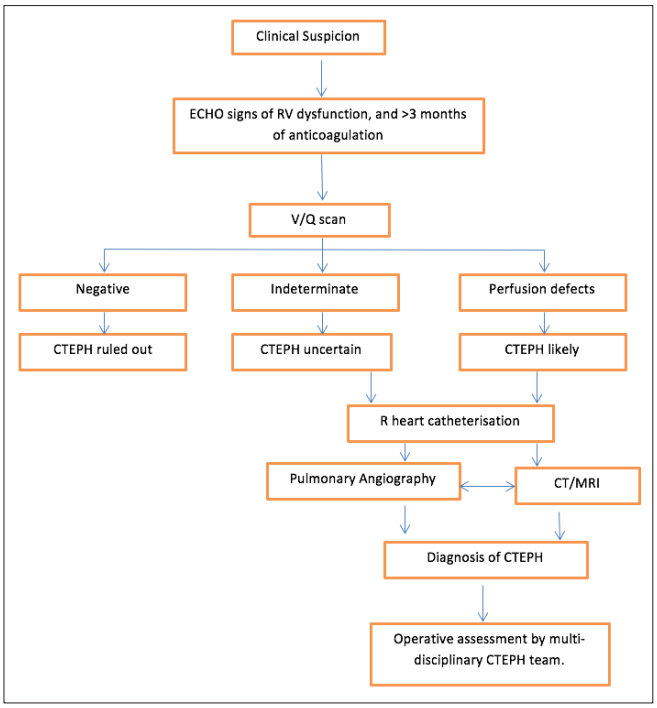
PTE allows for the removal of central obstructing lesions, resulting in an improvement and often normalisation of pulmonary hemodynamics. Operable CTEPH patients treated with PTE have a better long term survival rate than those who are treated with medical therapy.

Diagnostic algorithm for CTEPH



Conclusion

CTEPH is a leading cause of severe pulmonary hypertension. The best approach to decreasing the morbidity and mortality as well as the large medical burden and expense associated with CTEPH is to prevent this condition. Although multimodality imaging is usually needed to make the diagnosis, an echocardiogram can predict the development of CTEPH. Failure to recognize CTEPH often results in a delay in diagnosis and this condition has a poor prognosis if left untreated.

Take home messages

- **It is important to distinguish CTEPH as a cause of Pulmonary Arterial Hypertension, because CTEPH is the only potentially curable form of pulmonary hypertension.**
- **An echocardiogram must be performed six weeks after acute PE to screen for persistent PH.**
- **All individuals in whom PH is suspected should receive a ventilation/perfusion scan to screen for CTEPH.**
- **All individuals diagnosed with CTEPH should be assessed for potentially curative PTE surgery by an expert center.**

MCQs

1. A 70 year old woman with a history of previous recurrent pulmonary emboli, but no other comorbidities presents with breathlessness over a number of months. Her INR has been within the therapeutic range. Serial Echocardiograms demonstrate persistent features of pulmonary hypertension. Which one of the following is the most important measure?

a) Persist with warfarin, the clot will resolve eventually.

b) Immediately work up for advanced oral therapies.

c) Refer her for consideration of pulmonary endarterectomy.

d) Change her anticoagulant.

e) Refer her for a balloon atrial septostomy.

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2. Which one of the following statements is true?

a) Six weeks after acute PE, an echocardiogram may help screen for persistent PH.

b) Lifelong anticoagulation is not required once CTEPH diagnosed.

c) A normal plasma D-dimer excludes CTEPH.

d) CTPA is the gold standard investigation for the diagnosis of CTEPH.

e) A normal chest x-ray excludes CTEPH.

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Answers

1. c

This description fits with a diagnosis of CTEPH and anticoagulation has been proved ineffective in reducing pulmonary pressures. Pulmonary thromboendarterectomy is a potential cure, and the treatment of choice.

2. a

An ECHO done at six weeks can predict the development of CTEPH.D-dimer is an insensitive and a nonspecific test for the diagnosis of CTEPH. Despite a high negative predictive value, D-dimer alone cannot be used to rule CTEPH in patients with PH.

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MANAGEMENT OF DIFFICULT ASTHMA

D Neville, T Brown, T Jones, A Chauhan

Abstract

We present the case of a 48-year-old gentleman with severe asthma refractory to conventional treatments. Despite high intensity asthma treatments, including maintenance oral prednisolone, his asthma remained poorly controlled with a devastating effect on his quality of life. He suffered frequent severe exacerbations often necessitating hospital admissions and multiple side effects relating to his chronic systemic corticosteroid use.

Bronchial Thermoplasty has been able to achieve significant improvements in his lung function, asthma control and most importantly his quality of life. We discuss the diagnosis and phenotyping of severe asthma as well as describing a management approach. The case presented highlights the importance of novel treatments for severe asthma, and reinforces key elements in the management of severe asthma to help clinicians further their knowledge and clinical skills.

Case History

A 48-year-old man with severe asthma dependent on maintenance oral corticosteroids (OCS) presented with a 2-year history of worsening exertional and nocturnal breathlessness, wheezing and chest tightness. He had suffered multiple exacerbations of his asthma requiring further increases in his dose of OCS and several hospital admissions, which had led to prolonged periods of time off work.

He was first diagnosed with asthma 5-years previously and initially improved on fluticasone/salmeterol 250/50 one puff twice a day (BD) and montelukast 10mg once daily (OD). However, his asthma control subsequently deteriorated despite up-titration of his asthma treatments in line with the National SIGN/BTS Asthma Guidelines. At the time of review his asthma treatments included fluticasone/salmeterol 250/50 evohaler 1 puff BD, fluticasone 500mcg MDI 1 puff BD, montelukast 10mg OD, tiotropium 2.5mcg respimat 2 puffs OD, theophylline 450mg BD and oral prednisolone 30mg OD. He was compliant with all medications.

He was an ex-smoker with a 15-pack year history and had never been exposed to asbestos. He had no pets at home and worked in an office for a glazing company having been unable to continue as a window fitter due to his symptoms. His past medical history included a hiatus hernia with Gastro-oesophageal Reflux Disease (GORD) and Obstructive Sleep Apnoea (OSA) treated effectively with overnight Continuous Positive Airway Pressure (CPAP). He had no identifiable food allergies and aspirin did not worsen his symptoms.

Examination

His respiratory examination demonstrated preserved chest expansion with a resonant percussion note throughout. Auscultation revealed vesicular breath sounds with a mild end-expiratory wheeze throughout both lungs.

Investigations

Spirometry, Fractional exhaled Nitric Oxide (FeNO) and airway resistances (using plethysmography) were measured and compared to previous values (Table 1). His Asthma Control Questionnaire (ACQ) score was elevated (0-7, good control being <1) and his Asthma Quality of Life Questionnaire score was markedly reduced (0-7, higher scores suggest better quality of life).(1–3) FeNO remained elevated despite high-dose inhaled corticosteroids alongside long-term high dose OCS (Table 1), reflecting persisting eosinophilic airway inflammation. Skin prick tests (SPT) and specific IgEs to common aeroallergens proved negative.

Investigation	June 2011 – baseline	June 2013	Nov 2013	March 2014 – acute exacerbation	Nov 2014 – pre BT	March 2015 – post BT
FEV1(L) (% predicted)	3.38 (94%)	2.58 (77%)	2.32 (64%)	1.38 (38%)	2.54 (74%)	3.01 (84%)
FVC (L) (% predicted)	4.47 (101%)	3.82 (86%)	3.32 (75%)	2.24 (57%)	4.03 (90%)	4.33 (99%)
PEF (L/min)	650	450	400	160	420	620
FeNO (ppb)	22	76	77	98	68	18
Airway Resistance (%predicted)					160% predicted	86% predicted
ACQ Score		3.8	1.9	4.0	1.9	0.3
AQLQ Score		4.6	5.2	3.8	4.3	6.3
Dose of OCS (prednisolone)	0mg	20mg	30mg	40mg	20mg	0mg
Dose of Methotrexate	0mg	0mg	10mg	12.5mg	12.5mg	0mg

Table 1: Lung Function Tests

Abbreviations: FEV1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity, PEF: Peak Expiratory Flow, FeNO: Fractional exhaled Nitric Oxide, ACQ: Asthma Control Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, OCS: Oral Corticosteroid, BT: Bronchial Thermoplasty

An echocardiogram showed normal cardiac structure and function with no significant valvular abnormality. Bloods tests revealed a peripheral eosinophil count of $0.7x10^9$/L, antineutrophil cytoplasmic antibody (ANCA) and antinuclear antibody (ANA) were negative and his total Immunoglobulin E (IgE) level was 74 IU/mL. A High Resolution CT Chest Scan demonstrated bronchial wall thickening consistent with poorly controlled asthma but no bronchiectasis, emphysema or evidence of fungal lung disease.

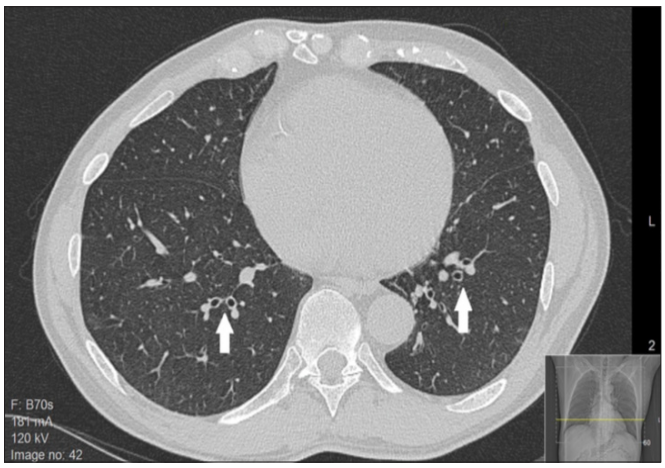

Figure 1: Bronchial wall thickening on High Resolution CT scanning with white arrows demonstrating the thickened airways.

MANAGEMENT OF DIFFICULT ASTHMA

D Neville, T Brown, T Jones, A Chauhan

Management

He was started on a steroid sparing agent (methotrexate 10mg weekly) in an attempt to wean down his maintenance OCS dose. Unfortunately, he suffered a further 3 exacerbations whenever his prednisolone dropped below 20mg. A trial of IM triamcinolone (a long acting corticosteroid) had no improvement in his symptoms or lung function. He started to develop serious steroid side effects (hypertension, diabetes and osteopenia) and was keen to come off long term OCS. He was treated with bronchial thermoplasty (BT).

Discussion

Asthma affects over 5.4 million people in the UK and whilst the majority can be treated effectively with available medications, over 250,000 (5%) experience persistent severe symptoms and frequent exacerbations despite maximal therapy.(4) The burden of severe asthma on the NHS is enormous accounting for over 50% of total asthma costs (£1 billion/year) with expensive medications and frequent exacerbations generating much of this cost.(5,6) Asthma remains responsible for more than 1,200 deaths each year, with those suffering severe and poorly controlled asthma facing the greatest risk. The recent UK National Review of Asthma Deaths (NRAD) highlighted poor recognition of asthma severity as a key factor associated with asthma mortality. (7)

Patients with severe asthma bear the greatest burden of asthma morbidity. They experience more frequent and severe symptoms and exacerbations which reduce their quality of life, impair their ability to work and place an enormous burden of anxiety on them and their families. Recent severe asthma guidelines have highlighted the unmet clinical need in this patient group and recognised the need for further research into the underlying mechanisms driving their disease. (8)

The most important consideration when first assessing difficult asthma is confirming a correct diagnosis. There is no single diagnostic test for asthma but the diagnosis relies on demonstrating evidence of variable airflow obstruction, airway hyper-responsiveness and/or airway inflammation in the context of relevant symptoms.

Evidence of variable airflow obstruction can be recorded by twice daily Peak Expiratory Flow (PEF) monitoring or by reversibility testing on spirometry. An average daily diurnal PEF variability of > 10% confirms changing airflow obstruction or bronchodilator (BD) reversibility, with an increase in Forced Expiratory Volume in 1 second (FEV1) ≥ 12% or 200mL post bronchodilator inhalation.(9) Our patient recorded a 15% increase in post-BD FEV1 confirming his diagnosis. When a diagnosis is inconclusive on spirometry, evidence of bronchial hyper-responsiveness can be obtained by performing a challenge test such as a methacholine challenge.

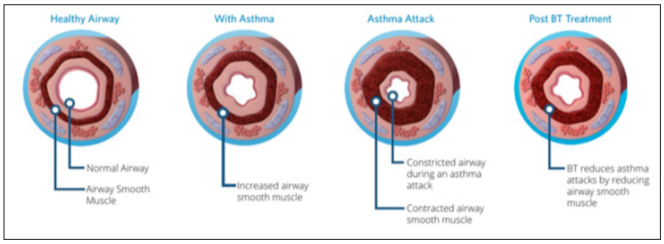

Figure 2: Airway changes in asthma and following BT (image used with permission from BostonScientific)

This involves monitoring a patient's FEV1 while they inhale increasing concentrations of nebulised methacholine. The test is positive if a 20% reduction in FEV1 is observed at a concentration of methacholine below 16mg/ml. (9,10) Histamine, mannitol and exercise testing can also be used. Asthma is an inflammatory airways disease, triggered by exposure to inhaled irritants or infections.

This inflammation can be driven by eosinophil and/or neutrophil activation. By confirming the predominant cell type that drives airway inflammation, patients can be phenotyped into eosinophilic or neutrophilic asthma. This information, along with clinical symptoms, can be used to guide management. (8) FeNO testing is a non-invasive way of estimating eosinophilic airway inflammation, with values over 50 parts per billion (ppb) suggesting on-going eosinophilic inflammation.(11)

Better characterisation of the inflammatory state of the airways can be achieved with sputum induction and sputum cell count measurement. Airway eosinophilia is predictive of steroid responsiveness, while those with an airway neutrophilia react poorly to corticosteroid treatment and may need other treatment such as a macrolide antibiotic.(12)

Simple steps in the management of asthma are important at any level of severity. Ensuring a patient is receiving their currently prescribed medication is imperative, both in terms of inhaler technique (which is often overlooked and poorly taught) and medication adherence. Identification and treatment of co-morbidities such as GORD, OSA, and sino-nasal disease can also significantly improve symptoms.

Furthermore, recognition of fungal disease associated with asthma, namely Severe Asthma with Fungal Sensitisation (SAFS) and Allergic Bronchopulmonary Aspergillosis (ABPA) enables the clinician to initiate additional anti-fungal treatment, which can improve asthma control. It is also important to consider exposure to irritants in the working environment that can either cause occupational asthma or worsen pre-existing asthma (work-aggravated asthma). Escalation of treatment can be considered if a patient is taking their medication correctly and consistently yet they remain symptomatic.

MANAGEMENT OF DIFFICULT ASTHMA

D Neville, T Brown, T Jones, A Chauhan

Novel management options

There are new pharmacological and interventional treatments emerging for severe asthma. Novel biological therapies primarily target elements of the allergic (Type 2) inflammatory cascade such as IgE (omalizumab) and IL5 (mepolizumab). Many trials of other monoclonal antibodies are currently underway in asthma and clinical trials can provide a route by which patients can gain access to new therapies.

Bronchial thermoplasty (BT) is the delivery of controlled radiofrequency energy to the airway walls using a specially designed catheter. Severe asthma is characterised by increased airway smooth muscle mass (figure 3) due to chronic inflammation and this contributes to the poor lung function and symptom control. BT aims to reduce airway smooth muscle mass, decreasing the ability of the airways to constrict in severe asthma and it may also reduce the secretion of inflammatory cytokines within the airway.(13)

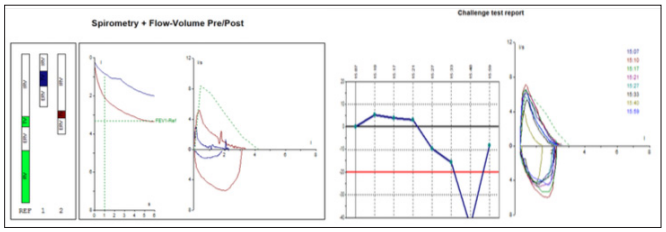

Figure 3: Bronchodilator reversibility (Left) showing spirometry and flow volume loop pre- (blue) and post- (red) salbutamol, with the green line showing the predicted loop. Methacholine challenge (Right) showing bronchial hyper-responsiveness with a greater than 20% drop in FEV1 at 16mg/mL methacholine.

Treatment is given in 3 sessions, each targeting a different part of the lung, with an interval of at least 3 weeks between each session. It is delivered only in specialist centres and each procedure takes around 45 minutes (Figure 4).

Evidence shows that patients treated with BT have an improvement in their quality of life and lung function, as well as having fewer hospital admissions with improvements maintained for at least 5 years. It is a safe procedure but can cause complications such as infections and a worsening of symptoms during the treatment period and longer term outcomes (> 5 years) are still unknown. (13)

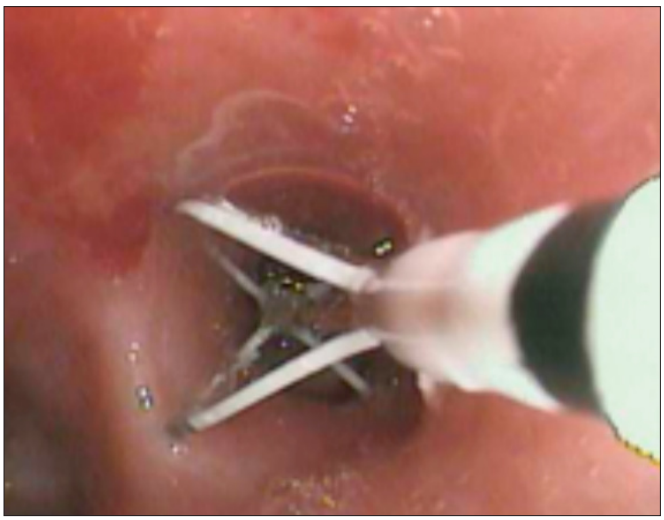

Figure 4: The Alair© Bronchial Thermoplasty catheter in situ during a procedure.(Image used with permission rom BostonScientific)

Progress

4 months after BT, our patient's lung function had dramatically increased (Table 1). He had significant improvement in his symptoms and exercise tolerance. He had suffered no exacerbations and had managed to completely wean himself off OCS, methotrexate and theophylline. For our patient the effect was dramatic. His subsequent improvement and quality of life can be summed up in his own words:

"As an asthmatic I tended not to go to any wedding, parties or the theatre, and going out to dinner with friends could be embarrassing. Let's face it - who wants to hear someone coughing and that horrible wheezing sound that you make. Now I'm back; this year I've already had two theatre trips, one wedding and playing football with my granddaughter is a delight knowing I don't have to kick the ball 100 yards just so I get some rest:".

Conclusion

Novel treatments including monoclonal antibodies and bronchial thermoplasty are becoming more common. When correctly targeted, these new treatments can have a large effect on patients' disease control and quality of life. Prior to consideration of escalation of therapy, use of current therapy and identification of other co-morbidities must be systematically assessed, with inhaler technique and medication adherence being frequently identified problems.

MANAGEMENT OF DIFFICULT ASTHMA

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Acknowledgements

We would like to thank the patient for allowing us to use the case and his quotation and Boston Scientific for allowing us to use their images of BT.

Abbreviations

FEV1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity, PEF: Peak Expiratory Flow, FeNO: Fractional exhaled Nitric Oxide, ACQ: Asthma Control Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, OCS: Oral Corticosteroid, BT: Bronchial Thermoplasty.

MCQ's

1) A 26-year old female attends clinic with poorly controlled asthma for the past 6 months. You saw her three months ago and escalated her treatment to budesonide/formoterol and this helped initially but the benefits only lasted a few weeks. Her peak flow chart shows significant diurnal variability, her FeNO is raised at 71 ppb and her ACQ score is elevated at 2.5. Which of the following should not be done at this review?

A. Improve inhaler technique

B. Refer for methacholine challenge to confirm diagnosis

C. Provide self-management plan

D. Review allergies and exposures

E. Increase inhaled steroid dose

2) A 47-year old male on budesonide 200/formoterol 6 two puffs twice a day attends clinic with significant wheeze and shortness of breath over the past 3 months. His FEV1 is reduced at 75% predicted, his FVC is stable at 101% predicted and his FeNO is elevated at 58 ppb. Which of the following is most appropriate to help his symptoms based on this information?

A. Add montelukast 10mg at night

B. Increase his budesonide/formoterol to three puffs BD and use this inhaler for relief of his symptoms also.

C. Add tiotropium 2.5micrograms two puffs once a day

D. Add azithromycin 250mg three times a week

E. Refer for consideration of Bronchial Thermoplasty

3) Which of the following is most likely to be seen on a High Resolution CT in severe asthma?

A. Bronchial Wall thickening

B. Bronchial Dilatation

C. Pulmonary Infiltrates

D. Mucoid Impaction

E. Lymphadenopathy

4) A 38 year old male attended the asthma clinic on budesonide 200 / formoterol 6 two puffs three times a day, montelukast 10 mg once daily, tiotropium 2.5 mcg two puffs once daily and prednisolone 15 mg once daily. He is still wheezy and his ACQ is 2.8. He is obese with a BMI of 40kg/m2 and describes falling asleep easily when watching TV, snoring and morning headaches.

He also has an irritating cough at night-time when he lies flat. He has a peak flow diary that shows no diurnal variability over the last 2 weeks. His SPTs show a sensitivity to aspergillus and his total IgE is 900 (markedly elevated) with a raised specific IgE to aspergillus. Which of the following is NOT an appropriate investigation?

A. Refer for a sleep study

B. High resolution CT chest

C. Bronchodilator Reversibility testing

D. Cardiopulmonary Exercise Testing (CPET)

E. Sputum fungal culture.

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5) A 35 year old male on high doses of ICS, LABA and LAMA attends clinic with a high ACQ and a low AQLQ. His FEV1 is 65% predicted without significant reversibility, but airway hyper-responsiveness is confirmed with a methacholine challenge. Sputum induction is performed, and this shows significant neutrophilia. Which of the following treatment changes is most appropriate?

A. Addition of oral steroids

B. Addition of second LABA

C. Removal of LAMA

D. Addition of omalizumab

E. Addition of azithromycin

Answers

1.B.

The peak flow variability is evidence of poorly controlled asthma, a methacholine challenge is not necessary at this point. Reviewing inhaler technique is very important as this case suggests the patient may have started using her inhaler incorrectly over time. Increasing her ICS dose should help if her technique is correct, reviewing her allergies and exposures (has she got a new cat? does she have hay fever? etc.) could suggest other ways to help control her asthma. A self-management plan is vital for all asthmatics.

2.B.

This man's elevated exhaled nitric oxide measurement is suggestive of persisting eosinophilic inflammation which should respond to inhaled steroids, assuming his inhaler technique is good. The use of a combination Inhaled corticosteroid (ICS) and long-acting beta2 agonist (LABA) as a single inhaler for both maintenance and reliever therapy (SMART), is a proven treatment strategy that allows self-control for patients and reduces exacerbation frequency.(14)

Montelukast is beneficial in a group of asthma patients, often those who are aspirin sensitive, while tiotropium may benefit those with significant airflow obstruction. Adding a macrolide or Bronchial Thermoplasty should be reserved for those with severe asthma resistant to standard therapies.

3.A.

Bronchial wall thickening is common in uncontrolled asthma. Permanent bronchial dilatation is characteristic of bronchiectasis. Pulmonary infiltrates suggest other pathology such as a pulmonary vasculitis. Lymphadenopathy suggests infection, malignancy or granulomatous diseases such as sarcoidosis. Mucoid impaction may be seen in severe asthma but is less common than bronchial wall thickening and may be suggestive of Allergic Bronchopulmonary Aspergillosis (ABPA) or other coexisting pathology.

4.D.

Cardiopulmonary exercise testing is beneficial in determining whether a person's breathlessness is of respiratory or cardiac cause, but not in the situation described. HRCT chest and sputum fungal culture may show evidence of ABPA, a sleep study may show evidence of OSA while wheeze alone is not diagnostic of asthma and bronchodilator reversibility may confirm (or refute) the diagnosis of asthma.

5.E.

Macrolides such as azithromycin are one of the few treatment options available for neutrophilic airway inflammation in asthma.(12) Reduction of his inhaled steroid dose may also be appropriate, as excessive ICS may increase frequency of infections. There is no evidence to suggest additional long acting beta agonists would be of any use and may worsen side effects. The LAMA should not be stopped unless it is not proving beneficial and long term oral steroids should be avoided where possible, particularly in non-eosinophilic disease.

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MODERN MANAGEMENT OF ADVANCED COPD

J John, N Jarad

Abstract

For a long time medicine has viewed severe emphysematous chronic obstructive pulmonary disease (COPD) with nihilism. Techniques now exist which go further than palliation and symptom control. This article uses a case report as a starting point for discussing the modern management of severe COPD. The discussion covers background pathophysiology, well-established medical and rehabilitation therapies, and more modern interventional therapies that have been shown to improve objective and subjective measures of disease severity.

Interventional therapies discussed include endobronchial valves and coils, both of which are devices that are inserted using bronchoscopy. The selection criteria for the use of valves or coils in patients with COPD are addressed, and the current evidence for their use is highlighted.

Case Report

Mrs H is a 66 year old female with severe chronic obstructive pulmonary disease (COPD). During a one year period prior to endobronchial valve insertion she required three hospital admissions for infective exacerbations of COPD, as well as needing additional courses of oral steroids and antibiotics every 6-8 weeks from her GP to help control exacerbations. She has a background of a 40 pack year smoking history. She stopped smoking 16 years ago.

Before endobronchial valve insertion her exacerbations tended to be severe as well as frequent. They often required hospitalisation with prolonged admission. Breathlessness and high-pitched wheeze would typically be present during disease stability but increased during exacerbations.

Her underlying COPD combined with the frequency of her exacerbations had a significant impact on Mrs H's quality of life. She required a stair lift in her home owing to significant breathlessness on exertion. Frequent exacerbations also meant that she had been sustained on a high dose of corticosteroids for a considerable time period, since exacerbations would recur before the steroid dose was tapered significantly. She was therefore at risk of the numerous side effects associated with high dose corticosteroid use. Her quality of life tests showed a high impact of disease. Her COPD Assessment Test (CAT) score (1) was 33/40. In this scoring system, the greater the value the worse is the quality of life. A score of 36 or more are usually seen near the end of life for COPD patients.

When reviewed in COPD clinic her regular medications were salbutamol and ipratropium home nebulisers QDS, fluticasone and salmeterol combination inhaler BD, carbocisteine 750mg PO TDS, aminophylline 225mg PO BD, prednisolone 25mg PO OD, alendronic acid 70mg PO OW, adcal D3 T BD, citalopram 40mg OD, lansoprazole 15mg OD, paracetamol 1g QDS. She was also taking azithromycin 250mg OD as prophylaxis against infective COPD exacerbations.

Her chest X ray showed upper lobe emphysema, which was confirmed with HRCT thorax, as seen in figure 1.

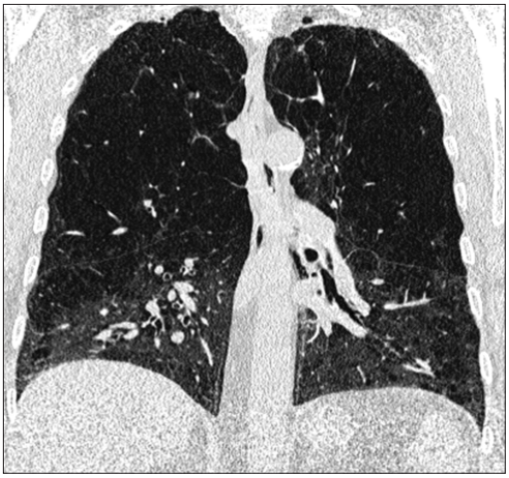

Figure 1: Coronal chest CT scan of Mrs H prior to endobronchial valve placement. Please note the upper lobe emphysema with relatively healthy looking lower lobes.

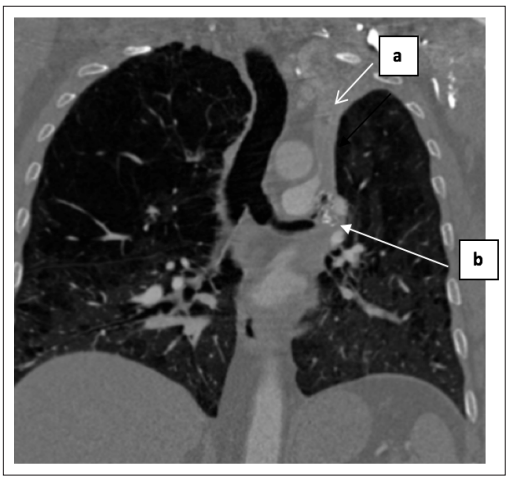

Figure 2: Coronal CT scan of the chest of Mrs H, demonstrating collapse in the left upper lobes (a) with two appropriately positioned endobronchial valves visible (b). The left lower lobe expanded to fill the air space.

The lung function tests of Mrs H prior to endobronchial valve placement are outlined in table 1.

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Test	FEV1	FVC	FEV1/FVC	TLC	RV	TLco	Kco
Actual	1.04	2.75	44	5.92	3.13	2.81	0.68
% predicted	50	109		129	181	39	43

Table 1: Detailed lung function tests. FEV1: Forced expiratory volume in the first second, FVC: Forced vital capacity, TLC: Total lung capacity, RV: Residual volume, TLco: Transfer factor of carbon monoxide, Kco: transfer co-efficient (this is the transfer factor corrected by the alveolar volume).

Mrs H underwent further assessments and was found to meet eligibility criteria for a lung volume reduction procedure using endobronchial valves (see table 2 for eligibility criteria). Her echocardiogram indicated no evidence of raised pulmonary artery pressures, she had successfully stopped smoking and undergone pulmonary rehabilitation, her FEV1 was less than 50% predicted and residual volume over 180% predicted. Furthermore, there were no significant comorbidities anticipated to interfere with the outcome of valve insertion.

Valves were sited into the proximal bronchi of the left upper lobe using bronchoscopy, resulting in collapse of the lobe and expansion of the left lower lobe (figure 2). After the procedure she made an uncomplicated recovery and was discharged after three days.

On follow up at one year, Mrs H had since been admitted with one COPD exacerbation. Her CAT score went down from 33 to 15. She had been able to swim, go to the gym and lose weight. Her FEV1 at 2 years post-procedure was 1.74 (85% predicted). Her 6 minute walk distance at one year was 380 meters.

Discussion

COPD is a collective term given to irreversible and progressive damage sustained to the bronchi and lung tissue, resulting in sub-optimal respiratory function showing as airway obstruction on spirometry. Smoking is by far the most significant cause of COPD. There are three underlying pathological forms of COPD: emphysema (parenchymal damage), chronic bronchitis (inflammatory airway narrowing and sputum production), and mixed emphysema and bronchitis.

Emphysema is characterised by alveolar destruction, which leads to enlarged terminal air spaces. The result is a loss of lung surface area for gas exchange and a loss of intrinsic elastic recoil of the lung tissue. Emphysematous airways also tend to collapse down during expiration resulting in air trapping in distal airways on expiration. This expiratory collapse occurs because the small damaged airways are not held patent because of the loss of normal interstitial lung architecture (figure 3).

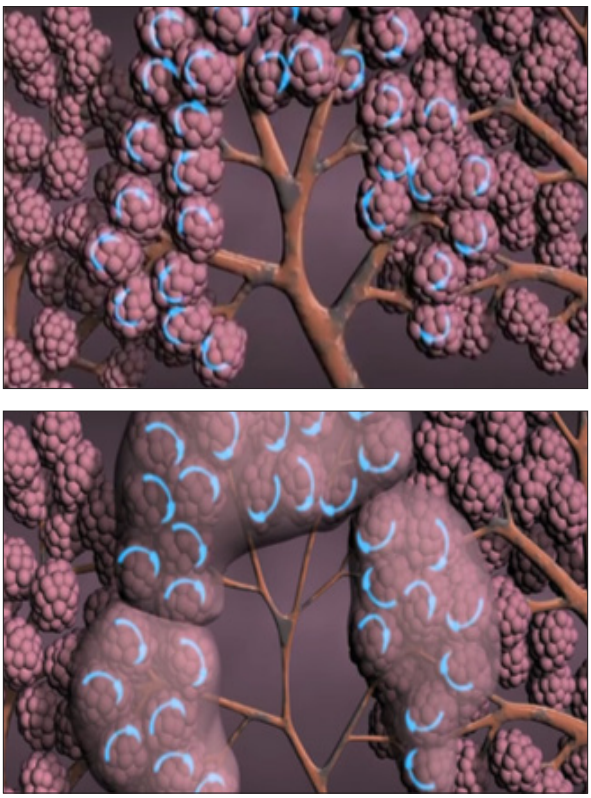

Figure 3: Schematic representation of normal lung tissue and normal airways (left) and emphysematous lung tissue and airways. Enlarged airspaces and the thinning of the airways tends to result in easy collapsibility. Reproduced with permission from Pulmonx®

Chronic bronchitis is the chronic inflammation of bronchi, with associated mucous secretion, causing narrowed airways and hence obstruction of airflow. Evidence suggests that progression of COPD is correlated closely with extent of emphysematous change seen on imaging, suggesting that emphysema plays a larger role in COPD progression than chronic bronchitis (2).

COPD is typically diagnosed on spirometry. The diagnostic criteria are met when the ratio of forced expiratory volume in the first second (FEV1) divided by the forced vital capacity (FVC) is less than 0.7. Severity of COPD is often assessed according to the percentage of predicted FEV1 for the patient. Severe COPD is when the FEV1 is reduced to less than 50% predicted, based on patient age, height and gender.

The impact of severe COPD on daily activities of patients has been studied (3). Mornings tend to be the worst time. Due to breathlessness and fatigue, patients are often struggle with activities including; putting on socks and shoes, washing and drying themselves, dressing, going up and down stairs, and leaving the house.

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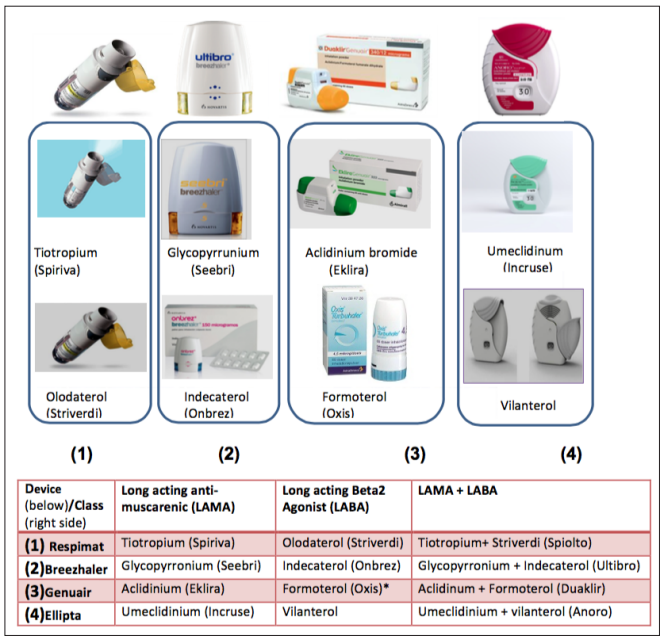
Management of severe COPD

The approach to management of COPD is multifactorial. Smoking cessation is by far the most significant intervention. Smoking cessation reduces annual decline in FEV1 as well as the frequency of exacerbations. Strategies to assist patients towards smoking cessation should be developed, the easiest of which is advice given during healthcare encounters, in keeping with NICE recommendations and recent evidence (4).

Stable disease is managed with short and long-acting inhaled bronchodilators. Over the past 5 years several potent long acting $Beta_2$ agonist (LABA) and long acting anti-muscarinic (LAMA) inhalers have become available in different devices. Moreover, various LABA and LAMA combination inhalers are available. Figure 4 illustrates the available LABA's, LAMAs and combination inhalers.

Combined LABA and LAMA medications are more potent than old inhalers. Their effectiveness has been shown to be sustained over a 12 month period. The improvement in health related quality of life has also been demonstrated. Certain combination inhalers have also shown a considerable reduction in number of exacerbations.



Device (below)/Class (right side)	Long acting anti-muscarenic (LAMA)	Long acting Beta2 Agonist (LABA)	LAMA + LABA
(1) Respimat	Tiotropium (Spiriva)	Olodaterol (Striverdi)	Tiotropium+ Striverdi (Spiolto)
(2)Breezhaler	Glycopyrronium (Seebri)	Indecaterol (Onbrez)	Glycopyrronium + Indecaterol (Ultibro)
(3)Genuair	Aclidinium (Eklira)	Formoterol (Oxis)*	Aclidinum + Formoterol (Duaklir)
(4)Ellipta	Umeclidinium (Incruse)	Vilanterol	Umeclidinium + vilanterol (Anoro)

Figure 4: The available inhaled long acting anti-muscarinic (LAMA) agents and long acting Beta2 agonists (LABA). The name between brackets is the commercial name for each component. The top row of inhalers are combination inhalers. (Formoterol is available in a turbohaler device but not in a genuair device.)

The introduction of many inhaled medications over a relatively short period has provided opportunity for patients and health care workers to choose the best device for treatment. However, it has also created confusion as to which to choose and how to replace old inhalers with new ones (figures 5).

Figure 5: Inhalers used by a hospitalised patient with COPD. There are 2 inhalers of combined inhaled steroids and long acting $Beta_2$ agonists (seretide and relvar) and also a long acting anti-muscarinic agent. The patient's inhalers are provided in 3 different devices.

Specific attention needs to be paid to the ability of patients to understand the purpose of inhalers, and to patients' ability to use them correctly (figure 6). Inability to understand inhalers is commonplace, and increases with age and with reduced mini-mental test score (figure 7) (5).

Figure 6: (A) A patient with deforming rheumatoid arthritis and COPD. The patient was unable to use both inhaled devices prescribed to her, and needed to rely on carers to do it. (B); The same patient did not notice that the Ellipta device was empty (indicated by the red window on the device).

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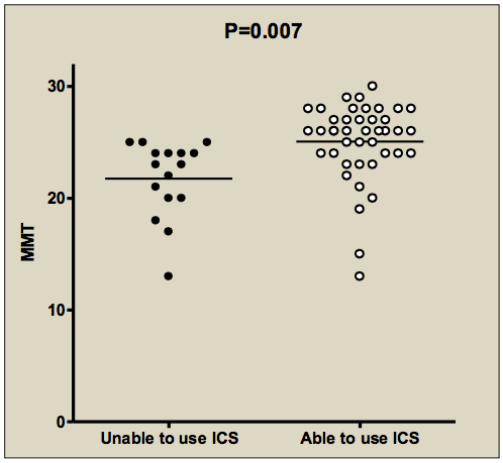

Figure 7: Reduced ability to use inhaled corticosteroids (ICS) in patients with reduced mini-mental test (MMT) score (after Walsh and Jarad 5).

Home nebulised bronchodilators can be considered for patients with advanced disease who might struggle with inhaler technique, or who achieve a favourable symptomatic benefit with nebulisers.

Pulmonary rehabilitation

Pulmonary rehabilitation courses have revolutionised the care of advanced COPD. The courses typically last for 1 hour and run twice weekly for 6-8 weeks. The course has three components: education, exercise assessment and exercise prescription to be done at home.

Pulmonary rehabilitation has been consistently shown to increase exercise capacity, improve quality of life and reduce length of stay during exacerbations (4, 6).

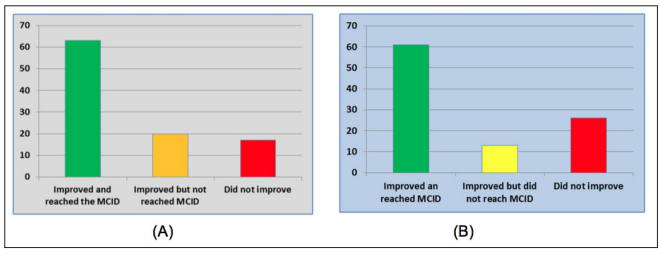

Figure 8: Data from 7000 UK patients who underwent a pulmonary rehabilitation programme. 6 minute walk distance reached at 3 months after the programme (A), and change in health related quality of life measures (B). Y-axis indicates the percentage of patients who improved and reached the minimally Important Clinical Difference (MICD) (green), those who improved but did not achieve MICD (orange, yellow) and those who did not improve (red). Adapted from reference (6).

Despite the well-founded benefit of pulmonary rehabilitation the uptake and completion rates are modest. A recent publication of a large audit run in London by the Royal College of Physicians found that many COPD patients are not referred for pulmonary rehabilitation. In addition, significant proportions of those who are referred either do not attend the initial session or do not complete the programme. Strategies to increase the uptake and complete the programme are under development.

Oxygen therapy

Ambulatory and long-term oxygen therapies are provided to a significant proportion of patients with severe COPD. Ambulatory oxygen is used to improve exercise tolerance, and long-term oxygen therapy is used to improve survival. The criteria for long term oxygen therapy are; PO_2 less than or equal to 7.3kPa, or 7.85kPa and with evidence of cor-pulmonale, right heart failure or polycythaemia.

Many patients assume that long-term oxygen therapy will improve breathlessness, and while this may happen it ought to be emphasised that is not the indication for long-term oxygen therapy driven through oxygen concentrators.

Bundle of care

Given the multi-faceted nature of management of advanced COPD, the British thoracic society proposed a bundle of care for all COPD patients, delivered at the point of discharge from hospital (7). The bundle of care consists of; smoking cessation advice, referral for pulmonary rehabilitation, ensuring correct inhaler technique, referral for oxygen therapy and end of life conversation when appropriate.

Interventional therapies for emphysema

The methods discussed so far improve the care of patients with COPD. However, patients with emphysema tend to respond variably and less well to bronchodilators compared with asthma patients. Due to the severe and irreversible tissue damage involved in the condition, physicians have had a nihilistic attitude towards emphysema.

Over the past few years, however, several interventional methods of managing emphysema have been introduced. The overall purpose is to manage hyperinflation through volume reduction strategies. Studies are continuing to emerge which show that removing, collapsing or reducing the volume of the most affected parts of the lungs causes reduction in breathlessness, improved lung function tests and increased survival.

Volume reduction surgery was found to be effective in selected patients with upper lobe emphysema and reduced exercise capacity (8). However, surgical lung volume reduction in patients with severe emphysema was associated with increased mortality and morbidity.

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Minimally invasive techniques carried out using bronchoscopy have recently been introduced. The two most studied methods separately involve endobronchial valves (blocking devices) and endobronchial coils (non-blocking devices). The criteria for using valves and coils are outlined in table 2.

Stopped smoking for at least 6 months
Underwent pulmonary rehabilitation programme
FEV1 less than 50% of predicted value
Residual volume of over 180% of predicted value
Six minute walk distance more than 100 metre and less than 450 meter.
Pulmonary artery pressure of < 50 mm Hg
No co-morbidity that interferes with outcome of care

Table 2: Criteria for lung volume reduction therapies.

Given the relatively high prevalence of emphysema and the rapid introduction of these methods of treatment, multi-disciplinary teams consisting of respiratory physicians, thoracic surgeons and thoracic radiologists have been formed to best select methods of treatment for each individual patient. As we will outline, these interventional methods appear very promising and are already yielding good results, however selection criteria do make these options unavailable to many patients with COPD at present.

Endobronchial valves (EBVs)

EBVs are one-way valves contained in an expandable nitinol cage (figure 9). The strongest evidence comes from the Zephyr valve (Pulmonx- Redwood City, California).

Figure 9: Several Zephyr emphysema valves.

EBVs are used in patients with upper lobe or lower lobe emphysema. This is unlike volume reduction surgery, where only upper lobe emphysema is considered. The valves are introduced through bronchoscope and deployed in all of the bronchi leading to the target lobe.

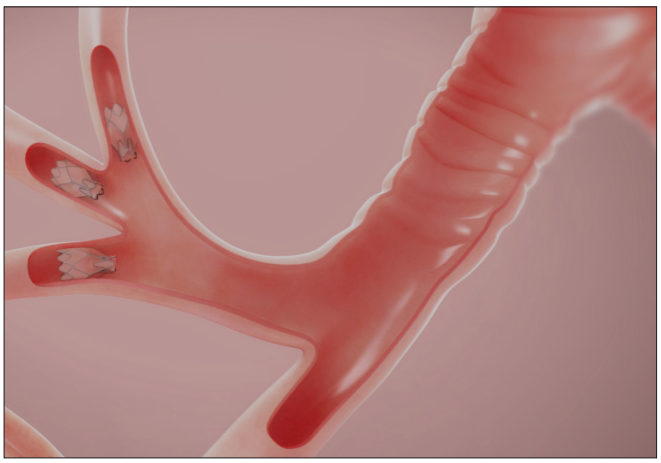

Figure 10: Schematic representation of three endobronchial valves blocking all bronchi leading to the right upper lobe. Reproduced with permission from Pulmonx®

A successful procedure results in collapse of the target lobe and an expansion of the adjacent lobe.

A lack of collateral ventilation between the target lobe and the adjacent lobe is a pre-requisite for the success of this procedure. Collateral ventilation describes when small channels exist which directly connect the airways of adjacent lobes. Their presence would result in unsuccessful collapse of a lobe using endobronchial valves by providing an alternative means for air to enter the target lobe.

The absence of collateral ventilation is often deduced by assessing the intactness of the inter-lobar fissures on CT scan and through physiological methods carried out during the procedure. In the latter, the outflow from a lobe blocked by an inflated balloon decreases within minutes when there is no collateral ventilation and remains unchanged when there is collateral ventilation.

Retrospective analysis and prospective clinical studies 9-11 have all demonstrated overall significant improvement in lung function, exercise capacity and quality of life in patients with heterogeneous emphysema and no collateral ventilation who received endobronchial valves (figure 11). It should be noted however that despite careful pre-procedure selection and investigation of patients, the response to valves is variable, with some patients showing negligible benefit for reasons not yet fully understood.

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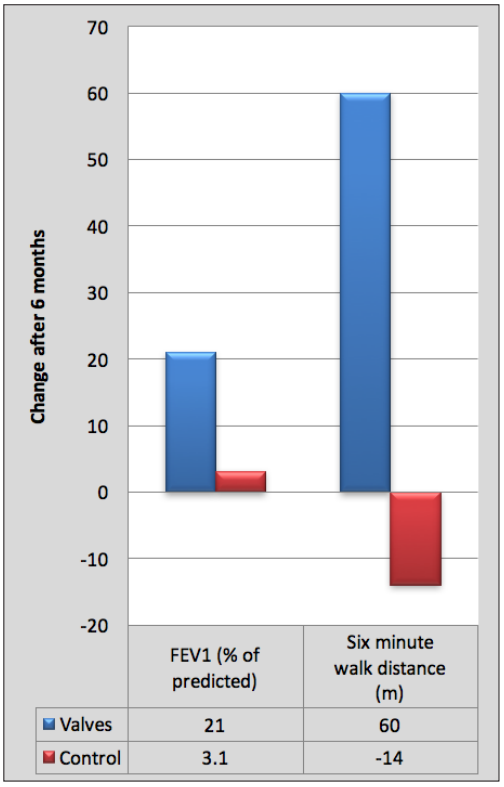

Figure 11: Change in FEV1 and 6 minute walk distance in a group of patients who underwent endobronchial valve insertion compared to an age and gender matched control group. Adapted from Klooster et al (reference 11).

Endobronchial valve insertion can be complicated with repeated chest infections and haemoptysis. Pneumothorax is a complication of concern that happens in up to 20% of patients.

Endobronchial coils

Endobronchial coils are wires made of nitinol that are designed to take their shape once deployed using bronchoscopy. The coils are introduced through a bronchoscope. They are held in a catheter and then pushed to the desired area of the lungs. As soon as the coil leaves the catheter it takes its 'birth shape'.

Coils help with emphysema through a combination of two mechanisms – the first is fortifying the floppy emphysema associated airways, and the second is volume reduction by folding emphysematous lung tissue. Typically 8 – 12 coil are introduced in each lobe and two lobes are normally treated. For coils to function appropriately there must be sufficient lung tissue. Unlike EBVs, coils are shown to be effective irrespective of the degree of collateral ventliation. Figure 12 shows coils in two lower lobes.

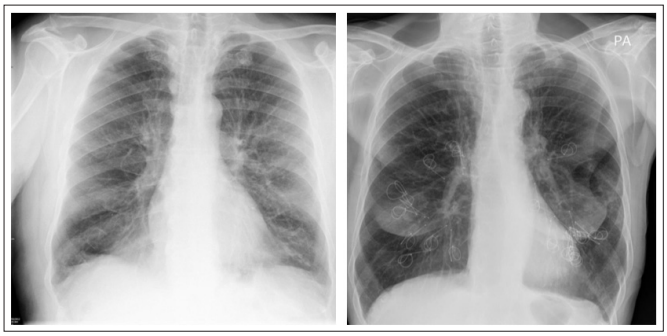

Figure 12: A 68 year old lady with emphysema before (left) and after (right) insertion of endobronchial coils in both lower lobes. An improvement of 46.6% in FEV1 was demonstrated, and a 200m increase in the 6 minute walk distance.

Two prospective studies have demonstrated effectiveness at 6 months (both studies) (12,13) and at 12 months (one study) (13). The studies also demonstrated a good safety profile in patients with emphysema.

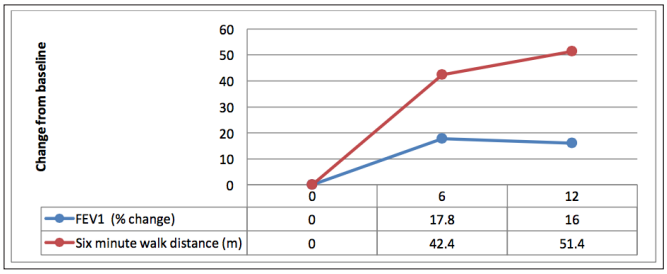

Figure 13: Improvement in FEV1 and 6 minute walk distance 6 and 12 months after insertion of endo bronhcial coils. Adapted from Deslee et al (reference 13)

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Lung transplant

Unilateral or bilateral lung transplantation is a high-risk but potentially curative option for patients with severe COPD. As for the other interventional methods described, the selection criteria are very specific. Furthermore, availability of lung donor specimens in the UK is low.

End of life care

Recognising end of life in COPD patients is not as straightforward as is often the case in lung cancer. The natural history of the disease is not linear, and patients with severe COPD remain alive for a long period of time. Pragmatic conversations about choices regarding death are often difficult to contemplate when patients consider themselves to be not too unwell.

Many patients only view hospital management with the aim of restoring their functional status, and would be distressed by end of life discussions; regardless of how well they are delivered.

However, the factors in table 3 are broadly shown to be poor prognostic factors that might prompt end of life conversations and end of life management. A shorter life expectancy is associated with increasing numbers of these prognostic criteria being met in an individual.

FEV1 < 30 % predicted
Breathlessness confining patients to within the house
At least two hospitalisations with exacerbations
The need of NIV for management of acute exacerbations
The need of mechanical ventilation for management of acute exacerbations
Low body mass index, low albumin, and anaemia

Table 3: Poor prognostic factors in COPD.

Questions

1: Which of the following are typically side effects of long-term oral corticosteroid use:

a) Osteoporosis
b) Diabetes mellitus
c) Central obesity
d) Easy bruising
e) All of the above

2: Potential side effects of salbutamol include all except:

a) Tachycardia
b) Increased risk of glaucoma
c) Transient hypokalaemia
d) Tremor
e) Anxiety

3: Which of the following lung function tests would most likely be seen in a patient with severe COPD with significant emphysema (% = % predicted for age, height, gender)?

a) FEV1 60%, FVC 65%, Total lung volume 65%, Gas transfer coefficient 40%
b) FEV1 55%, FVC 110%, Total lung volume 120%, Gas transfer coefficient 45%
c) FEV1 40%, FVC 110%, Total lung volume 115%, Gas transfer coefficient 45%
d) FEV1 110%, FVC 115%, Total lung volume 115%, Gas transfer coefficient 100%
e) FEV1 60%, FVC 65%, Total lung volume 65%, Gas transfer 90%

4: A patient attends the emergency department with an infective exacerbation of COPD. They have been given 40mg prednisolone, salbutamol and ipratropium nebulisers and intravenous antibiotics. Their GCS is 15, however they are short of breath and wheezy.

Their oxygen saturations are 89% on 4 litres/minute of oxygen delivered using a simple facemask. An arterial blood gas shows the following; pH 7.29, pO2 7.9 kPa, pCO_2 9.2 kPa, lactate 1.2 mmol/L, standardised bicarbonate 32 mmol/L, base excess +9 mmol/L. What is the most appropriate next management step?

a) Increase the oxygen flow rate
b) Repeat the ABG in 1 hour following further nebulisers
c) Fast bleep your senior to discuss starting non-invasive ventilation (NIV)
d) Commence CPR
e) Lie patient flat to allow them to breathe more easily

5. One of the following statements is correct for volume reduction:

a) Surgical management of emphysema can be offered to patients irrespective of the affected lobes of the lungs
b) Endobronchial valves are contra-indicated in patients with lower lobe emphysema
c) Endobronchial valves need to be inserted so they obstruct all the bronchi leading to the target lobe
d) Endobronchial coils should not be provided in patients with inter-lobar collateral ventilation
e) Endobronchial valve insertion improves FEV1 but not the exercise capacity

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Answers

1. Answer: e)

All of the above.

2. Asnwer: b)

Increased risk of glaucoma. This is an adverse effect associated with anti-muscarinic inhalers used in COPD.

3. Answer: c)

The lung pattern here is obstructive, and the % predicted FEV1 is less than 50%, which in the context of COPD would classify it as severe. a) = restrictive pattern, b) = less severe obstructive pattern, d) = normal, e) = restrictive

4. Answer: c)

The blood gas shows a respiratory acidosis with partial metabolic compensation, due to acute on chronic type 2 respiratory failure. This patient will most likely need NIV in order to counteract the acute accumulation of carbon dioxide which is causing the acidosis.

5. Answer: c)

In order to be successful valves must prevent airflow to an entire lobe. This is because collateral airway ventilation exists WITHIN lobes, and so volume reduction would not be achieved if some bronchi were left open. All of the other statements are false.

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NON-INVASIVE VENTILATION IN THE MANAGEMENT OF ACUTE COPD: A CASE BASED DISCUSSION

E Shahabuddin, H Moudgil

Abstract

Adult patients with respiratory disease may have had little or no response to initial treatment and stable patients may deteriorate within minutes. We will use a case example of a patient with Chronic Obstructive Pulmonary disease who developed Type 2 Respiratory failure to illustrate appropriate options for escalation, including non-invasive ventilation inclusion and exclusion criteria as outlined in the British Thoracic Society guidelines.

We also discuss referring to the High Dependency Unit and the importance of establishing a ceiling of care. We will provide a skill set directed at arterial blood gas interpretation. Through this article we hope to prepare the reader for the unpredictable challenges involved with being a Junior Doctor attending adult patients with respiratory disease

Case Illustration

A 70 year old usually confined to her home but managing with most activities of daily living presented to the Accident & Emergency (A&E) Department. She gave a background history of severe COPD on Long term oxygen therapy (LTOT), known right upper lobe bronchial carcinoma diagnosed on radiology within the previous six months, hip replacement surgery and prior deep vein thrombosis (DVT).

She had initially attended her General Practitioner (GP) with a three day history of worsening cough with breathlessness and when initially triaged in A&E her Early Warning Score (EWS) was 7. She was not febrile and haemodynamically stable but was drowsy and cyanosed with oxygen saturations of 85% on air. Chest auscultation confirmed symmetrical but limited air entry to the lungs with bilateral wheeze. There was no peripheral oedema.

She was referred to the medical teams diagnosed as an exacerbation of COPD with a lower respiratory tract infection (CURB 65 = 1) and had been prescribed regular nebulised bronchodilators (salbutamol/ipratropium), oral steroids, and intravenous antibiotics.

Her chest radiograph (CXR) confirmed hyperinflation but no pneumothorax or infection related consolidation as shown in figure 1 (Note it is an AP film and thus difficult to interpret). Electrolytes were within the normal range but inflammatory and infective markers raised with a mild neutrophilia and C reactive protein (CRP) at 153 (normal range <5). An Electrocardiogram (ECG) showed no acute changes.

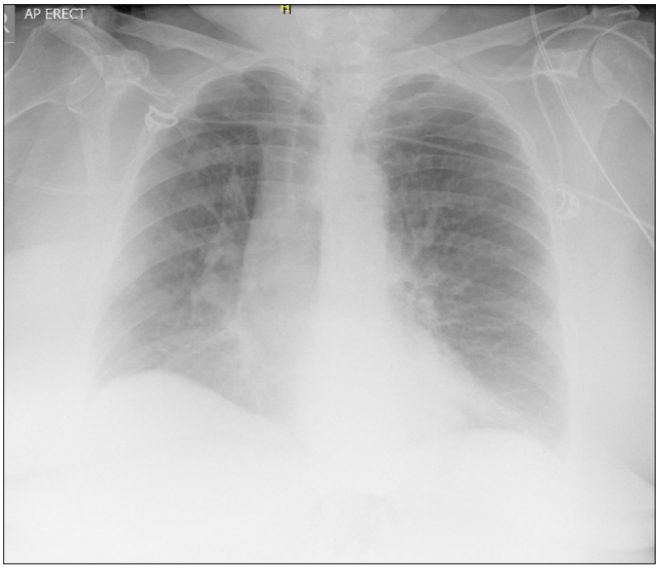

Figure 1: Chest radiology at admission with minor right lower zone consolidation.

Arterial blood gases (ABG) on air before any treatment showed hypoxia with respiratory failure (PaO_2 7.9, range 10-14 kPa) and hypercapnia ($PaCO_2$ 15.2, range 4.5-6.7 kPa) confirming type II respiratory failure with severe acidosis (pH 7.21, range 7.35-7.45). Repeated ABG an hour later whilst on treatment including controlled oxygen confirmed some improvement, respectively PaO_2 8.5 kPa but remaining hypercapnic with $PaCO_2$ 10.9 kPa and acidotic with pH 7.29. The patient was becoming exhausted, triggering need for clinical decisions on escalation of treatment.

She was started on an infusion of intravenous aminophylline and transferred to the respiratory ward for BiPAP as the ceiling of treatment. Her ABG improved but she had been uncomfortable with the nasal mask. Initial pressure settings on the Bi-PAP machine had been with IPAP 14, EPAP 5, back-up ventilator rate 12, with oxygen at 28%, and IPAP was quickly escalated (ramped up) to 18. Figure 2 shows a typical set up for non-invasive ventilation and the nature of mask (full face mask- not commonly used).

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Figure 2: Niv/Mask Set Up.

The hypercapnia and wheeze settled over the next two days during which time efforts were made to wean off the BiPAP, starting with changing the prescription to alternating four hours on and off and stopping the intravenous aminophylline. When clinically stable with oxygen saturations maintained at a target 88-92%, opportunity was taken to re-assess the previously diagnosed lung carcinoma to inform on prognosis. The chest CT scan was unchanged from six months earlier.

A meeting was arranged involving the patient and her family to discuss resuscitation status and about future similar presentations. Heavily weighted by the patient's own wishes the decision was made for her to follow a path of palliative care in the community and not for further NIV. Her GP was informed of this decision.

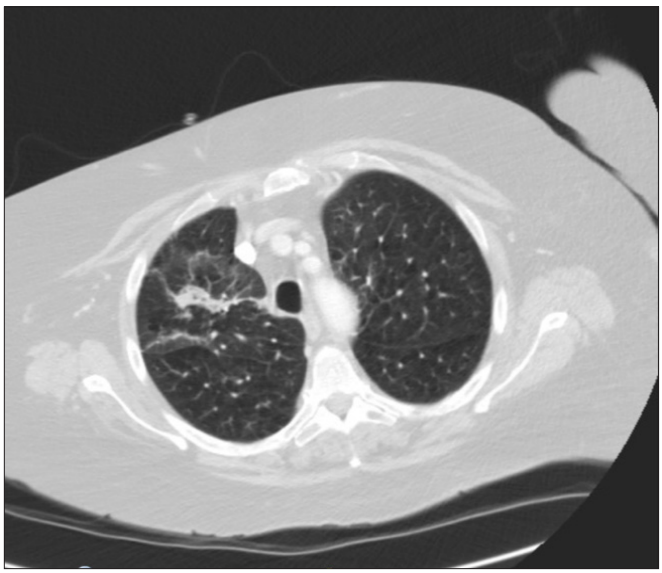

Figure 3: Chest CT scan showing 24 mm right upper lobe opacity.

Discussion

This case illustrates (1) a good outcome using NIV in managing acute type II respiratory failure with decompensated acidosis complicating acute exacerbation of COPD, (2) the need to promptly recognise the deteriorating patient with clinical signs and EWS as well as repeated ABGs, (3) offering a route to escalation or ceiling of treatment discussed with seniors and (4) the role of a patient centred approach in decision making and communicating with the GP.

BiPAP is increasingly being used in the acute setting and although at one time confined to the High Dependency or Intensive Care Units, its use has increased in respiratory and some medical wards as well as admissions units and some A&E departments. Use extends to not only COPD, but also weaning from mechanical ventilation and neuromuscular diseases.

The 2014 BTS/RCP audit of hospital services reported that 81% of respiratory wards offered NIV for acute COPD complicated by type II respiratory failure. [1] A 28 bedded respiratory unit such as ours typically has four patients at any one time on such machines at various stages of their exacerbation. Data show that mortality rate is reduced by 50 % with numbers needed to treat (NNT) at 10 for each life saved. [2]

It is important to optimise treatment for airflow obstruction usually over the first hour from presentation and an expectation is that you will develop competence with not only undertaking ABGs but also interpret findings. The minimum is being able to differentiate between respiratory or metabolic acidosis and qualify further as type I or II respiratory failure as highlighted in skill set Box 1; also identified are other conditions also giving rise to respiratory failure and where NIV is also considered.

Type 1 Respiratory failure (PaO_2 <8kPa, $PaCO_2$ <6.7kPa)

Develops from any lung disease (pneumonia, fibrosis, COPD, asthma), or vascular abnormality (Pulmonary embolus, pulmonary vasculitis or a right to left shunt).

Type II Respiratory failure (PaO_2 <8kPa, $PaCO_2$ >6.7kPa)

COPD, Obesity hypoventilation, cystic fibrosis or intercostal muscle weakness or diaphragm weakness.

Box 1: Respiratory failure.

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Whereas indications for NIV are obvious, it is more important to be aware of contra-indications for ward based care abbreviated from BTS guidelines as listed in Box 2.[3] Patients are sometimes initiated against protocol advice with more severe acidosis and usually considered more palliative with ceiling of treatment as ward based care.

Indications

Type II respiratory failure with mild acidosis (pH 7.26 to 7.35) with $PaCO_2$ >6.7

Contraindications

Facial burns, trauma, recent facial or upper airway surgery
Fixed airway obstruction, recent upper gastrointestinal surgery
Haemodynamically unstable requiring inotropes/pressors (unless in a critical care unit)
Life threatening hypoxaemia
Pneumothorax (unless intercostal drain inserted)
Copious respiratory secretions
Bowel obstruction
Vomiting
Severe co-morbidity
Confusion/agitation
Patient declines treatment

Box 2: Indications/contraindications to NIV in adults.

As in this illustrated case, patients may also have exacerbating factors including minimal consolidation but it is important to exclude pneumothorax or large pleural effusions. Patients may fail to respond to treatment with NIV and as such decisions to continue should be regularly reviewed initially after four hours. Others may simply be intolerant of NIV masks due to claustrophobia or are unable to tolerate or synchronise with the inspiratory/expiratory pressures.

Junior doctors should be aware of NIV/BiPAP guidelines [3] and the British Thoracic Soceity /Royal College of Physicians audit [1] suggests that 90% of Trusts offer some form of in-house training; this then includes developing a confidence in use of the tight fitting nasal or face mask as well as the NIV machines and usually settings for IPAP (to reduce hypercapnia), EPAP (to improve oxygenation) etc. which are more protocol driven.

The body acts to maintain a constant pH to optimise enzyme function and metabolic pathways. Metabolic acidosis is detected centrally by chemoreceptors in the medulla oblongata and peripherally in the carotid bodies and corrected acutely by stimulating hyperventilation to excrete carbon dioxide (CO_2). In contrast, as with this illustration, a metabolic compensation may develop over days/weeks in cases of CO_2 retention with the kidneys retaining more bicarbonate buffer (HCO_3^-): it was raised at 33 mmol/l (range 22-26) suggesting a chronic pattern which was then not being adequately compensated.

Before establishing NIV it is important to decide on the ceiling to treatment and in particular where failure would mean escalation to intubation and mechanical ventilation through intensive or high dependency care (ITU/HDU). It is necessary to make early decisions and involve seniors as well as any outreach ITU/HDU teams in a multi-disciplinary way. In decision making it is expected that there is familiarity with the case including weighing up any prior ITU admission, co-morbidities, LTOT, body mass index (BMI), baseline physiology including baseline ABGs or spirometry when stable, characteristics including quality of life (independence, mobility, care), etc. Where possible it is important to also establish any prior advance directives including regarding resuscitation the patient may have indicated.

MCQs Self-Assessment

1. A 65 year old with known COPD presented to A&E with increasing breathlessness. She had widespread coarse crackles and wheeze despite nebulised salbutamol and ipratropium bronchodilators and was drowsy with a respiratory rate of eight. On 35% oxygen her saturation was 85% with ABG pH 7.29 PaO_2 7.0 $PaCO_2$ 9.0 HCO_3^- 32. What would be the next best approach?

A) Persist with multiple (back-to-back) salbutamol nebulisers

B) Increase the oxygen and give high dose steroids

C) Call Intensive Care Unit

D) Regular nebulised salbutamol and ipratropium, high dose steroids, and repeat ABG after an hour and if no improvement start NIV

E) More than one approach

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2. A 74 year old man, usually independent, is being treated for right basal pneumonia and when reviewed on the ward saturates at 78% on 8L of oxygen. Respiratory Rate (RR) is 26/minute and Heart Rate (HR) 120/minute with bi-basal crackles. Repeat CXR shows new left basal consolidation and ABG pH 7.36 PaO_2 6.9 and $PaCO_2$ 4.0. How would you best manage this patient?

A) Increase the oxygen to 15L

B) Change his antibiotics

C) Increase the oxygen to 15L and discuss with Intensive Care Unit

D) Give IV diuretics

E) Give regular nebulisers and steroids

3. An 83 year old with a background lung cancer, ischaemic heart disease, hypertension, poor mobility with a frame and dependent on carers four times daily is admitted with increasing shortness of breath. She is on 15L oxygen with saturations of 88% despite clear chest radiograph and despite intravenous antibiotics appears fatigued. ABGs are difficult. How would you approach this patient?

A) Change the prescribed intravenous antibiotics

B) Start therapeutic Low Molecular Weight Heparin (LMWH)

C) Call for Intensive Care Unit review

D) Discuss Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) with senior

E) Continue antibiotics, consider therapeutic LMWH but call senior for decisions on ceiling of treatment

4. A 55 year old with known COPD is admitted with worsening breathlessness and evidence for bilateral widespread wheeze. CXR shows no consolidation, oxygen saturations are 90% on 2L/min with ABG pH 7.40 PaO_2 8.0 $PaCO_2$ 9.0. How would you initially manage this patient?

A) Increase his oxygen aiming for saturations >94%

B) Discuss with Intensive Care Unit

C) Continue regular nebulised bronchodilators and steroids, then repeat ABG

D) Call senior immediately and consider NIV

E) Start intravenous antibiotics

5. A 60 year old with known COPD, a step-down from Intensive Care Unit who three days earlier was treated with BiPAP, now develops a pyrexial illness with temperature 38.5 C, HR 110, BP 102/70, Saturations 90% on air, with right basal crackles (blunted right costophrenic angle on CXR) with no wheeze. ABG shows pH 7.38, PaO_2 9.3 $PaCO_2$ 5.5 HCO_3- 30. He remains on nebulised bronchodilators. How would you next manage this patient?

A) Recheck observations in an hour and if no improvement start antibiotics

B) Discuss with Intensive Care Unit

C) Add steroids and Oral doxycycline

D) Intravenous fluids and antibiotics to treat Hospital acquired pneumonia (HAP)

E) Intravenous fluids and antibiotics, with high flow oxygen to treat HAP and restart NIV

Answers

1. Option E

Although usual practice is to optimise therapy and recheck ABG as the patient is in the range to treat with NIV (mild respiratory acidosis), caution is needed here as patient is not only drowsy but also has reduced respiratory rate (eight) which might represent developing extreme exhaustion and therefore the patient should also be discussed with the intensive care unit.

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2. Option C

He is severely hypoxic secondary to pneumonia without hypercapnia or significant acidosis and thus is not a candidate for NIV, he may be a candidate for CPAP but would merit review by Intensive Care Unit. Although there may be a role for each of the other options particularly if there has been progressive disease unresponsive to initial antibiotics or fluid overload if treating sepsis, the best approach is to increase his inspired oxygen concentration and have a discussion with Intensive Care Unit.

3. Option E

Although there are multiple co-morbidities and frailty, both infection and pulmonary embolic disease represent a potentially reversible cause and as such it is important to empirically treat but discuss and establish ceiling of care (rather than only DNACPR) at an early opportunity.

4. Option C

His oxygen saturations are within target range for exacerbation of COPD (88-92%), despite hypercapnia he does not need immediate NIV as he has a compensated respiratory acidosis indicative of chronic hypercapnia which is not an indication for acute NIV treatment. The best approach is to persist with medical management treating airflow obstruction and monitor progress with repeated ABG.

5. Option D

It is likely that the patient has developed HAP and should be managed as per sepsis protocols. PaO2 of 9.0 is usually adequate in patient with COPD and care should be taken when giving oxygen (work to target saturations). The current ABG is satisfactory in context of not needing to restart NIV but if giving oxygen it is important to monitor ABG.

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OPPORTUNISTIC LUNG INFECTIONS IN HAEMATOLOGY PATIENTS

J Brown, S Mithra

Opportunistic Infections In Haematology Patients – A Wide Differential

Major suppression of the immune system makes patients susceptible to pneumonia caused by a large range of microorganisms, creating a significant diagnostic challenge. Due to more effective chemotherapy regimes (not always requiring inpatient administration) that also often contain high dose steroids and frequent use of stem cell transplantations, patients with haematological malignancies are at particularly high risk of developing opportunistic lung infections.

Between 40-60% (1) of haematology patients will present with pulmonary infections during their management, and these are associated with high morbidity and often are a direct cause of mortality (2). Prompt recognition and management is vital in these cases as fulminant infection can rapidly develop. Non-infective causes of lung disease are also common and need to be considered in the differential diagnosis.

This article will discuss the types of opportunistic infections that are encountered in haematology patients along with their management principles and radiological findings. A clinical case will help illustrate the clinical approach to an immunocompromised patient with potential lung infection.

Case Study

A fifty-one year old man with no significant past medical history was noted to be pancytopenic (see learning point 1) during routine investigation of a lipoma and was subsequently diagnosed with biphenotypic acute leukaemia. He had no symptoms prior to presentation and was transferred for commencement of chemotherapy 4 days after the pancytopenia was noted.

Learning Point 1: Definitions

Neutropenia – a neutrophil count of less than 1.0X10^{9}ml on a full blood count differential panel.

Pancytopenia – reduction in all the formed elements of blood, signifying an underlying problem in the bone marrow, with low platelet and total white cell counts and reduced haemoglobin concentration

Leukaemia – a white cell malignancy characterised by high numbers of abnormal immature white blood cells (classified according to lineage; either myeloid or lymphoid); starts in the bone marrow. Biphenotypic acute leukaemia has features of both acute myeloid leukaemia (AML) and acute lymphoid leukaemia (ALL)

Prior to starting the second cycle of chemotherapy, he was re-admitted to hospital after a collapse. Blood tests revealed he had been persistently neutropenic between these two admissions (total duration of 1 month post chemotherapy). He was pyrexial, with a productive cough and coarse bibasal crepitations on examination.

Baseline observations	Temperature 38.6, Blood pressure 90 mmHg systolic (after 2.7 L intravenous crystalloid), Heart rate 115 bpm, RR 35, Oxygen saturations 95% on 8L/min oxygen (dropping to 85% on air)		
Blood results on admission	Hb 83 g/L WCC 0.01 x 10^9/L Platelets 29 x 10^9/L CRP 346 mg /L	Na 134 mmol / L K+ 4.5 mmol / L Urea 11.7 mmol / L Creatinine 85 mmol / L	ABG on 8L/min Oxygen pH: 7.27 pO2: 8.5 kPa pCO2 6.4 kPa HCO3- 17.6 mmol/L

Table 1: Initial observations and blood results.

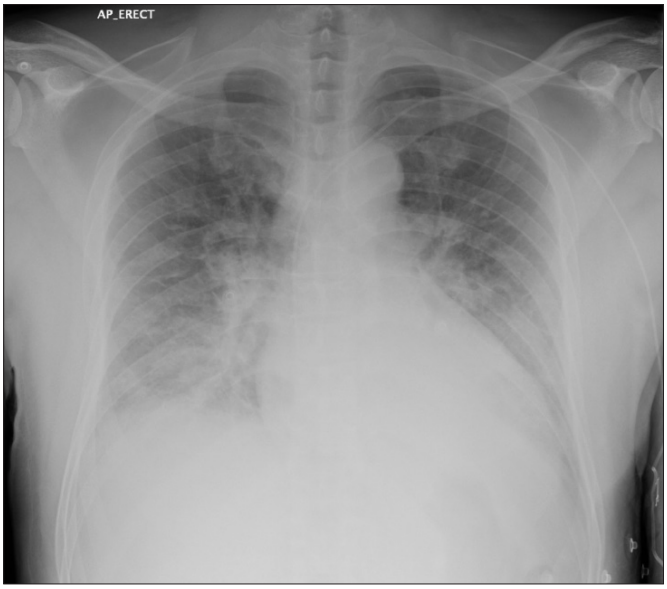

Figure 1: Bilateral lower zone changes, consistent with pneumonia but not specific. Note also, presence of a left-sided subclavian venous access catheter (PICC line).

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The results of the key initial investigations are shown in table 1 and the admitting chest X ray in figure 1. His blood gases showed a metabolic acidosis with a low pO_2.

Due to his high oxygen requirements, evidence of respiratory failure and consolidation on chest X-ray, he was admitted to the intensive care unit for Optiflow non-invasive ventilation and inotropic support.

He was initially treated empirically with Piperacillin/Tazobactam at 4.5g four times daily and Caspofungin 70mg once daily (to cover the possibility of aspergillosis due to his prolonged neutropenia).

To define the chest X ray abnormalities in more detail and thereby suggest the causative organism, a CT scan was obtained which demonstrated bilateral patchy consolidation suggestive of bacterial pneumonia (Figure 2). On the second day of admission the blood cultures grew Klebsiella pneumoniae resistant to amoxicillin, piperacillin/tazobactam and trimethroprim but sensitive to carbapenems and ciprofloxacin. Hence his treatment was changed to meropenem 1g three times daily, and his pyrexia faded over the next four days.

He remained on the intensive care unit for 1 week, moving to the haematology ward once he was maintaining his oxygenation comfortably with saturations >96% on air. By day 8, his neutrophil count had recovered to 1.01 x 10^9/ml with a total white cell count of 1.26 x 10^9/ml. He remained in hospital for a further 18 days and was on meropenem for 9 days in total, making a good recovery with no persisting respiratory symptoms. Repeat chest X-Ray (after 6 weeks) showed good resolution of the basal consolidation.

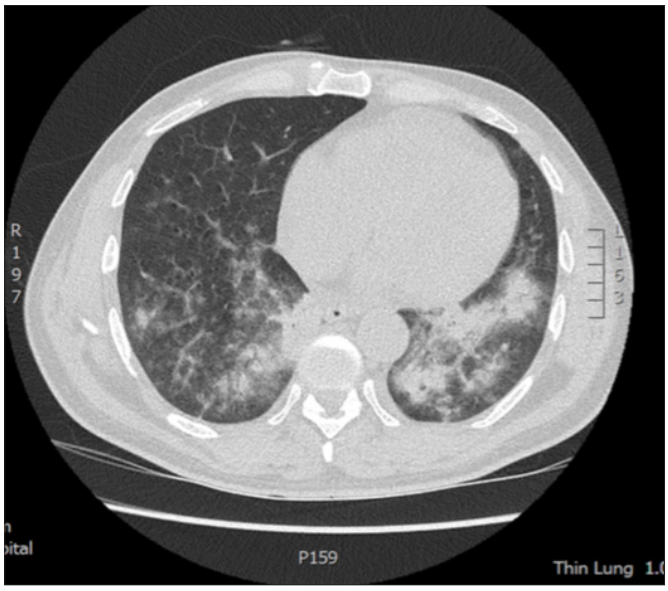

Figure 2: CT thorax showing bilateral patchy consolidation in both lower lobes. Differentials include bacterial pneumonia, viral infection and possible invasive filamentous fungal chest infection (eg aspergillosis).

What causes immunodeficiency in haematological malignancy?

There are a number of mechanisms by which immunodeficiency occurs in haematological malignancy (2,3), each of which predisposes to a different range of potential pathogens . These mechanisms include both the diseases themselves and the treatments for these diseases such as chemotherapy and haematopoetic stem cell transplant (HSCT).

There are three main patterns of immunodeficiency (2, learning point 2):

· Neutropenia; usually caused by cytotoxic chemotherapy, marrow infiltrations or aplastic anaemia. A neutropenic state predisposes to bacterial or, if prolonged (>2 weeks), filamentous fungal lung infections. This is a very common finding in haemato-oncology patients receiving chemotherapy, and immediately after HSCT.

· Deficiencies in cell mediated immunity;; caused by long term immunosuppressive drugs (corticosteroids, tacrolimus, ciclosporin), lymphoproliferative disorders and after HSCT. Places patient at risk of intracellular pathogens such as Nocardia species, mycobacteria, herpesviruses (especially CMV), respiratory viruses, the fungus Pneumocystis jirovecii (Pneumocystis pneumonia, PCP) and parasites (toxoplasmosis) (2,3).

· Deficiencies in antibody mediated immunity;; causes include post-HSCT, myeloma, CLL, and rituximab therapy for lymphoma, as well as inherited and acquired primary immunodeficiencies. Associated with cutaneous herpesvirus and bacterial lung infections (2,3).

Allograft HSCT leads to more prolonged and profound immune defects than autograft HSCT and therefore has a high incidence of associated opportunistic infections.

Learning Point 2: Immunological Response Mechanisms

Cell mediated immunity – lymphocyte recognition of microbial antigens leading to cytokine release and activation of other immune system cells (phagocytes, lymphocytes), or direct killing of infected host cells.

Antibody mediated immunity – antibody production in response to a foreign antigen (by B-cells) that will recognise and bind to this antigen again on repeated exposure, thereby promoting microbial killing by phagocytosis.

OPPORTUNISTIC LUNG INFECTIONS IN HAEMATOLOGY PATIENTS

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Principles of Assessment

As with all presentations of acute medical problems, a thorough and detailed history is vital to reach a reasonable differential diagnosis. Haematology patients present with the usual symptoms of respiratory compromise (shortness of breath, cough, wheeze and chest pain) but lung infections can also cause fever and marked systemic symptoms (myalgia, anorexia and lethargy) without localising lung symptoms. Duration of the symptoms helps determine underlying cause with bacterial and viral infection developing more commonly over days and atypical and fungal infections over longer periods of time (weeks) (4).

The drug history needs to include both current drugs and recent treatments including intermittent therapies such as rituximab or chemotherapy courses. Neutropenia is a common side effect of haematological therapy (usually seen between 7-21 days after administration) and care must be taken to account for any potential drug interactions (e.g with other drugs causing pancytopenia such as carbimazole, clozapine and anti-epileptic medications) (5). The duration of neutropenia may be longer during subsequent cycles of chemotherapy due to cumulative effect of the medication. This is when the chance of developing an opportunistic infection is at its highest.

Learning Point 3: Prophylactic Medications

Haematology patients are often already on long term antibiotics to prevent development of infections. These include:

Aciclovir - antiviral prophylaxis

Co-Trimoxazole (Septrin) – anti-Pneumocystis prophylaxis (also prevents Nocardia)

Itraconazole/Posaconazole – antifungal prophylaxis (especially Aspergillus)

Depending on the causative pathogen, crepitations, squeaks and wheezes are possible findings on examination of the lungs. However, it is important to note that examination is often unremarkable for some pathogens *(eg Aspergillus, P. jirovecii)* (5). Low saturations and tachypnoea suggest extensive consolidation (bacterial pneumonias) or a bilateral interstitial process related to viral or *P. jirovecii* infections.

A full set of bloods (including blood film, clotting and CRP) will help direct further management;; rapid increases in CRP levels to very high levels over 24 to 48 hours would suggest bacterial infection. Respiratory viral swab should be considered, especially if the patient has myalgia or coryzal symptoms. Blood cultures, line cultures and when indicated by symptoms urine/stool/sputum cultures should be taken.

Febrile neutropenic patients need prompt delivery of broad spectrum antibiotics according to trust guidelines within an hour. Correction of blood dyscrasias should also be part of management particularly if haemoglobin is below 80g/L or if the platelets fall below 20 x 10^9ml.

Causes Of Pulmonary Infection In Haematology Patients – The Differential Diagnosis & Investigations

The table below summarises the main findings for opportunistic infection in haematology patients (8). The plain chest X ray film is often non-specific and can be even be normal. CT scanning (in particular HRCT) can define the pattern of radiographic disease much more accurately and thereby suggest the diagnosis (especially in the case of invasive aspergillosis and PCP) (9). More invasive investigations may be necessary such as bronchoscopy to obtain bronchial lavage from the affected lobe, or in rare cases CT guided or even surgical biopsy (7). Biopsies are particularly effective ways to diagnose peripheral macronodules caused by aspergillosis or Nocardia species.

	Bacterial	**Invasive Filamentous Fungi (mainly *Aspergillus* species)**	***Pneumocystis jirovecii* Pneumonia**	**Herpesviruses**	**Respiratory Viruses**
Common Presentation	- Fever - Tachypnoea, - Hypoxia - Cough - Purulent sputum - Crepitations over affected lobe(s) - Rapid onset over days	- Persistent fever - Cough - Pleuritic chest pain - Haemoptysis - Few signs (pleural rub rarely) - Develops over days to weeks	- Exercise induced dyspnoea and hypoxia - Dry cough - Few signs - Develops over days to weeks	- Fever - Cough - Hypoxia - Bilateral crepitations - Rapid onset over days	- Coryza - Mylagia - High fever - Cough - Hypoxia - Bilateral squeaks and crepitations - Rapid onset over days
At risk patients	- Neutropenia - HSCT - Immunosuppressive therapy	- Prolonged neutropenia >10 days - HSCT - High dose systemic corticosteroids	- HSCT - High dose systemic corticosteroids - T cell immunosuppression	- HSCT - High dose systemic corticosteroid - T cell immunosuppression	- HSCT - High dose systemic corticosteroid - T cell immunosuppression
Pathogens	- Gram negative bacilli *(Pseudomonas aeruginosa Klebsiella, Eshcerichia .coli, Acinetobacter baumannii)*, - Gram positive cocci *(Staphylococcus aureus, Streptococcus pneumoniae)*	- *Aspergillus fumigatus* - *A.flavus* - *A.niger* Rare: - *Mucor* - *Pencillium* - *Scedosporium*	- *Pneumocystis jirovecii*	- Cytomegalovirus (CMV) - Herpes Simplex Virus (HSV)	- Influenza - Parainfluenza - Respiratory Syncytial Virus (RSV) - Adenovirus - Metapneumovirus - Coronavirus
Pathogenesis	- Oropharyngeal commensals - Acquired from hospital environment - Blood-borne, via a central line catheter (PICC line, Hickman line or Portacath) (9).	- Inhalation of ubiquitous airborne spores (7) - Defective phagocyte function / numbers	- Impairment of cellular and humoral immunity - Uncontrolled replication of *Pneumocystis*.	- Usually reactivation of latent infection - T-cell mediated immune deficiency	- Droplet spread from infected individual - T-cell mediated immune deficiency (4)
'Classic' Imaging appearances	- Consolidation (lobar, segmental) with air-bronchograms.	- Macronodular lesions with "ground glass halo" or cavitation with a central mycetoma (air crescent sign) (3)	- Extensive bilateral ground glass infiltrates with peripheral sparing and upper zone dominance	- Bilateral Ground glass / alveolar opacities	- Bilateral Ground glass / alveolar opacities. - Bilateral treeree-in-bud (3).
Treatment	- Broad spectrum antibiotics; eg Piperacillin/Tazobactam	- Amphotericin - Voriconazole or posaconazole - Caspofungin	- High dose Co-Trimoxazole - Steroids (if hypoxic) - Or Clindamycin and Primaquine	- CMV: ganciclovir or foscarnet - HSV: aziclovir	- Zanamivir (Influenza)

Table 1: Differential Diagnosis.

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Learning Point 4: Non-infectious causes of respiratory compromise

In addition to the infectious causes, there are a number of non-infectious causes (9) to consider in the differential diagnosis such as:

- Pulmonary oedema
- Acute respiratory distress syndrome (ARDS)
- Transfusion associated lung injury (TRALI)
- Drug induced lung disease: chemotherapeutic drugs such as bleomycin, rituximab, methotrexate
- Radiotherapy pneumonitis
- Lung graft versus host disease causing bronchiolitis obliterans
- Organising pneumonia

When to call for help

Patient management frequently requires the involvement of a multidisciplinary team including respiratory, haematology, microbiology, radiology and often intensive care teams. If the patient is on active chemotherapy with presumed neutropenic sepsis (or deranged clotting parameters), early referral to the haematology team is advised.

As antibiotic resistance is becoming more prevalent, review of previous cultures and discussion with the microbiology teams should happen early to ensure adequate cover. Trust guidelines will have recommendations of empirical broad spectrum antibiotics so as not to delay initial treatment. Should there be no improvement in blood pressure or saturations, referral to critical care may be considered for early administration of non-invasive ventilation.

Conclusion

Respiratory disease forms a large proportion of complications in haematology patients. It is important to remember that more than one type of infection can be present simultaneously and that non-infectious causes must be considered.

Although there are multiple pathogens that can cause opportunistic infections they do have distinctive clinical patterns and are associated with different types of immunosuppression, which allows the diagnosis to be suspected in many cases. However, aggressive empirical therapy and investigation is still frequently necessary. A thorough clinical investigation carried out in collaboration with haematology, respiratory and microbiology teams is vital to properly improve patient outcomes.

Multiple Choice Questions

1. A 54 year old man is referred to the Respiratory Outpatients Department with increasing dyspnoea and dry cough over the last 4 months. There is evidence of pallor, clubbing, end-inspiratory crepitations at the lung bases (which are dull to percussion). Chest X-Ray shows reticulonodular shadowing and CT Thorax reveals honeycomb patterning. He undergoes spirometry which shows a restrictive pattern. A diagnosis of pulmonary fibrosis is suspected. Which of the following drugs is the least likely to cause a pulmonary fibrosis?

a. Bleomycin

b. Amiodarone

c. Ramipril

d. Methotrexate

e. Nitrofurantoin

2. A 48 year old lady, who has undergone a allograft HSCT for AML 12 months ago presents with a 8 week history of progressive dyspnoea. She is not febrile. On auscultation of her lungs there is a widespread expiratory wheeze. X-Ray looks normal and the CRP is not raised. Spirometry shows an obstructive picture. What is the most likely cause?

a. Pneumocystis jirovecii pneumonia

b. Drug induced lung pathology

c. Bacterial infection

d. Graft versus host disease causing bronchiolitis obliterans

e. Aspergillus infection

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3. You review a 54 year old man who had an autograft HSCT for myeloma 3 months previously. He now presents with a 4 week history of progressive dyspnoea and a dry cough. On examination there are no respiratory signs except for a high respiratory rate (30/minute). Saturations on air are 98% but he desaturates to 87% on mobilising. Chest X-Ray is reported as normal, but you think may show a subtle interstitial infiltrate. He has not been on antifungal prophylaxis. Given the most likely diagnosis, what is the next most appropriate investigation to help confirm the diagnosis?

a. Blood cultures

b. High resolution CT Thorax

c. Sputum culture

d. Respiratory swab

e. Spirometry

4. A 60 year old lady who has completed her third cycle of chemotherapy for ALL and has had a persistent neutropenia is admitted with high fevers and a cough. Admission CXR revealed an area of air space shadowing in the right upper lobe. She was commenced on empirical antibiotics (piperacillin-tazobactam) for neutropenic sepsis, but the fever persisted. HRCT was performed with report including "right upper lobe macronodule with surrounding ground glass attenuation" corresponding areas to the CXR abnormality. What is the most likely diagnosis?

a. Invasive aspergillosis

b. Cytomegalovirus pneumonia

c. Pneumocystis jirovecii pneumonia

d. Pulmonary oedema

e. Streptococcus pneumoniae pneumonia

Answers

1. C - Ramipril

Many drugs can cause a disease similar to idiopathic pulmonary fibrosis. In addition to chemotherapeutic agents such as bleomycin or methotrexate, long term use of nitrofurantoin (as Urinary Tract Infection prophylaxis) or amiodarone can cause interstitial lung disease and pulmonary fibrosis. Ramipril is a common cause of chronic cough but does not cause interstitial lung disease.

2. D – Bronchiolitis Obliterans

Allograft HSCT can cause a lung graft versus host disease that causes bronchiolitis obliterans. This is a non-infectious cause of small airways obstruction and as such does not present with fever. The chest X-ray is usually unremarkable but the lung function tests will show an obstructive picture that is often poorly reversible with treatment.

PCP and drug-induced pathology both may also present with progressive dyspnoea over weeks but do not usually cause a wheeze or obstructive lung function, and the chest X ray is likely to show interstitial infiltrates. Aspergillus or bacterial pneumonias tends to present with fever and neutropenia and an abnormal chest X ray.

3. B – High resolution CT Thorax

The key points are the history of progressive dyspnoea and exercise induced desaturations in a patient with a T cell immune defect; this points to a diagnosis of P. jirovecii pneumonia. The chest X ray can look normal, but an HRCT would reveal ground glass alveolar infiltrates with a characteristic upper lobe predominance and sub-pleural sparing and as such would be the best next step in investigating the underlying cause.

Blood and sputum cultures, spirometry and respiratory swab for viruses may form part of the management plan to help exclude other diagnoses but do not help identify P. jirovecii pneumonia.

OPPORTUNISTIC LUNG INFECTIONS IN HAEMATOLOGY PATIENTS

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4. A - Invasive aspergillosis

Pulmonary nodules surrounded by ground glass attenuation is commonly referred to as a "halo sign". This is an early radiographic finding of invasive filamentous fungal infection, and represent small areas of haemorrhage around the area of infection. The commonest cause of invasive filamentous fungal infections are Aspergillus species, especially

A. fumigatus. The most important risk factors for invasive aspergillosis are prolonged neutropenia or high dose systemic corticosteroid treatment. . S. pneumoniae pneumonia should respond rapidly to piperacillin-tazobactam and causes consolodiation rather than a macronodule. CMV, P. jirovecii, and pulmonary oedema usually cause bilateral interstitial infiltrates, not a macronodule.

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THE SPONTANEOUS PNEUMOTHORAX

A Paracha, M Paracha

Case

A 42 year old lady arrived in the Accident and Emergency Department in respiratory failure with a reduced level of consciousness. Shortly after arrival, she had a cardiac arrest with pulseless electrical activity (PEA); advanced life support was commenced with cardiopulmonary resuscitation, endotracheal intubation and 3 doses of adrenaline 1mg intravenously with return of spontaneous circulation after 13 minutes.

Subsequently, a more thorough history indicated that the patient had been unwell for the last two weeks with symptoms of an upper respiratory tract infection, and was treated with antibiotics and steroids by her General Practitioner two days ago. She had no significant past medical history, smoked 7 cigarettes per day, and was a non-drinker.

An urgent chest X-ray revealed a large right pneumothorax (See image 1) and an intercostal drain was inserted which resulted in improved oxygenation. A later review of the chest X-ray revealed that she also had a smaller left-sided pneumothorax at initial presentation that became worse subsequently (See image 2).

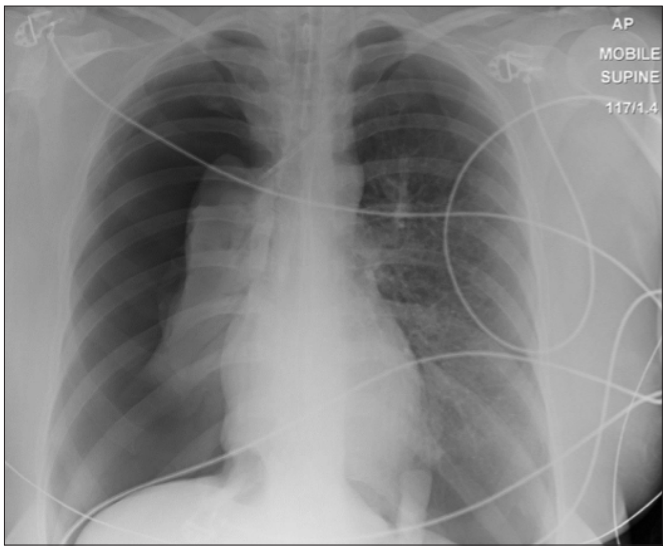

Image 1: Initial Chest X-Ray showing a large right pneumothorax.

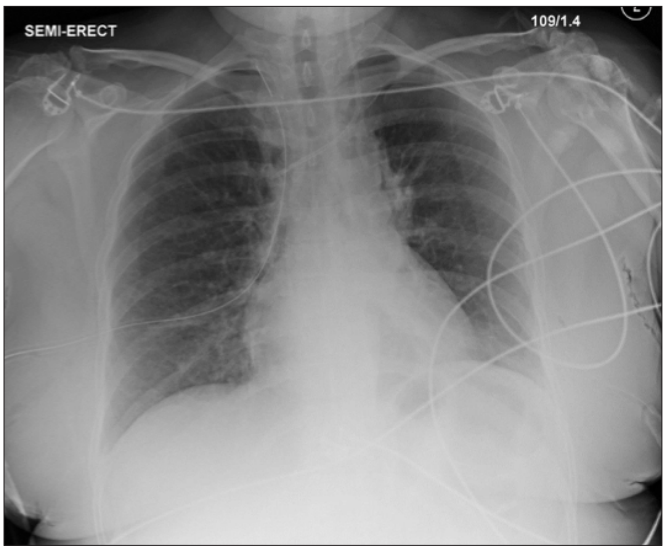

Image 2: Chest X-Ray the following day showing a new left pneumothorax and recovering right-sided pneumothorax.

This highlighted the importance of systematically reviewing imaging. A second chest drain was inserted on the left side and the patient made a quick recovery.

A non-contrast computerised tomography (CT) Scan (See image 3) revealed findings suggestive of lymphangioleiomyomatosis (LAM), a rare type of cystic lung disease. CT abdomen excluded an angiomyolipoma. Video-assisted thoracoscopic surgery (VATS) and pleural abrasion was performed with lung biopsies, which confirmed the diagnosis. The patient was discharged after two weeks.

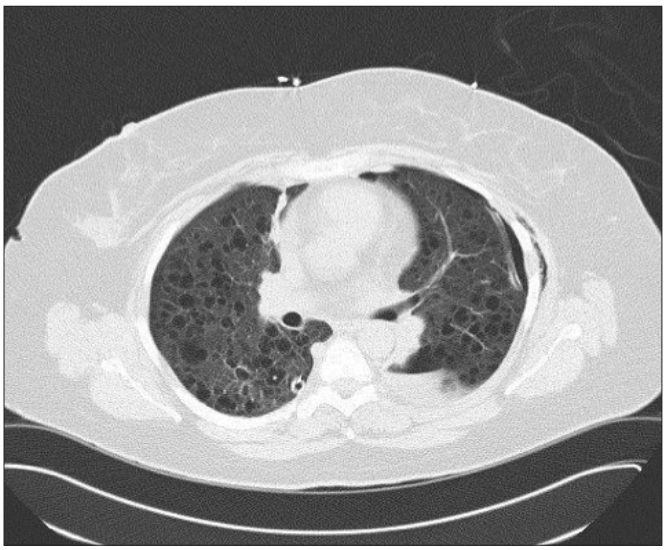

Image 3: Non-contrast CT thorax showing extensive bilateral thin walled cysts with uniform distribution highly suspicious of LAM.

THE SPONTANEOUS PNEUMOTHORAX

A Paracha, M Paracha

Discussion

A pneumothorax is a collection of air in the pleural space (See diagram 1). It is an important acute respiratory condition, which most junior doctors will encounter. The term 'spontaneous' means there was no provoking factor, eliminating external trauma as the aetiology. Estimated incidence is 24/100,00 in men and 10/100,000 per year in women in England and Wales with smoking significantly increasing risk by 22 times in men and 8 times in women. (1)

Spontaneous pneumothoraces are classified into primary and secondary (See table 1). Differentiating between these is important, as patients with SSP are more symptomatic and have poorer outcomes (2) due to reduced pulmonary reserve. (3) Consequently, even a small pneumothorax in a patient with severe chronic obstructive pulmonary disease (COPD) can cause type 2 respiratory failure.

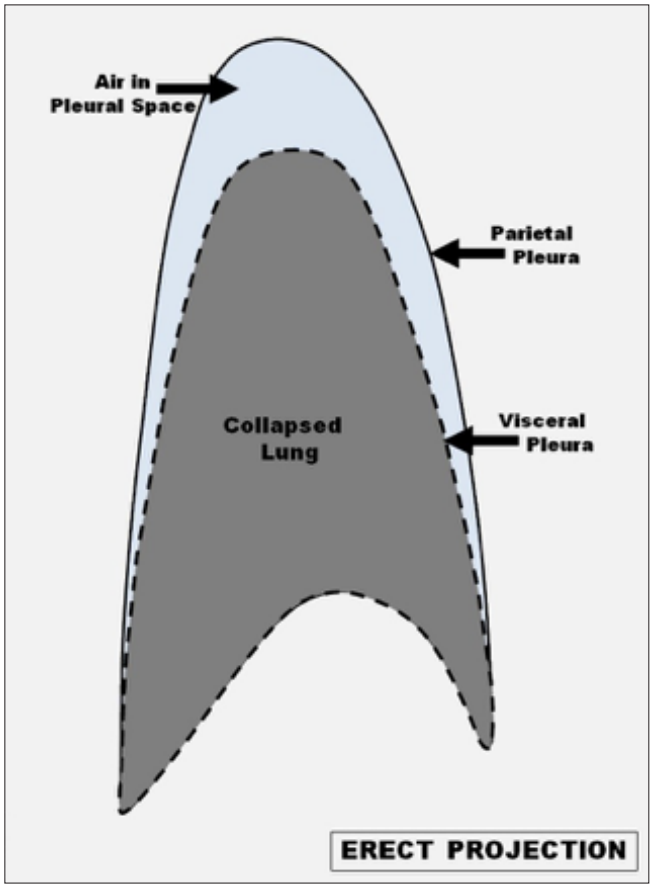

Diagram 1: A Pneumothorax.

Case courtesy of Dr Nikos Karapasias, Radiopaedia.org, rID: 25667

	Causes/Risk Factors	The 'Typical' Patient
Primary Spontaneous Pneumothorax (PSP) **Occurs without a precipitating event in an otherwise healthy person**	• Rupture of subpleural bleb or bulla • Smoking • Family history	• Young male, typically early 20s • Tall stature • Low body weight • Smoker • Acute dyspnoea and chest pain occurring at rest
Secondary Spontaneous Pneumothorax (SSP) **Occurs as a complication of an underlying lung disease**	• COPD • Cystic fibrosis • Primary or metastatic malignancy • Tuberculosis • Infective - necrotising pneumonia • Connective tissue disease • Cystic lung disease e.g. Lymphangioleiomyomatosis, Pulmonary Langerhans Cell Histiocytosis	• Underlying lung disease • Increased severity = increased incidence

Table 1: Spontaneous Pneumothorax Causes, Risk Factors and Typical Features.

Conversely, PSP patients can present with little or no dyspnoea and chest pain may be a more prominent feature. (2) Although they may be hypoxic, hypercapnia rarely results. By definition, PSP occurs in healthy individuals with no overt lung disease, however, anatomical and histological abnormalities such as subpleural blebs, bullae and destructive changes have been found. (2, 4) Aside from this, a tension pneumothorax is a medical emergency and should always be promptly assessed for.

Signs and symptoms

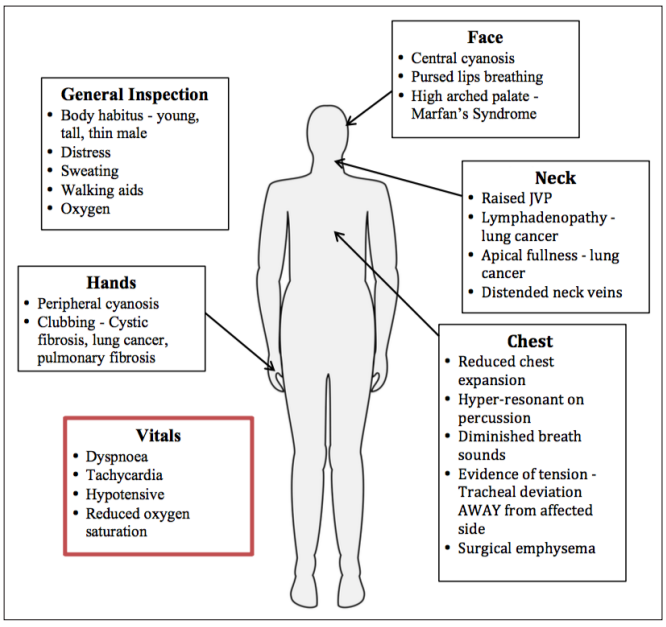

Diagram 2: Signs and symptoms of a pneumothorax.

THE SPONTANEOUS PNEUMOTHORAX

A Paracha, M Paracha

Tension Pneumothorax: A Medical Emergency

When the accumulating air in the pleural space begins to exert pressure upon thoracic and mediastinal structures, this is known as a 'tension pneumothorax'. A 'one-way valve' is created; with every breath more air escapes into the pleural cavity but does not return. This can result in haemodynamic instability and therefore patients may exhibit signs of shock.

Scenarios in which tension pneumothorax is more common include invasive ventilation, trauma, resuscitation and in underlying lung disease. It is a life- threatening emergency requiring immediate action via oxygen and emergency needle decompression (see 'Needle aspiration'). The sound of air leaving the thorax confirms the diagnosis and converts the tension pneumothorax into a simple pneumothorax. Rapid chest drainage should then be performed.

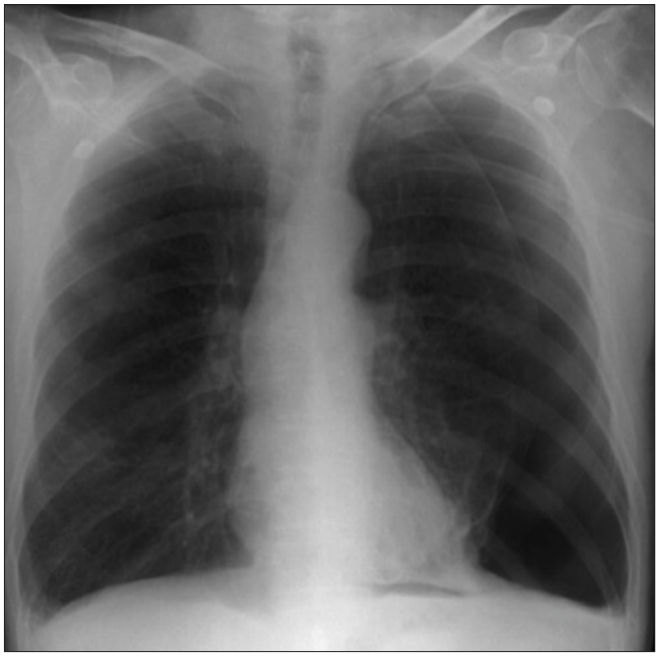

Image 4: X-Ray showing tension pneumothorax of the left lung. Classic radiological features of tracheal deviation and mediastinal shift to the contralateral side and depression of the hemidiaphragm are present. Case courtesy of AProf Frank Gaillard, Radiopaedia.org, rID: 15374.

Investigations

Imaging is the mainstay for diagnosing pneumothoraces that do not have signs of tension or haemodynamic instability:

- Standard erect chest X-ray in inspiration is the best initial investigation.
- CT scan can be used in uncertain or complex cases.

The size of the pneumothorax is determined via the visible rim of air between the chest wall and lung at the level of the hilum. (2) If suspected, investigations for other conditions (See Table 2) should also be part of the initial workup.

Differential diagnoses for sudden onset of dyspnoea

- **Pneumothorax**
- **Pulmonary embolism**
- **Acute left ventricular failure**
- **Acute exacerbation of asthma and COPD**
- **Anaphylaxis**

Management

The British Thoracic Society has a set of clear guidelines to aid decisions surrounding patient management (See image 5) based on the following principles:

1. Clinical compromise and/or shortness of breath.

2. PSP or SSP: Generally speaking there should be a lower threshold for active intervention for SSP. Patients with a small, asymptomatic PSP can be treated conservatively.

3. Size of the pneumothorax: 2cm is the magic number; a pneumothorax larger than this will need to be actively managed.

THE SPONTANEOUS PNEUMOTHORAX

A Paracha, M Paracha

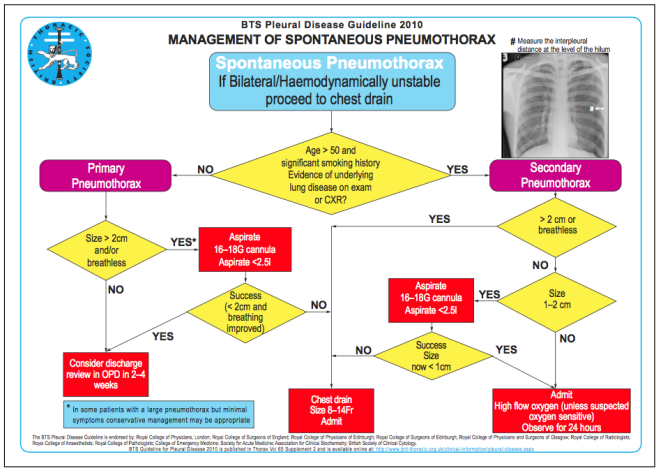

Image 5: Needle Aspiration.

• Use a 16-18G intravenous catheter placed in the mid-clavicular line at the second or third intercostal space. Length should be judged on body habitus. This is important, as injury to the lung must be avoided whilst attempting to successfully release the air.

• A large syringe is then used to withdraw air from the pleural space, the patient can be asked to exhale to avoid air entering the cavity. Withdrawal of more than 2.5 litres of air indicates persistent leak and the need for a chest drain (5).

Chest Drain

• A small bore (8-14 Fr) chest drain inserted by the Seldinger technique is sufficient in the majority of cases. Prior to insertion ensure adequate analgesia, sedation (if possible) and oxygen as required. In addition, double check the details of the patient and confirm the correct side by reviewing the chest X- ray. The drain is then inserted by a trained professional, within the 'safe triangle' to avoid damage to surrounding structures (See Image 6).

A passive drainage system using underwater seal drainage (See Image 7) or unidirectional flutter valve should be employed. Suction is not routinely needed (5).

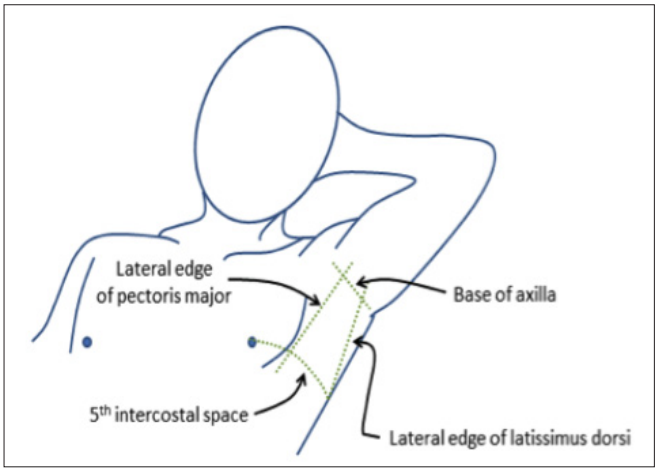

Image 6: The 'safe triangle' for insertion of chest drains.
Courtesy of: http://ceaccp.oxfordjournals.org/content/8/6/204.full

Management of a Chest Drain

• The water seal chamber should rise with inspiration and fall with expiration if working correctly. If it does not appear to be working ensure the tube is not kinked or occluded.

• Air leak should be assessed daily. It is best to document its relation to the respiratory cycle in terms of whether it is inspiratory, expiratory, continuous or on coughing. The drain should not be removed until air bubbling ceases.

• Never lift the drain above the patient or clamp a bubbling drain.

• Consider referral to cardiothoracic surgery if there is persistent air leak after 5-7 days (5).

Image 7: Underwater seal drainage system.
Courtesy of: www.icid.salisbury.nhs.uk.

THE SPONTANEOUS PNEUMOTHORAX

A Paracha, M Paracha

Prognosis and Recurrence Prevention

Although deaths from spontaneous pneumothoraces are rare, recurrence rates are high. Retrospective studies show recurrence rates of up to 54% within the first 4 years in PSP patients (6, 7) and up to 50% over three years among patients with COPD. (8)

A preventative procedure is generally recommended after the second or third episode of PSP, except cases in which a second episode is thought to pose a threat e.g. pilots or patients living in remote areas. In SSP, secondary prevention is recommended after the first episode, as a recurrence can be life threatening. (3) Emphasis should also be placed on smoking cessation in both types (2).

Options for preventing recurrence include medical and surgical procedures. Pleurodesis is a procedure that obliterates the pleural space, so gas can no longer accumulate. A number of different agents are available; the most commonly used is talc (predominantly hydrated magnesium silicate). (9) Evidence favours surgical chemical pleurodesis using video-assisted thoracoscopic surgery (VATS), however for patients unsuitable for surgery, medical pleurodesis can be performed via a chest drain. (2) Other surgical options include pleurectomy with pleural abrasion (open or using VATS).

Multiple Choice Questions

1. A 28 year old tall, slim male presents to the Accident and Emergency Department due to a sudden onset of sharp chest pain and breathlessness. On examination the trachea is central and he is haemodynamically stable but there is reduced breath sounds on the right hand side. What is the most appropriate initial investigation?

A. CT scan

B. Erectchest x-ray

C. Pulmonary function tests

D. Electrocardiogram

E. Needle aspiration

2. A 26 year old man with no past medical history visits the Accident and Emergency Department due to sudden onset of shortness of breath and chest pain. Chest X-ray reveals a 1cm left-sided pneumothorax with no tracheal deviation. Despite oxygen he still feels breathless. What would be the most appropriate next step?

A. Insert chest drain

B. Discharge and review in outpatients in 2-4 weeks

C. Needle aspiration

D. Pleurodesis

E. CT thorax

3. A 45 year old woman is being discharged following a primary spontaneous right pneumothorax that recovered after needle aspiration. She currently works as a nurse and smokes 15 cigarettes per day; she was previously fit and well. What further advice or treatment would you recommend to her?

A. Medical pleurodesis using talc

B. Surgical pleurodesis and lung biopsy

C. Pleurectomy

D. Annual chest x-rays

E. Smoking cessation and outpatient appointment in 2-4 weeks

4. A 72 year old man with a history of severe COPD and diabetes arrives in the Accident and Emergency Department due to a sudden onset of severe breathlessness. Respiratory examination reveals hyperesonance, reduced chest expansion and reduced breath sounds on the left, the trachea is deviated to the right side. What is the best initial step?

A. Oxygen and emergency needle decompression of right lung

B. Oxygen and emergency needle decompression of left lung

C. Insert chest drain

D. Nebulised salbutamol

E. Continuous positive airway pressure (CPAP) treatment

THE SPONTANEOUS PNEUMOTHORAX

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5. A 65 year old man, with a history of emphysema, has been having persistent air leak after being admitted due to a pneumothorax 4 days ago. What is the most appropriate next step?

A. Refer to thoracic surgeons

B. Discharge and review in outpatient department in 2 weeks

C. Medical pleurodesis

D. Watch and wait

E. Insert new chest drain

MCQ Answers

1. B

Erect chest x-ray is the most appropriate investigation for a suspected pneumothorax if the patient is stable and a tension pneumothorax has been ruled out.

2. C

A patient with a PSP >2cm and/or breathlessness should be treated via needle aspiration

3. E

A patient can be discharged with follow up in the outpatients department following a PSP that has recovered via needle aspiration. Smoking cessation is recommended for all patients after a pneumothorax.

4. B

Signs and symptoms suggest SSP. Trachea deviates AWAY from affected side in tension pneumothorax. Tension pneumothorax requires prompt treatment with oxygen and needle decompression.

5. A

Persistent air leak for 3-5 days requires referral to thoracic surg

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THE INVESTIGATION & MANAGEMENT OF A PNEUMOTHORAX

D Barry, E Heiden, AK Banerjee

Abstract

A Foundation Doctor working in an Acute Medical Unit or Emergency Department is very likely to encounter adults admitted with breathing difficulties. It is important to remember that young adults who are otherwise fit and well may develop a pneumothorax which could severely affect their ability to ventilate effectively, whilst patients admitted with long-term conditions such as COPD and fibrotic lung conditions can also develop a pneumothorax which can lead to a rapid clinical deterioration.

The prompt assessment and management of these patients is critical. This article will discuss the key aspects to the condition, important investigations, management options and important information to pass on to the patient prior to their discharge from hospital.

Definition

A pneumothorax is defined as a clinical situation in which air becomes trapped in the pleural cavity; the area between the chest wall and lung. Pneumothoraces can occur spontaneously or as a result of trauma. This article will focus on those which occur spontaneously. They can occur in people with otherwise normal lungs; a primary spontaneous pneumothorax (PSP), or in association with an underlying lung condition: a secondary spontaneous pneumothorax (SSP).

Epidemiology

PSP's classically occur in tall thin men aged between 20-40. They have an incidence of between 7.4-18 per 100,000 population (1) and are six times more common in men than in women (2). PSP's most commonly result from the rupture of an apical pleural bleb. It is postulated that these are due to congenital defects in the alveolar walls, possibly due to connective tissue variances (3). After the age of 40, the pneumothorax is more likely to be secondary in nature. COPD is the most common underlying cause although there are many other causes including asthma, lung cancer, tuberculosis and pulmonary fibrosis. On average, one third of patients who experience a pneumothorax will have a recurrence, which is more likely in those who continue to smoke.

Morbidity and mortality

There are roughly 167 men per million population admitted with either a PSP or SSP4 . Mortality rates in the UK vary between 0.62 per million per year in women to 1.26 per million in men.

Clinical features

A pneumothorax often presents with acute chest pain usually on the affected side. It is often associated with breathlessness; although the severity of the presenting complaint can be wide. In particular, patients with a PSP can often experience minimal breathlessness at rest, but are likely to become breathless on minimal exertion (3).

A pneumothorax often presents with acute chest pain, usually on the affected side. It is often associated with breathlessness although the severity of symptoms can be wide. In particular, patients with a PSP can often experience minimal breathlessness at rest, but are likely to become breathless on minimal exertion (3).

Progressively worsening shortness of breath can represent an enlarging pneumothorax. Most instances of PSP occur whilst the person is at rest (5). Meanwhile, SSP's are more likely to present with more pronounced breathlessness, which correlates with the degree of respiratory compromise. It is important to remember that a pneumothorax can also closely mimic an exacerbation of a patient's underlying condition.

Risk Factors

- *Male sex*
- *Smoking*
- *Young (primary pneumothorax)*
- *Tall*
- *Positive Family history (e.g. Marfan's syndrome)*
- *Underlying respiratory disease (including Cystic Fibrosis)*
- *Previous pneumothorax*

Symptoms

- *Chest pain*
- *Anxiety*
- *Breathlessness*
- *Worsening of underlying respiratory condition (e.g. wheeze and cough in COPD)*

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Signs

- *Hypoxia*
- *Tachycardia*
- *Respiratory Distress*
- *Decreased or absent lung sounds*
- *Diminished movement*
- *Resistance to ventilation*
- *Tracheal deviation (towards the contralateral side)*

Investigations

Chest Radiograph

In the vast majority of cases a plain Chest Radiograph(CXR) is the diagnostic test. Classically it will show a lack of lung markings peripherally with a visible lung edge. An erect CXR during inspiration is recommended for the initial diagnosis of a pneumothorax (6). The size of a pneumothorax does not always correlate with symptoms. The definition of a 'small' pneumothorax is one where the distance between the lung margin and chest wall measures less than 2cm, at the level of the hilum.

A 'large' pneumothorax measures greater than 2cm and represents an approximate pneumothorax of 50% by volume (6). Inversion of the image on the modern hospital PACS system may make the lung edge more visible and lack of lung markings clearer to see, as does rotating the image through 90 degrees.

CT Chest

CT is the gold standard in the evaluation of pneumothoraces. They are also useful to differentiate large bullae of emphysema which may look like a pneumothorax on the CXR. In SSP's they are useful in the diagnosis of the underlying lung disease. CT scanning is recommended for uncertain or complex cases and when parts of the underlying lung appear tethered to the chest wall on the CXR, to guide chest drain insertion (6).

Arterial Blood Gas

Arterial blood gasses(ABG) are routinely used to assess the degree of hypoxaemia associated with the pneumothorax, in patients with respiratory distress. The ABG of a patient with a SSP will likely show a degree of hypoxia and possibly hypercapnia, which will give a guide as to the urgency of treatment. (7)

Ultrasound

Ultrasound can also be used to diagnose pneumothoraces. Early research showed that ultrasonography was only more valuable than conventional CXR when rapid conventional radiography was not possible or practical (8).

A more recent meta-analysis has shown that it is particularly useful in patients who have received a traumatic injury and would therefore undergo a supine CXR (9). It has been shown that the supine CXR has a low sensitivity in detecting intra-pleural air (10). There are many potential avenues of research and development in the area of ultrasonography for the investigation of pneumothorax (10).

Tension Pneumothorax

A tension pneumothorax is a medical emergency and requires prompt assessment and management. It occurs following the progressive build-up of air within the pleural space which subsequently pushes the mediastinum to the opposite hemi-thorax, resulting in obstruction of venous return to the heart. This inhibition of venous return leads to hypotension, haemodynamic collapse and eventually, cardiac arrest.

Patients typically present with acute respiratory distress and agitation. Examination may reveal a raised JVP, hypotension, reduced breath sounds on the affected side with tracheal deviation to the contra-lateral side and a hyper-resonant percussion note.

A tension pneumothorax should be managed with prompt administration of oxygen and insertion of a large bore cannula into the second intercostal space, mid-clavicular line on the side of the suspected pneumothorax. Management should precede further investigation or confirmation of a tension pneumothorax on CXR.

The cannula should be left in place until a functioning inter-costal chest drain can be positioned. Care should be taken to ensure that the cannula does not block or fall out before the inter-costal drain is inserted.

THE INVESTIGATION & MANAGEMENT OF A PNEUMOTHORAX

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Management

Patients with underlying lung disease are less likely to tolerate a pneumothorax; therefore, the distinction between a primary and secondary pneumothorax must be made early. If a patient experiences breathlessness as a result of their pneumothorax, they must undergo intervention, regardless of whether or not there is underlying lung disease.

The British Thoracic Society has developed a flow diagram in their Pleural Disease Guideline, to direct clinicians in the management of spontaneous pneumothoraces. A copy of the diagram should be easily accessible in all acute hospitals.

Suction

There is no evidence that routine suction is of any value. It is reserved for cases when, despite insertion of a chest drain, the pneumothorax persists beyond 24-48 hours. This is characterised by the persistent bubbling of air through the under-water seal of the chest drain.

Decisions to start suction should always be made by a respiratory specialist. Optimal pressures of 1-2 KPa have been suggested in order to speed up resolution by overcoming the rate of air leak into the pleural space from the lung.

Clamping Chest Drain

Chest drain tubes for pneumothoraces generally should not be clamped. Clamping a chest drain whilst there is a continuing air leak may result in a tension pneumothorax or worsening surgical emphysema. Therefore, a bubbling drain should never be clamped. Chest drains for fluid drainage can be clamped to control drainage rates as necessary.

Chemical pleurodesis

Medical talc combined with a sterile dilutant can be flushed through a chest drain, once the lung has fully re-expanded and there is no sign of a continued air leak into the pleural cavity. Chemical pleurodesis is only very rarely indicated and primarily reserved for patients with poor functional status, with repeated pneumothoraces on one side, who are not fit for surgery.

It has a success rate of approximately 60%; this is increased to 90% with talc poudrage; when a talc slurry is introduced following medical or surgical thoracoscopy. The procedure can be very painful; patients must be consented prior to undergoing chemical pleurodesis and adequate analgesia, including intra-pleural local anaesthetic, must be administered.

Surgery

Indications for surgery include a recurrent ipsilateral pneumothorax, a contra-lateral pneumothorax, professions at risk (for example divers) and patients with a persistent air leak despite drainage. There is no defined timing for referral to thoracic surgeons for patients with a non-resolving pneumothorax, but most centres advocate five days. Patients can either undergo an open thoracotomy or Video-Assisted Thoracoscopic surgery (VATS).

The aim of surgery is to resect or suture any visible blebs or bullae, whilst ensuring apposition of the opposing pleural surfaces, in order to seal them together.

Complications

Surgical emphysema occurs when air tracks from the pleural space into the subcutaneous tissues. It can occur spontaneously before drain insertion. It may be due to a blocked or kinked chest drain, or when the drain is poorly positioned, with drain fenestrations within the chest wall. Re-insertion of the drain may be necessary.

Re-expansion pulmonary oedema occurs when alveolar capillaries, damaged by the pneumothorax, become further traumatised during lung re-expansion. Although generally a rare complication it is more common following a large pneumothorax and symptoms include breathlessness, cough and chest pain, whilst the lung re-expands. Rarely, pulmonary oedema can cause respiratory failure, particularly when a pneumothorax has remained un-drained for several days.

One of the most common clinical issues is failure to re-expand with persistent bubbling of the chest drain due to failure in healing of the bronchopleural fistula. There is also the possibility of pleural infection and drain induced/spontaneous haemothorax. If the patient has an underlying lung disease a SSP can cause respiratory failure.

Discharge

Patients treated for a PSP by simple aspiration should undergo regular observations to ensure they are clinically stable prior to discharge. SSP treated with simple aspiration should be admitted overnight, prior to discharge.

Patients who have had a chest drain to relieve their pneumothorax can be discharged after drain removal if they remain stable. A follow-up CXR should be arranged within two weeks, to confirm resolution of the pneumothorax.

THE INVESTIGATION & MANAGEMENT OF A PNEUMOTHORAX

D Barry, E Heiden, AK Banerjee

Patient Advice

1. Avoid air travel for two weeks following complete resolution on CXR.

2. Lifelong avoidance of diving unless the patient has undergone bilateral surgical pleurectomy

3. To seek medical attention immediately should they develop any further breathlessness.

4. Strong smoking cessation advice and link to risk of recurrence or chest pain.

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UNILATERAL PLEURAL EFFUSIONS: INVESTIGATION & MANAGEMENT

AR Willsher, JA Nightingale

Abstract

Pleural effusions are common and present symptomatically, usually with breathlessness (1). While they may be simple and self-limiting, they can be a manifestation of serious pathology. We will discuss the investigation and management options in these patients. With regard to management, chest drains remain a vital tool (3). Their use and consequent day-to-day management is largely restricted to specialist wards and so the majority of foundation trainees will rarely encounter them. We will discuss their use, assessment of the patient with a chest drain and common complications.

Case History

PL is a 75-year-old lady who presented to the respiratory clinic with a 2-week history of increasing breathlessness and dry cough. She was an ex-smoker and lived alone. Her past medical history included B-cell lymphoma, uterovaginal prolapse and depression. Her drug history included lansoprazole and venlafaxine. She had no known drug allergies.

On admission, her oxygen saturation was 98% on air with a respiratory rate of 18. Chest examination revealed reduced expansion and reduced breath sounds on the left with a dull percussion note. Blood tests, including a serum calcium, were unremarkable. Chest x-ray showed a large, unilateral, left-sided pleural effusion.

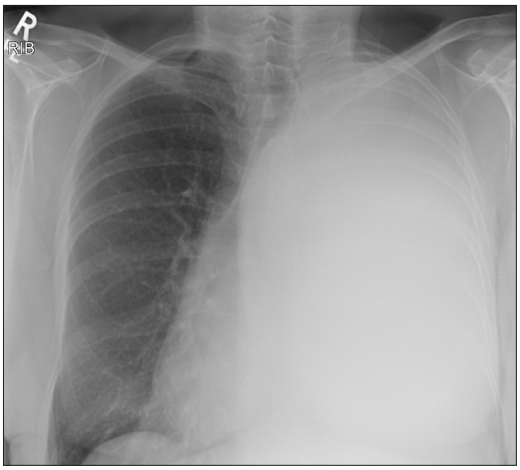

Figure 1: Unilateral left-sided pleural effusion.

She was subsequently admitted to Hospital and a small-bore chest drain was inserted under ultrasound guidance using the Seldinger technique (2, 3). A sample of dark brown pleural fluid was aspirated and tested for LDH, pH, protein and sent for cytology and gram stain, culture and sensitivity (4).

The chest drain was allowed to drain 1 litre of fluid, before being clamped overnight. This pattern of drainage was due to continue until less than 200ml in a day was drained (3). Chest X-ray performed after insertion showed correct placement of the chest tube.

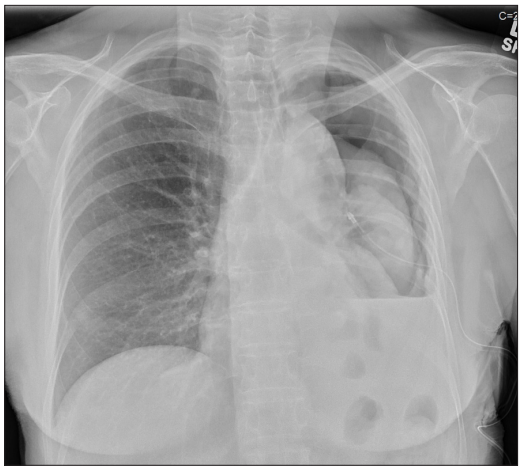

Figure 2: Evidence of chest drain tubing within pleural cavity.

PL managed well with the chest drain over the next few days and was able to mobilise around the ward. During this time, the drainage bottle was changed but unfortunately nursing staff failed to place water in the new bottle. A repeat chest x-ray was performed, which showed a reducing effusion but development of a hydropneumothorax with no evidence of tension. The decision was made to use suction to aim to reduce the pneumothorax and it was explained to the patient, along with the importance of managing the drainage bottle (3, 4).

The initial results from the aspirate indicated an exudate and cytology confirmed a diagnosis of adenocarcinoma (1). A staging CT scan was performed and the patient was discussed at the lung cancer multi-disciplinary team meeting.

PL had her chest drain removed and was well enough to be discharged home. She would be re-admitted in 2 weeks to have a PleurX drain inserted and would be seen in oncology outpatients regarding chemotherapy. Pleurodesis was not possible due to the presence of a 'trapped' lung (5). Four months later, PL has her PleurX drain in situ and has received 3 cycles of carboplatin and gemcitabine chemotherapy. The fourth cycle has currently been delayed due to pancytopaenia.

Discussion

History and examination

Pleural effusions arise due to excessive production of fluid, in some cases with an inability or a reduced ability to resorb fluid (1). As they are common, with many causes (Box 1), it is vital that a thorough patient history and examination is undertaken. Pleural effusions can be broadly separated into transudates and exudates (1).

Transudative pleural effusions are usually bilateral and arise due to changes in the regulation of pleural fluid resorption; namely an increase in plasma osmotic pressure and/ or raised pulmonary/ systemic hydrostatic pressure (6). Exudative effusions are usually unilateral and arise due to an inflammatory process within the pleura, which increases pleural permeability allowing leakage of protein and fluid into the pleural space (6).

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Transudates	
Common causes: • Left ventricular failure • Liver cirrhosis • Hypoalbuminaemia	Less common causes: • Hypothyroidism • Nephrotic syndrome • Mitral stenosis • Pulmonary embolism • Constrictive pericarditis • Urinothorax • Ovarian tumour– Meig's syndrome • Ovarian hyperstimulation • Superior Vena Cava Obstruction
Exudates	
Common causes: • Malignancy o Carcinoma of the bronchus o Mesothelioma o Metastatic malignancy • Parapneumonic	Less common causes: • TB • Pulmonary infarct • Connective tissue disease • Benign asbestos effusion • Post-MI • Acute pancreatitis • Yellow-nail syndrome • Drugs i.e. methotrexate, amiodarone (7) • Fungal infections

Box 1: Causes of pleural effusion.

Consequently, it is important that a thorough past medical history and drug history, past and current, is taken. Lifestyle factors such as smoking and asbestosis exposure may also be relevant. Examination findings should determine the side(s) of the pathology.

Investigation

Every patient with a suspected pleural effusion should have a posteroanterior chest x-ray performed (1). If bilateral effusions of transudative origin are suspected, no further pleural investigation is required (1) although further investigations such as echocardiography may be needed to determine the cause. However, a sample of fluid should be aspirated under ultrasound guidance by a trained physician if the effusion is unilateral or a presumed transudative effusion does not respond to therapy (1, 3).

A blood gas machine provides a pH and aliquots of fluid should also be sent to microbiology, cytology and biochemistry to measure protein, LDH, glucose levels and for culture. Fluid may also be sent for amylase levels in the case of suspected acute pancreatitis or oesophageal rupture (check local guidelines).

The protein level can help determine if pleural fluid is a transudate or exudate and Light's criteria can be used if this is inconclusive (7) (Box 2). Of note, Light's criteria can be unreliable in patients with congestive cardiac failure as diuretic therapy may increase serum LDH and protein levels (1).

For fluid with a protein concentration of 25-35 g/l

• If at least one of following is present fluid is virtually always an exudate

– Protein/serum protein ratio > 0.5
– LDH/serum LDH ratio > 0.6
– LDH > 2/3 of upper limit of normal of serum LDH

• If none present fluid is a transudate

Box 2: Light's Criteria.

If a pleural effusion is found to be an exudate and no cause is apparent from microbiology or cytology results it may be necessary to proceed to pleural biopsy. Generally, this is performed via video-assisted thoracoscopic surgery (VATS), a type of thoracic surgery performed using a fibreoptic scope and instruments inserted through small incisions in the chest wall known as "ports".

These small ports reduce the risk of infection and wound dehiscence and allow for a faster recovery by the patient. The procedure can be performed under local or general anaesthetic (8). It is important to note that a VATS procedure is only possible whilst fluid remains present in the pleural cavity. In view of this, a decision to drain an effusion is often delayed until a clear diagnosis has been established in case a VATS procedure may be required.

Pleural Drainage

As in the case history presented, if the patient is symptomatic, unilateral pleural effusions may require insertion of a chest drain to remove fluid and allow re-expansion of the lung. This should be performed under ultrasound guidance by a trained physician, using aseptic technique (3).

It is advised that this procedure is only carried out during 'normal' working hours; if there is a requirement for drainage of pleural fluid outside of these hours, for example for an extremely breathless patient, it is advised to aspirate 1-1.5 L of pleural fluid under supervision (2, 3). A recent chest x-ray should always be available prior to chest drain insertion with the sole exception of a tension pneumothorax (3).

Chest drains are usually managed on respiratory wards by nursing staff trained in their management. However, they may be encountered on on-call shifts and it is important to recognise when they are not working or when complications have arisen. The main complications related to chest drain insertion/usage are infection, surgical emphysema, pain, haemorrhage, tube blockage/dislodgement and visceral damage (3).

Assessment of the Patient with a Chest Drain

When reviewing a patient with a chest drain, it is important to examine the chest wall for signs of infection and the tube for any evident blockage. Patency of the drain should be assessed by determining whether the drain is 'swinging'. 'Swinging' refers to the natural rise and fall of water within the system with changes in pleural pressure during the respiratory cycle and can be prompted by asking the patient to inhale/exhale deeply. If the drain is not swinging this indicates that it is no longer in open communication with the pleural space either due to blockage or displacement. If not, the drain should be flushed with 20ml normal saline to try to unblock it.

In the case of a pleural effusion, one should determine if the drain is still draining; the drain chart should be useful here. Of note, a chest drain should not be allowed to drain more than 1.5 litres of fluid in the first hour after placement or at any one time, as rapid re-expansion of the lung may lead to pulmonary oedema that can be life-threatening (3). If the chest drain is 'swinging' and has drained less than 200ml in the preceding 24 hours, it may be ready to be removed (3).

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One must also check that the water in the bottle covers the drain tip, the bottle is kept upright and below the level of chest drain insertion (3). It is important to seek senior help if you believe a tube requires removal, re-siting or is no longer functioning correctly.

In the case presented the chest drain was not managed correctly; when the drainage bottle was changed a new bottle was attached without the fluid required to lead to an underwater seal. This allowed air to enter the pleural cavity and converted the patient's effusion into a hydropneumothorax. Further management involved attempted drainage of the fluid and air from the pleural space by placing an effective drain and when this was not successful the drain was placed under suction.

Unfortunately this was also unsuccessful as the patient had a 'trapped lung', a situation that means the lung is not able to re-expand even once the pleural fluid is removed. Incomplete lung re-expansion may be due to encasement of the lung by malignancy, thick visceral peel, pleural loculations and adhesions within the collapsed lung (the most likely cause following an infective pleural effusion), proximal large airway obstruction or a persistent air leak in the case of a pneumothorax.

In our patient's case the lung was trapped and would not have re-expanded even if the chest drain had been managed perfectly.

Pleurodesis

In patients with malignant effusions there is a high risk of recurrence of the effusion following successful drainage or aspiration as the pleura remains abnormal. In view of this it is usual practise to consider a pleurodesis in these patients. Pleurodesis involves the instillation of a chemical sclerosant, such as talc or bleomycin, into the pleural space, either via a chest drain or under direct vision at the time of a VATs procedure (5).

This causes an inflammatory response, which resolves by scarring of the visceral and parietal pleura obliterating the pleural space and hence preventing re-accumulation of the pleural fluid. This inflammation is responsible for the commonest side effects of pleurodesis, namely chest pain and fever.

The most important determinant of the likely success of pleurodesis is complete re-expansion of the lung, confirmed radiologically. Most studies suggest the lack of a response following instillation of a sclerosant is associated with incomplete lung expansion. Where complete lung re-expansion is not possible, pleurodesis may still be attempted or alternatively a long-term indwelling pleural catheter may be inserted, as was the case with our patient.

MCQs

1) It is midnight and you (foundation doctor) have clerked a patient on the admissions unit who you believe has a unilateral pleural effusion. They are symptomatic, but stable. What is the most appropriate course of action regarding their effusion?

a) Gather equipment required for a chest drain and contact your senior
b) Gather equipment required for aspiration and contact your senior
c) Monitor the patient and wait until morning
d) Aspirate pleural fluid yourself
e) Consent the patient for chest drain insertion and contact your senior

2) A patient requires a non-urgent chest drain and is on life-long warfarin for atrial fibrillation. What is the most appropriate action?

a) Withhold 1 dose of warfarin and insert the drain the following day
b) Measure the INR and if >1.5 discuss with haematology regarding reversal
c) Insert the chest drain while the patient is on warfarin
d) Stop warfarin and commence enoxaparin
e) Stop warfarin and commence a heparin infusion

3) You are called to see a patient with a chest drain which the nurses on the ward claim has not drained any fluid in 10 hours. On examination, you notice that the sutures holding the tube in are loose and consequently the tube appears dislodged. What is the most appropriate course of action?

a) Push the tube back in and tighten the sutures
b) Request a chest x-ray
c) Phone for senior help
d) Assess the patient using ABCDE approach
e) Request a pleural ultrasound

4) The underwater seal is the most important element of the chest drainage system because:

a) It indicates patency of the tubing by rising and falling (swinging) with inspiration and expiration
b) It allows air to enter the pleural space but prevents air from exiting the pleural space through the chest tube
c) It allows fluid or air to exit the pleural space but prevents air from entering the pleural space through the chest tube
d) It allows air to move freely in and out of the pleural space through the chest tube.
e) It allows the amount of fluid drained from the pleural space to be measured.

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5) You are called to the ward to assess a patient with a chest drain in situ that the nursing staff are concerned is no longer 'swinging'. On examining the patient you confirm this is the case. Which of the following is the most likely cause?

a) The tubing is coiled on the bed with a straight path to the chest drain
b) The patient has developed a drain-related infection
c) The patient is ambulatory
d) The patient's pleural effusion has drained to dryness
e) The tubing is blocked

Answers

1. Answer: B

According to BTS guidelines, only in an emergency should a chest drain be inserted overnight (3). If there is significant respiratory compromise, it could be appropriate to aspirate some fluid. This should be performed under ultrasound guidance and by a trained personnel. It is only appropriate to consent a patient if you able to facilitate an informed decision.

2. Answer: B

A non-urgent chest drain should not be inserted if INR >1.5. Local guidelines can be followed or haematology contacted regarding reversing the warfarin.

3. Answer: D

Provided that the patient is stable, you can commence requesting investigations to clarify the extent of remaining fluid/ air and requesting senior help regarding potential re-siting of the drain. A tube must never be passed back through an insertion site due to risk of infection (3).

4. Answer: C

The underwater seal drainage system is an important part of the chest drain apparatus, allowing safe drainage of fluid or air (in the case of a pneumothorax) from the pleural space. The underwater seal acts as a one-way valve through which air or fluid is expelled from the pleural space by a combination of positive expiratory pressure and gravity but air is prevented from re-entering during inspiration.

The drainage tube is submerged to a depth of 2-3cm in the water of the chest drainage bottle. This ensures minimum resistance to drainage but maintains the underwater seal even in the face of a large inspiratory effort.

5. Answer: E

When a chest drain is correctly inserted in the pleural space the water level in the attached tubing will fluctuate or 'swing' due to changes in intrapleural pressure with respiration. If a chest drain is no longer swinging this indicates that either the tubing is blocked or that the tip of the chest drain no longer resides within the pleural space.

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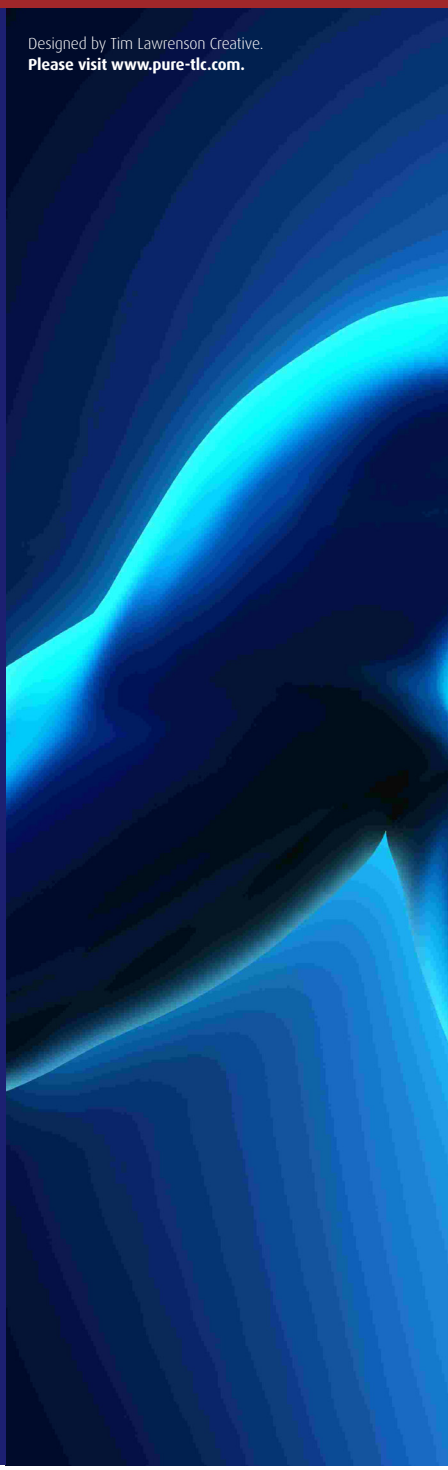

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