Malignant pleural mesothelioma associated with recurrent pneumothorax

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Shareable abstract (@ERSpublications)
Secondary pneumothoraces can be the first presentation of pleural malignancies and may also complicate their course. They are often associated with prolonged air leaks, and cardiothoracic intervention can be required. https://bit.ly/3DEvPem

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An 84-year-old male presented with a few days of progressive dyspnoea. He had no constitutional symptoms or pain. He was a never-smoker and had significant asbestos exposure from 40 years ago when he worked in the local shipyards. His past medical history included controlled severe asthma, hypertension, a hiatus hernia, atrial fibrillation, fibromyalgia and thyroid nodules.

On examination, he was comfortable at rest and was in rate-controlled atrial fibrillation, with saturations of 96% on air and a respiratory rate of 16 breaths per min. He had no clubbing or palpable lymphadenopathy. He had reduced air entry in the left hemithorax. There was no peripheral oedema. He had very mild inspiratory and expiratory crackles at the right base.

A chest radiograph showed a left-sided pneumothorax (figure 1), with a very small associated pleural effusion. Haematological and biochemical investigations were normal. An echocardiogram carried out recently was normal.

Task 1

What is the most appropriate course of action?

a) Conservative management and discharge
b) Conservative management in a place of safety
c) Needle aspiration of the pneumothorax
d) Insertion of small bore intercostal chest drain
e) Insertion of large bore chest drain
f) Referral to cardiothoracic surgery

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He became more breathless so a 12Fr Seldinger chest drain was inserted in the fifth intercostal space in the triangle of safety and secured appropriately. However, that drain became dislodged (the patient got the tubing caught on a chair) and was replaced with an anterior apical drain. Lung expansion was reasonable (but not full) on repeat imaging (figure 2). However, there was an ongoing air leak with continuous bubbling in the drainage bottle.

The patient's symptoms had by now completely resolved. A computed tomography (CT) scan showed non-apposition of the pleural surfaces (which precluded instillation of talc), with subtle reticulation at the

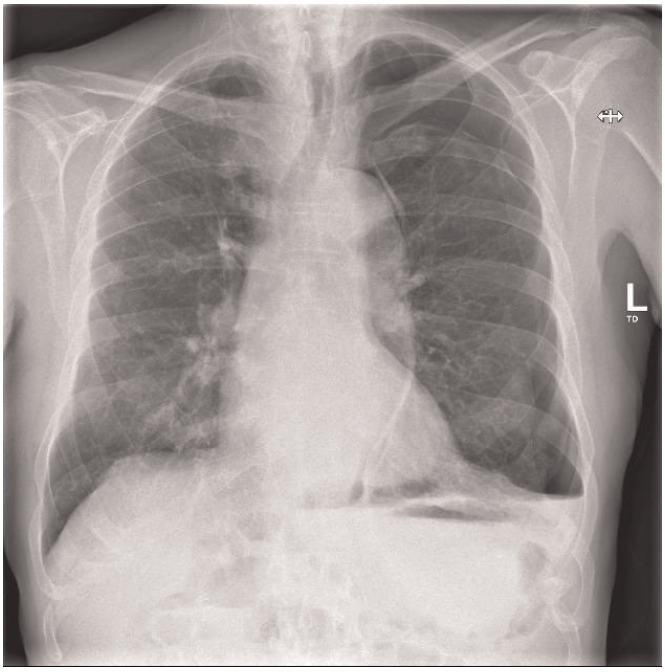

FIGURE 1 Chest radiograph showing a left-sided pneumothorax.

bases which could signify early asbestosis (figure 3). There was no obvious bullous disease. Suction was not felt to be a good idea as suction can cause a drainage dependent air leak as argued by WALKER *et al.* [3]. We felt we should give the pneumothorax time to heal.

The drain was connected to an ambulatory bag and the patient was reviewed regularly in the outpatient department. 4 weeks after the initial presentation, the air leak was still present. A left video-assisted thoracoscopy, bullectomy (as there were apical bullae seen at surgery) and talc pleurodesis was performed. The patient was discharged with a new chest drain and an ambulatory bag, which was subsequently removed. There was full lung expansion (figure 4).

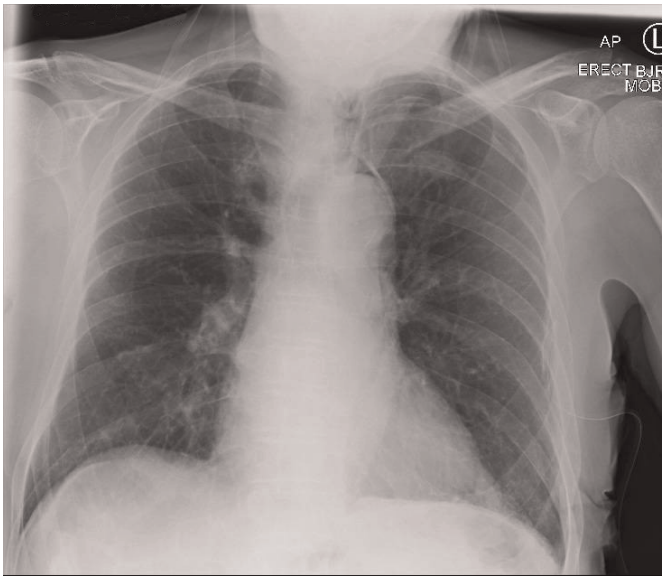

FIGURE 2 Chest radiograph showing lung expansion (not total) and good drain placement.

FIGURE 3 Computed tomography scan showing non-apposition of pleural surfaces and subtle basal reticulation.

Pathological analysis showed the congested and fibrotic pleura. The pulmonary parenchyma showed sub-pleural bullous spaces. There were plaque-like infiltrates and multiple nodules on the visceral pleura. There were multi-focal proliferations of epithelioid cells forming glandular structures. These stained with calretinin, pan cytokeratin anion exchanger (AE1/AE3) and cytokeratin (CK5/6), with loss of breast cancer gene 1 (BRCA1)-associated protein-1 (BAP1). There was infiltration into lung parenchyma at the stapled margin. The appearances were consistent with an epithelioid malignant pleural mesothelioma (MPM).

His performance status was 1. He was started on carboplatin and pemetrexed. Just before the fifth cycle, he started complaining of increased dyspnoea and a repeat CT scan was performed. Figure 5 shows a large left basal hydropneumothorax. There was no discernible increase in pleural thickening or metastases. Oxygen saturations were normal.

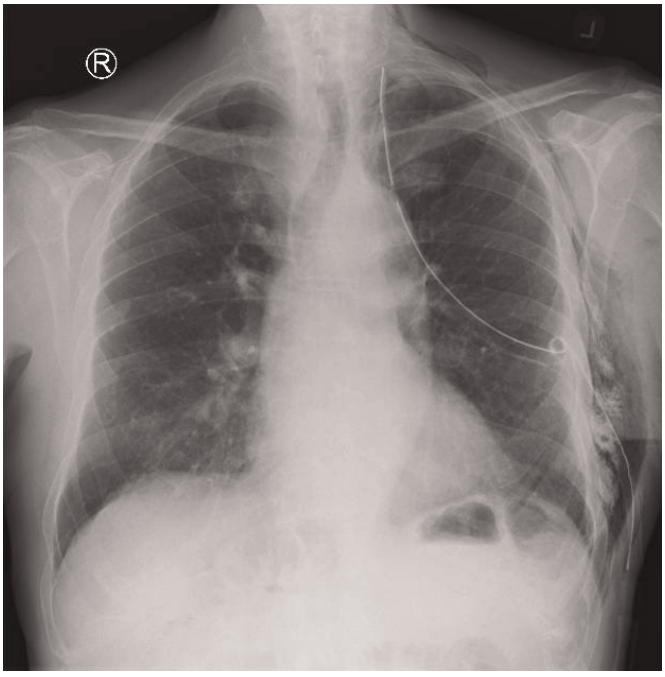

FIGURE 4 Chest radiograph showing full lung expansion post surgery.

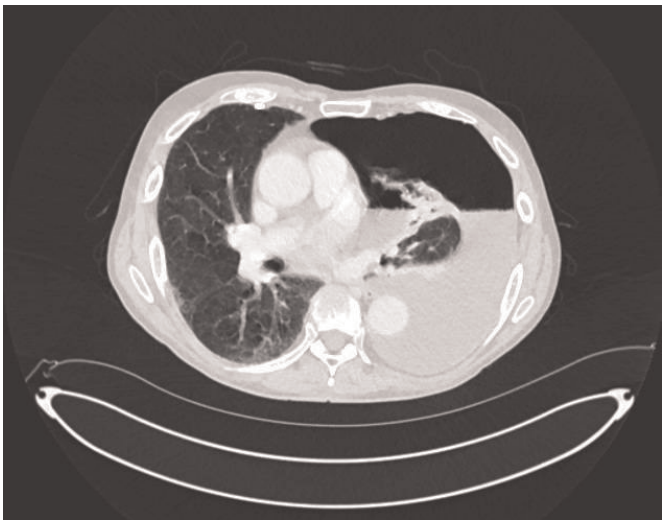

FIGURE 5 Computed tomography scan showing large left hydropneumothorax.

Task 2

What is the most appropriate course of action?

a) Observation
b) Insertion of a small bore drain
c) Insertion of a large bore drain
d) Offer ambulatory management with an indwelling drain and ambulatory bag
e) Re-referral to cardiothoracic surgery

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A patient-centred approach was adopted. Intervention was felt necessary and the patient was keen to proceed. A small bore or a large bore drain could be connected to an ambulatory bag but that could become dislodged, and we felt that the air leak might be prolonged due to the underlying pleural disease (blebs and mesothelioma). Indwelling pleural catheters (IPCs) have been used for prolonged air leaks [4]. A Rocket IPC was inserted under local anaesthetic with no complications. The IPC is a 16Fr drain and less likely to fall out as the cuff of the IPC causes an *in situ* fibrotic reaction.

2 weeks later, there was no output from the ambulatory bag and the patient reported no air coming out. The IPC was flushed, capped, and the patient observed for 4 h. There was no radiological or clinical change at that time. However, 5 days later, he developed increased breathlessness, and a chest radiograph showed lung deflation with the appearance of surgical emphysema (figure 6). The presumption was that the pneumothorax had recurred, and air leaked out of the IPC tract. The patient was admitted. The IPC was connected to an underwater seal with immediate bubbling from the drain and the patient felt better. However, there was still a persistent left basal pneumothorax and air leak which did not improve with low-pressure, high-volume wall suction (we do not use digital suction locally) for 48 h, this was on the advice of the cardiothoracic team. After that time, there was no radiological or clinical change.

Task 3

What is the most suitable option for the patient?

a) Talc slurry pleurodesis
b) Blood patch application
c) Placement of an endobronchial valve
d) Further cardiothoracic surgery

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The challenge faced in this case was the ongoing air leak and whether there was inadequate drainage, or lung entrapment by previous talc or the current mesothelioma. Significant lung entrapment was perhaps unlikely given the radiological appearances. To optimise the pneumothorax drainage, the lung needed to

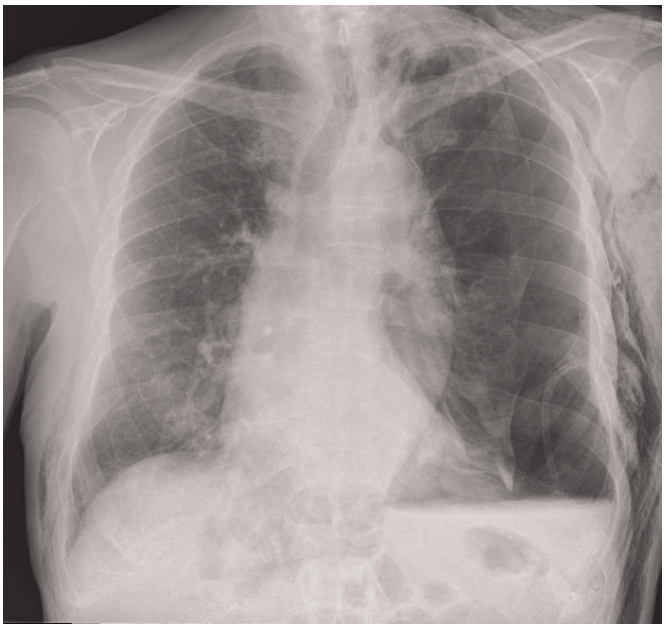

FIGURE 6 Chest radiograph showing pneumothorax recurrence and surgical emphysema.

expand. As the IPC was located anteriorly and basally, there was a tentative idea to place a further, larger chest drain for further drainage. This was a reasonable option considering he is an 85-year-old patient with mesothelioma receiving chemotherapy, with cardiac comorbidities and potential surgical challenges with previous talc pleurodesis. There was no merit in performing further talc slurry pleurodesis as there was no pleural apposition. Whilst blood patch can be an option in patients with secondary pneumothoraces with un-apposed pleural surfaces, there is a theoretical risk of empyema [5]. We were keen to preserve the fitness of this patient as much as possible, so that he should be able to receive systemic anti-cancer treatment in the future.

However, the patient was fit and willing to undergo further surgery. This would potentially have the benefit of identifying the cause of his air leak, and to determine if the lung was entrapped and to potentially perform further talc pleurodesis. He was thus transferred to the regional cardiothoracic centre.

At redo surgery, there was early mesothelioma disease apparent. The left lung was not entrapped and was capable of full re-expansion. There was no air leak on the underwater test and no features of infection. As the left lung reinflated fully, further talc poudrage was performed.

The pneumothorax was either due to his bullous disease or his pleural malignancy. It is recognised that bullous disease can happen in the absence of active smoking due to passive smoking inhalation, indoor and outdoor air pollution. However, there was possibly also disruption of the visceral pleural surface due to tumour infiltration. MPM presenting as a pneumothorax is rare and has been described in case series only. Mitsui *et al.* [6] described 16 cases from Japan, in one of the largest case series, with a median age of presentation of 58 years, with male and right-sided predominance. Interestingly, 11 (69%) suffered from pneumothorax recurrence. A summary of the evidence between 2000 and 2018 suggests similar results with a mean age of 67 years, affecting mostly males and their right hemithorax, the epithelioid tissue subtype is the most common type described [7]. Recurrence occurred despite the bullectomy, so we think this was all due to his mesothelioma.

The role of surgery in pneumothorax is well established but often debated. In primary pneumothoraces, recurrence after the first episode is the accepted criterion for surgical correction [1, 2]. If the patient is in a high-risk occupation such as being a diver or a commercial airline pilot, surgical correction at the first occurrence is also advised. In secondary pneumothoraces, referral to surgery is indicated for prolonged air leaks, and there is a debate as to whether this is after 3 or 5 days of continuous bubbling from a chest drain. It must also be noted that often pneumothoraces should be allowed time to resolve on their own, as the evidence would suggest that the visceral air leak can heal [1–3]. There is debate whether application of

suction can provide the pleural apposition to allow the leak to heal or whether suction exacerbates the leak. In this case, suction was not applied at the first pneumothorax but applied at the point of recurrence upon the advice from cardiothoracic surgery. It did not produce the required pleural apposition for the application of talc slurry. The theoretical risk of empyema was not one we, and the patient, were willing to take with blood patch pleurodesis. Similar reservations around endobronchial valves were expressed, as they can sometimes be associated with bronchial infections [8], but the valves were not required anyway.

The rates of recurrence after cardiothoracic surgery are very low. However, there is no evidence to infer the ideal timing of surgery in persistent air leak and an individualised approach should be adopted each time, as we did here. Thoracic surgery for pneumothorax usually includes bullectomy, a type of wedge resection using staplers, and surgical pleurodesis with talc. Other methods can include pleural abrasion and partial pleurectomies.

Following his video-assisted thoracoscopic surgery, the patient has remained well, and there are plans to restart chemotherapy.

Answer 1

b. This is most likely a secondary spontaneous pneumothorax (SSP) rather than a primary spontaneous pneumothorax (PSP) given the man's age, right-sided clinical examination findings and previous asbestos exposure [1]. Therefore, conservative management with discharge and outpatient review is unlikely to be appropriate, despite the normal vital signs. Needle aspiration has a good evidence base in PSP for relieving symptoms and improving the radiological appearance but does carry a risk of repeated procedures [2]. The evidence for needle aspiration in SSP is less clear, and often left to the discretion of the physician. If drainage is required in SSP, often a small bore Seldinger drain (traditionally defined as <20 French gauge (Fr)) is the first line intervention, with larger bore drains reserved for if the air leak is not contained by the small bore drain or if the air leak is prolonged with incomplete lung expansion. However, observation can also have a role to ascertain whether the pneumothorax remains stable or if symptoms get worse. A patient-centred decision was thus made given the lack of tension features and haemodynamic stability and he was admitted and observed for 48 h. Cardiothoracic surgery is not an appropriate first option as established guidance would suggest drainage first.

<< Go to Task 1

Answer 2

d.

<< Go to Task 2

Answer 3

d.

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Conflict of interest: The authors have no conflicts of interest.

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