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CASE REPORT

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Malignant pleural mesothelioma in a patient with pneumothorax: A cumbersome subtype both clinically and pathologically

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Abstract

Here, we report a case of malignant pleural mesothelioma (MPM) that was very difficult to diagnose. A 62-year-old woman with a surgical history of recurrent bilateral pneumothorax was admitted to our hospital with severe dysphagia. Computed tomography (CT) detected stenosis in the lower esophagus. Immunohistochemical examination of a biopsy sample from the stenotic region was suggestive of MPM. Chemotherapy was initiated, but the patient soon weakened and died. Autopsy revealed atypical cells, identical to those seen in the biopsy sample which had spread into the stenotic esophagus and entire thoracic cavity. Although neither pleural thickening/nodules nor asbestos bodies were observed, we finally diagnosed the tumor as a biphasic-type MPM. We re-examined previous surgical specimens of pneumothorax and acknowledged foci of bland mesothelial cell proliferation which had the same pathological findings as tumor cells at autopsy. The lack of asbestos exposure and pleural thickening, an initial manifestation of pneumothorax, and faint cytological atypia prevented an early diagnosis. In cases of recurrent pneumothorax in elderly patients, MPM should be included in the differential diagnosis.

KEYWORDS

initial symptom, malignant pleural mesothelioma, pathological diagnosis, pneumothorax

INTRODUCTION

Malignant pleural mesotheliomas (MPMs) are rare thoracic neoplasms that have recently increased in occurrence.[1] Their primary cause is asbestos, with tumors developing 30–40 years after exposure.[1] While chest pain and pleural effusion are the most common symptoms/signs,[2] a few patients present with pneumothorax.[3–5] Here, we report an MPM case that was difficult to diagnose due to a peculiar clinical course: the patient had no asbestos exposure, showed pneumothorax as an initial symptom, and died of malignant esophageal stricture.

CASE REPORT

A 62-year-old woman was admitted to our hospital with severe dysphagia. A year prior to admission, she had suffered from recurrent bilateral pneumothorax (Figure 1(a)) and was treated surgically each time. Although pleural effusion was present, pleural thickening/nodules were not found during surgery.

On admission, she was malnourished and exhausted. Computed tomography (CT) detected stenosis in her lower esophagus (Figure 1(b)). Upper gastrointestinal endoscopy did not show any tumors on the luminal surface of the

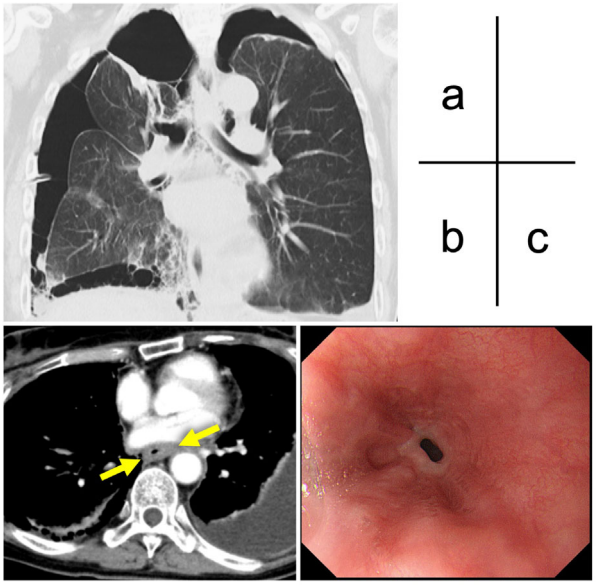

FIGURE 1 Past and present diagnostic imagings. (a) Chest computed tomography (CT) following previous hospitalization of the patient due to bilateral pneumothorax. There was a small amount of pleural effusion and neither pleural thickening or pleural nodules were observed. (b) Contrast-enhanced computed-tomography of the recent hospitalization. The lower esophagus had a thick wall and narrow lumen (arrows). (c) Endoscopic findings of the stenotic esophagus. The luminal surface showed no obvious neoplastic changes

stenotic esophagus (Figure 1(c)). An endoscopic ultrasound-guided fine-needle aspiration (EUS–FNA) specimen from the narrowed portion contained irregular-shaped clusters of atypical cells (Figure 2(a)). Immunohistochemically, atypical cells were positive for calretinin, podoplanin, epithelial membrane antigen (EMA) and CD146 (Figure 2(b)–(e)), suggestive of MPM.

The patient's family consulted a mesothelioma specialist for a second opinion but MPM was not diagnosed due to a lack of characteristic radiological findings. Nevertheless, after patient and family consent, we initiated chemotherapy (CBDCA+PEM) with a potential diagnosis of MPM. After one course of chemotherapy had been completed (two months hospitalization), her general condition deteriorated. She died shortly afterwards and an autopsy was performed.

Post mortem examination revealed a partial pleural adhesion and thin membrane-like structure covering the pleural surface as well as a pleural effusion (300–400 ml). Pleural thickening/nodules were not observed. The lower esophagus was thickened and contracted (Figure 3(a)). Histologically, the stricture showed robust proliferation of small atypical cells in the adventitia and muscular layer in a highly infiltrative manner (Figure 3(b)). Immunohistochemical findings of atypical cells were the same as those of the EUS–FNA specimen (Figure 3(c)–(f)). The final pathological diagnosis was biphasic-type MPM. Tumor cells, the cytological atypia of which was surprisingly mild, penetrated extensively into the entire thoracic wall, lungs, heart, stomach, and pancreas. No asbestos bodies were detected in the lungs.

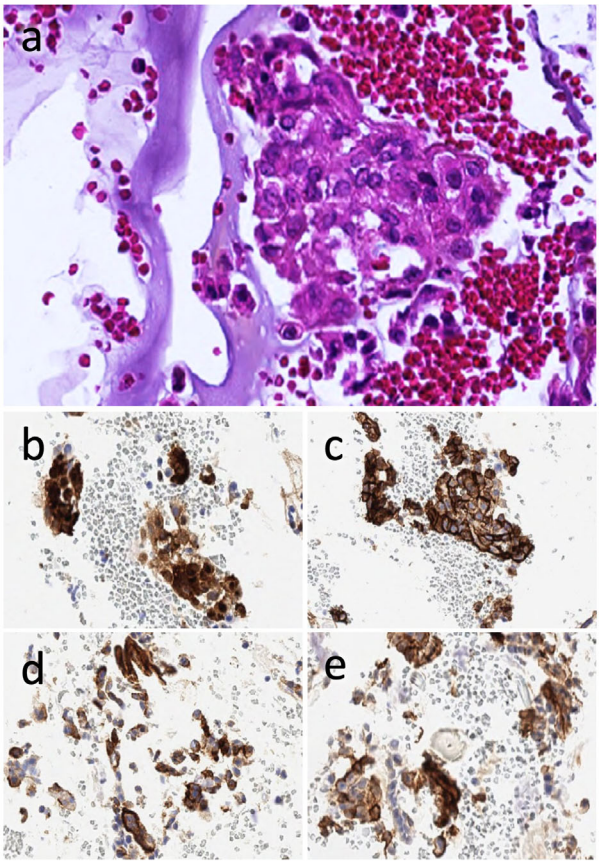

FIGURE 2 Morphological and immunocytochemical findings of the endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) specimen. (a) An atypical cell cluster was observed. Hematoxylin–eosin stain (original magnification, x400). Positive immunostaining for (b) calretinin, (c) podoplanin, (d) EMA and (e) CD146 suggested malignant mesothelioma as a possible diagnosis. Immunoperoxidase stain (original magnification, x100)

Previous surgical specimens of pneumothorax were re-examined and indistinct nests of proliferating mesothelial cells were found within the lung parenchyma (Figure 4(a), (b)). The cellular atypia was so mild that a distinction between reactive mesothelial hyperplasia and MPM was impossible. However, immunohistochemical findings (Figure 4(c)–(f)) were identical with those of the autopsy sample suggesting the lesions were MPM. Importantly, emphysematous change, a common pre-existing condition of pneumothorax, was absent.

DISCUSSION

Like common malignant neoplasms, the integration of clinical information, radiological imaging, and pathological findings is important for the early diagnosis of MPMs. Typically, a patient has a history of asbestos exposure, presents with respiratory symptoms and chest tightness due to massive unilateral pleural effusion, with pleural thickening/nodules visible on imaging.[1,2,6] In the present case, we failed

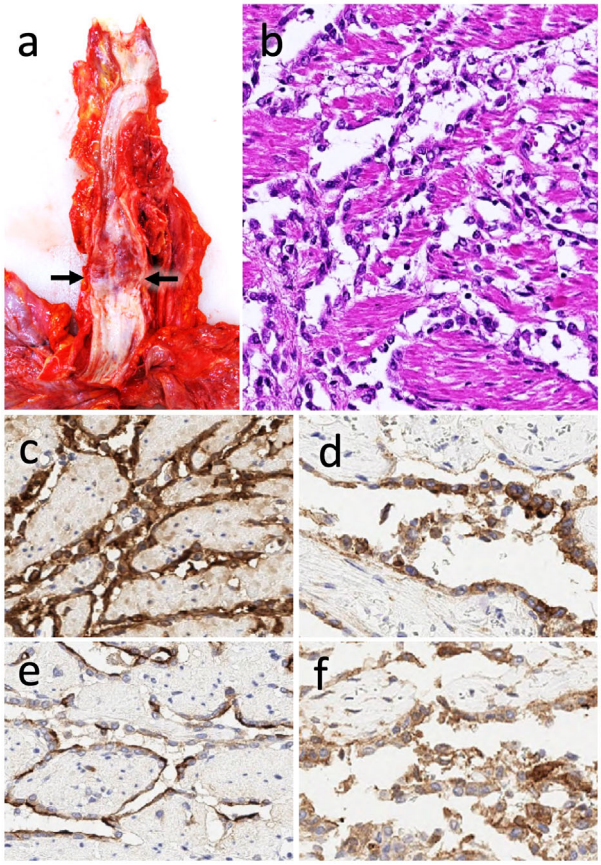

FIGURE 3 Autopsy findings. (a) Stricture was present in the lower esophagus (arrows). (b) Histologically, mildly atypical small cells infiltrating into interfascicular spaces of the strictured esophageal muscular layer were seen. Hematoxylin-–eosin stain (original magnification, x200). These cells were positive for (c) calretinin, (d) podoplanin, (e) EMA and (f) CD146 which indicated that the proliferative lesion was MPM. Immunoperoxidase stain (original magnification, x200)

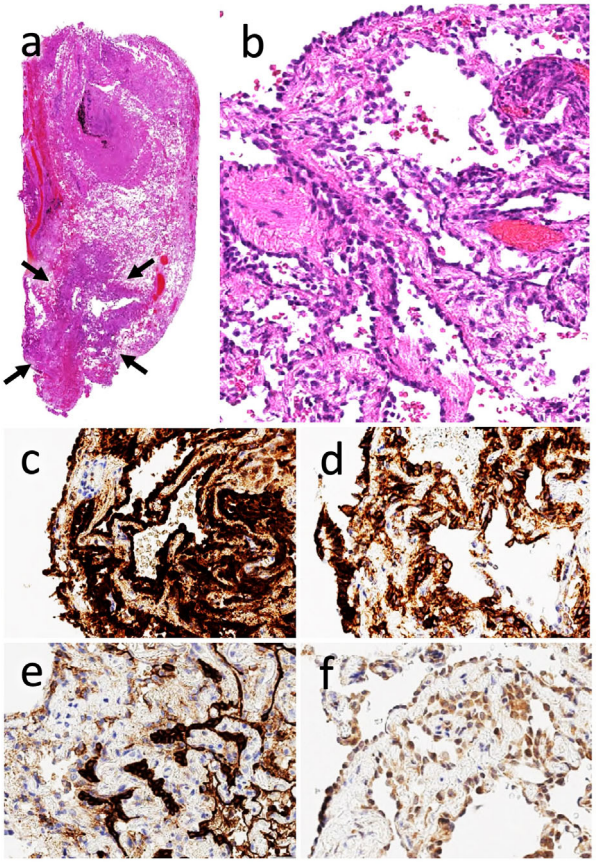

FIGURE 4 Previous surgical specimen of pneumothorax. (a) An atelectatic lesion was present (arrows). Loupe view (original magnification, x20). (b) Cells proliferating along alveolar walls were seen in the lesion. Hematoxylin–eosin stain (original magnification, x100). These cells were positive for (c) calretinin, (d) podoplanin, (e) EMA and (f) CD146. These findings were identical to those of the autopsy. Immunoperoxidase stain (original magnification, x200)

to make an early diagnosis because of an unusual clinical presentation, which started as a repeated bilateral pneumothorax and ended as a malignant esophageal stricture, with extremely mild cytological atypia.

Spontaneous pneumothorax is infrequently caused by neoplasms of which primary malignancies are few.[7] MPM seldom complicates pneumothorax during the illness, especially at initial presentation.[3–5] Pathological mechanisms of MPM-associated pneumothorax include the rupture of a necrotic tumor or ball–valve action by a tumor.[8] Patients with MPM usually present with pleural thickening/nodules, but a few exceptional cases show no such lesions.[9] In our case, the tumor cells were of a highly infiltrative nature and broadly spread without pleural thickening/nodules. This characteristic might have led to the pneumothorax although a particular trend in the histological type of pneumothorax-complicating MPM is unknown. Most MPMs arise unilaterally, with bilateral cases being less than 20%[10] and very few in patients with MPM.[11]

As well as metachronal bilateral pneumothorax, broad tumor proliferation in thoracic cavities induces esophageal stricture. Pseudoachalasia due to malignancies is found in 2.4%–4% of clinically diagnosed achalasia patients, with MPM accounting for only 7.5%.[12,13] An MPM patient with initial symptoms of dysphagia by tumor-related esophageal stricture was first reported in 1983.[14] Our case is considered even more rare, with esophageal stricture leading to a diagnosis of MPM.

Although asbestos exposure is an important risk factor for MPM, occupational asbestos exposure is evident in only about 80% of MPM patients and even fewer for women.[15] The lack of asbestos exposure was also one of the reasons an early diagnosis was not achieved.

In summary, the present MPM case was exceptional both clinically and pathologically due to a lack of asbestos exposure and pleural thickening, bilateral pneumothorax as an initial manifestation, and faint cytological atypia. These prevented an early diagnosis, with an EUS–FNA specimen from the esophageal stricture finally leading to an accurate diagnosis. In cases of recurrent pneumothorax arising in elderly patients without emphysematous changes, subclinical MPM should be included in a differential diagnosis.

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