

Malignant pleural mesothelioma presenting with remitting–relapsing pleural effusions: report of two cases

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Abstract

Pleural effusions are common and are associated with malignancy in one sixth of cases. Malignant pleural effusion (MPE) is typically persistent and progressive, prompting further investigations if the initial tests are not diagnostic. A spontaneously remitting effusion is commonly presumed to be benign, and further investigations may not be performed. We present two cases in which the presenting pleural effusion spontaneously resolved but recurred (in one case, multiple times), leading to further investigations that revealed an underlying malignant pleural epithelioid mesothelioma. These cases demonstrate the need for clinicians to be aware that remitting effusions can occur in the context of pleural malignancy and should be kept under observation, with a low threshold for further investigation if relapse occurs.

Introduction

Pleural effusions are common; malignancy accounts for one in six cases [1]. MPE is the first clinical presentation of 90% of mesothelioma and 25% of lung cancer patients. MPE arises from cancer-induced plasma extravasation ± obstruction of pleural lymphatic outflow [2]. It usually continues to accumulate unless the patient receives effective cancer therapy or develops (spontaneous or therapeutic) pleural symphysis. Hence, traditional teaching suggests that an effusion that spontaneously resolves is unlikely to be malignant. We report two patients presenting with a pleural effusion that resolved rapidly without treatment but subsequently recurred. Both were eventually diagnosed with malignant mesothelioma.

Case Report

Case 1

A 63-year-old man developed pleuritic chest pain and a left-sided pleural effusion (Fig. 1), which largely resolved without intervention when seen at our pleural referral service 2 weeks later. Bedside ultrasound found only a trace

(0.5 cm depth) of residual anechoic fluid at the costophrenic angle, and lung gliding was preserved.

The patient was known to have asthma, type II diabetes mellitus, hypertension, and prior alcohol-related pancreatitis. He never smoked and was on no new medications. He was working as a carpenter with asbestos exposure and also spent three childhood years living in an asbestos mining town where his father (who died eventually of mesothelioma) worked.

Extensive investigations found no cause for the effusion, including echocardiography, computed tomography (CT) pulmonary angiography, vasculitic screen, mesothelin level etc. There were no pleuro-parenchymal abnormalities on CT apart from pleural plaques.

Because of its rapid spontaneous resolution, the provisional diagnosis was that the effusion was likely of benign aetiology, such as a benign asbestos pleural effusion (BAPE). Over the following 4 months, however, the effusion recurred and resolved spontaneously on two further occasions (Fig. 1) but was too small for aspiration. He underwent diagnostic video-assisted thoracoscopic surgery (VATS), which found abnormal parietal pleura amongst pleural plaques. Pleural biopsy revealed malignant

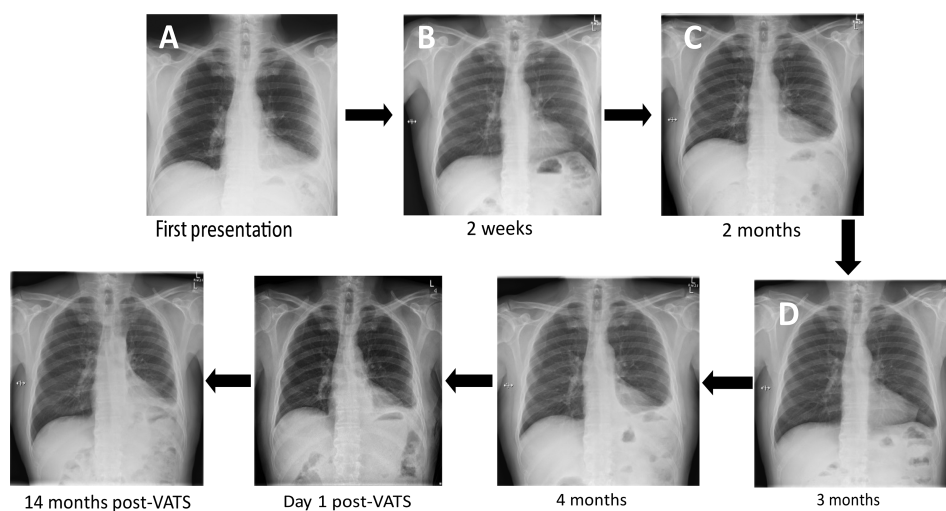


Figure 1. Serial chest X-rays (CXRs) of patient 1. (A) First presentation with left pleural effusion. (B) First clinic visit at 2 weeks, resolution of left pleural effusion on CXR, trace fluid at left costophrenic angle on ultrasound. (C) Second clinic visit at 2 months, recurrence of small left pleural effusion. (D) Third clinic visit at 3 months, effusion decreased significantly in size, measuring less than one rib space on ultrasound. (E) Fourth clinic visit at 4 months, recurrence of effusion, referred for video-assisted thoracoscopic surgery (VATS). (F) Day 1 post-VATS. (G) Follow up at 14 months post-VATS.

epithelioid mesothelioma. No pleurodesis was performed, but the effusion had not recurred after 14 months of follow up post-VATS.

Case 2

A 78-year-old man presented to the emergency department with a week of left-sided pleuritic chest pain. Chest X-ray (CXR) showed a left-sided pleural effusion. Clinical history, initial examination, and routine blood tests did not suggest any of the common causes of pleural effusions (e.g. heart failure or infection). He was a non-smoker and was on no medications. A vasculitic screen was negative. CT pulmonary angiography was negative for pulmonary emboli but revealed a moderate-sized loculated pleural effusion with sub-pulmonic and apical ($6 \times 5 \times 4$ cm) components.

He was assessed by the Pleural Unit 2 days after the initial presentation. By that time, his symptoms had resolved without treatment, and his effusion significantly reduced in size spontaneously. Bedside ultrasound only found a small residual basal effusion with complete resolution of the apical collection. His past history included sigmoid carcinoma with liver involvement treated successfully with surgery, chemotherapy, and radiofrequency ablation. He had been disease-free for 9 years. He was an installer of refrigerators and air-conditioning units, which involved drilling through asbestos walls and roofs.

Thoracentesis only yielded <20 mL of fluid, which was an exudate (pleural/serum protein = 40/66 mmol/L).

Cytology showed reactive mesothelial cells but no evidence of malignancy. Because of the significant spontaneous reduction of the effusion and the absence of suspicious features in the fluid analyses, the provisional diagnosis was a self-limiting benign effusion. The patient was kept under surveillance.

A repeat CT scan 2 months later revealed a recurrence of his effusion and possible mild pleural thickening. A repeat thoracentesis was non-informative, and an ultrasound-guided pleural biopsy showed benign fibrinous pleuritis. The patient declined further interventional procedures but agreed to further radiological surveillance.

The patient remained well, but the effusion persisted on CT a further 6 months later. Positron emission tomography-CT (PET-CT) showed fludeoxyglucose (FDG)-avidity in the left pleura, especially the costophrenic angle. The patient, on this occasion, agreed to VATS, which revealed parietal pleural nodularity, and biopsies confirmed epithelioid mesothelioma. The patient remained asymptomatic, and the effusion had not recurred at follow up 3 months post-VATS.

Discussion

Pleural effusion affects 3000 people/million population annually and can arise from over 60 causes, including malignancy [1]. MPE results from excess fluid formation (tumour-induced vascular hyper-permeability) and reduced drainage (lymphatic tumour infiltration) and usually continues to accumulate unless these mechanisms are

disrupted (e.g. chemotherapy) or if the pleural space is obliterated (e.g. by pleurodesis). Resolution of MPE without intervention is therefore rare, and spontaneous remitting–relapsing MPE has, to our knowledge, not been reported.

Clinicians, following conventional teaching will favour benign causes, over malignant ones, in the workup of a remitting–relapsing effusion [3,4]. This may delay invasive diagnostic procedures (as in our two cases). In patients with asbestos exposure, BAPE is a plausible benign cause of an exudative effusion. BAPEs are often small, and patients are asymptomatic. Its natural history is one of chronicity with frequent recurrences. In one retrospective series, 8 of the 22 patients with BAPE had more than one episode of pleural fluid recurrence either ipsilaterally or contralaterally [5].

Clinicians should be aware that, though uncommon, MPEs can present as remitting–relapsing effusions. Patients at risk of MPE with no definitive explanation for their effusion should at least be kept under surveillance, and clinicians should have a low threshold for further investigations (e.g. VATS) even if their initial effusion spontaneously settled.

Disclosure Statement

The patients provided written consent for the publication of their case histories and accompanying images.

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