

# Malignant pleural mesothelioma presenting as a spontaneous pneumothorax

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## Keywords

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## Abstract

Malignant pleural mesothelioma (MPM) is thought to arise from the mesothelial cells that line the pleural cavities. Most patients initially experience the insidious onset of chest pain or shortness of breath and have a history of asbestos exposure. MPM rarely presents as spontaneous pneumothorax. We report two male patients who presented with a spontaneous hydropneumothorax. One was exposed to asbestos and the other was not. Computed tomography showed tiny nodules with pleural thickness. They both underwent pleural effusion cytology and/or pleural biopsy. Therefore, the pathological diagnosis of MPM was obtained in both cases. We also reviewed 16 Japanese MPM cases with pneumothorax including our two patients. More than half of the patients suffered from pneumothorax repeatedly. We emphasize the need to obtain a pathological diagnosis of pleural effusion cytology and/or pleural biopsy in older patients presenting with a spontaneous hydropneumothorax.

## Introduction

Malignant pleural mesothelioma (MPM) is characterized by its association with asbestos, its long latency period, and the propensity for the diagnosis to be obtained in the later stages of the disease and typically presents with a pleural effusion and pleural thickening. Most patients initially experience substantial chest pain or dyspnea [1]. It rarely presents as spontaneous pneumothorax [2]. We here report two cases and review a series of 14 cases in Japan.

## Case Report

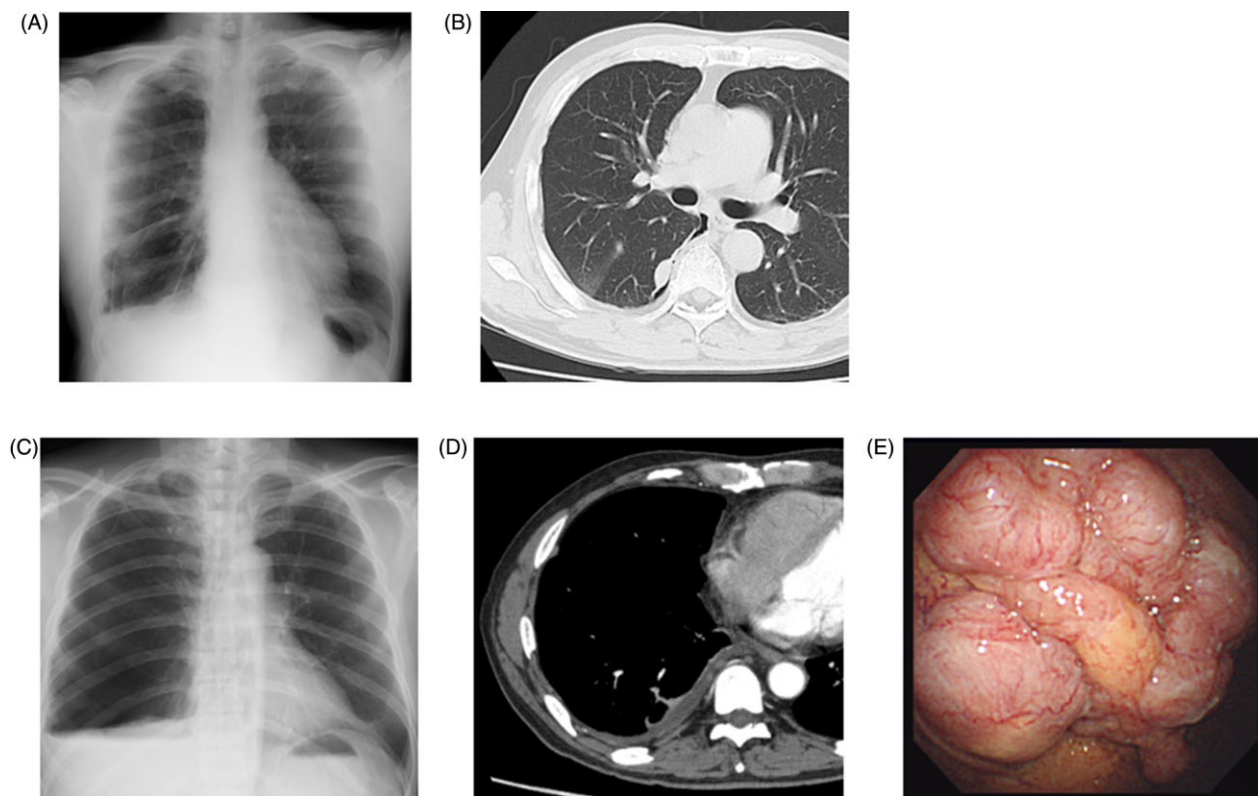
### Case 1

The patient was a 63-year-old man who had worked as an employee of an air-conditioning maintenance facility. He had a history of asbestos exposure and was a previous smoker with a 24 pack-year history. During a month before presentation, he experienced continuous cough. Right-sided mild pneumothorax and pleural effusion was detected on chest X-ray and the result of pleural effusion

cytology was negative. Despite chest tube placement, the pneumothorax failed to be resolved (Fig. 1A). Computed tomography (CT) scanning revealed collapse of the right lung and a few small nodules in visceral pleura without any bullae and blebs (Fig. 1B). The definitive diagnosis was obtained by pleural effusion cytology with additional immunocytological stain; positive calretinin and D2-40 while negative carcinoembryonic antigen (CEA). The pneumothorax was temporally resolved following chemical pleurodesis with intrapleural injection of OK-432. He eventually underwent right-sided extrapleural pneumonectomy followed by adjuvant radiotherapy of 40 Gy. The final pathological diagnosis was malignant epithelioid pleural mesothelioma of pT2N2M0 IMIG stage III.

### Case 2

A 57-year-old male patient presented with exertional dyspnea for 2 weeks. He was a current smoker with 27 pack-year history, while he had not been exposed to asbestos. Chest radiograph showed right hydropneumothorax and CT scanning showed pleural thickening with tiny



**Figure 1.** (A) Chest X-ray of case 1 reveals hydropneumothorax. (B) Chest computed tomography (CT) reveals small nodules of visceral pleura 15 mm in size. (C) Chest X-ray of case 2 reveals pneumothorax with mild pleural effusion. (D) CT scanning shows right pleural thickening at the right parietal pleura and a small amount of pleural effusion. (E) Endoscopic thoracoscopy shows multiple nodules studding on the internal surface of parietal pleura.

nodules at the right diaphragm and parietal pleura (Fig. 1C, D). The result of effusion cytology was negative. Therefore, thoracoscopic pleural biopsy was performed (Fig. 1E) and pathological diagnosis was epithelial MPM, where immunohistochemical stains were positive for calretinin, D2-40, CK5/6, CK (AE1/AE3), and CK (CAM5.2), while negative for Ber-Ep4 and CEA. Pneumothorax was treated by chemical pleurodesis with intrapleural injection of OK-432. After three cycles of neoadjuvant chemotherapy of cisplatin and pemetrexed, he underwent right-sided extrapleural pneumonectomy. The final pathological diagnosis was epithelial MPM with pT2N0M0 IMIG stage II.

## Discussion

MPM originates in the mesothelial cells and has an increasing incidence worldwide. Several epidemiological studies have revealed that it can be closely correlated with asbestos exposure. It is generally known that most patients present with insidious onset of chest pain and shortness of breath [1]. Spontaneous pneumothorax is a rare presentation of MPM

[2]. Spontaneous pneumothorax secondary to probable MPM was originally reported in 1956 by Eisenstadt [3]. In Japan, Ohkado et al. first reported a 49-year-old male patient with MPM detected by spontaneous pneumothorax in 1989 [4]. Using PubMed.gov, US National Library of Medicine, National Institutes of Health, and Ichushi Web, Japan Medical Abstracts Society, we found 15 Japanese cases reported and reviewed a series of 16 Japanese cases including our two cases (Table 1). The median age of the patients was 58 years (range 29–80 years). Thirteen (81%) patients were male, and three (19%) were female. There are nine right, six left, and one bilateral MPM with spontaneous pneumothorax reported. Only four (25%) of 16 patients had a history of asbestos exposure in this series, while four patients reported earlier had unknown history of asbestos exposure. Rate of exposure to asbestos tended to be low compared with that in other developed countries [1]. Pleural effusion was present in nine (56%) cases of this series. Eleven (69%) patients suffered from pneumothorax repeatedly.

The etiological mechanism of pneumothorax in MPM is not clear. However, three mechanisms have been recognized to explain how pneumothorax occurs secondary to

**Table 1.** Sixteen malignant pleural mesothelioma (MPM) patients with spontaneous pneumothorax in Japan.

Author	Year	Age (years)/ gender	MPM side	Asbestos exposure	Pleural effusion in onset	Number of pneumothorax before diagnosis	Estimated mechanism of pneumothorax
Okado <i>et al.</i> [4]	1989	49/M	L	Unknown	Present	2	Necrotic tumor
Nakazawa <i>et al.</i> [6]	1991	51/F	L	No	Present	1	Unknown
Kobayashi <i>et al.</i> [7]	1994	48/F	R	No	Absent	1	Necrotic tumor
Tanaka <i>et al.</i> [8]	1996	67/M	R	Unknown	Present	Many	Necrotic tumor
		70/M	R	Unknown	Present	Many	Necrotic tumor
Okumura <i>et al.</i> [9]	2002	77/M	L	Unknown	Absent	2	Necrotic tumor
Gotoh <i>et al.</i> [10]	2002	29/M	L	No	Absent	2	Unknown
Matsuge <i>et al.</i> [11]	2005	80/M	L	No	Absent	3	Ball-valve action
		45/M	R	No	Absent	3	Ball-valve action
Katayama <i>et al.</i> [12]	2006	71/M	R	No	Present	2	Necrotic tumor
Kono <i>et al.</i> [13]	2007	43/F	R	Yes	Present	1	Necrotic tumor
Makidono <i>et al.</i> [14]	2010	44/M	R	No	Absent	2	Unknown
Maebeya <i>et al.</i> [15]	2011	60/M	L	Yes	Absent	Many	Necrotic tumor
Takeuchi and Kaseda [16]	2012	74/M	L/R	Yes	Present	2	Necrotic tumor
Case 1		63/M	R	Yes	Present	1	Necrotic tumor
Case 2		57/M	R	No	Present	1	Necrotic tumor

malignant tumors. First, it may be caused by the rupture of necrotic tumor nodules. Second, the periphery tumor nodules cause a ball-valve action, which over distends the lung to form subpleural bullae, leading to rupture. Third, the tumor spreads to the pleura itself [5]. The first mechanism was the major reason of pneumothorax in our series, which led to recurrent or persistent pneumothorax. Although malignancies are an uncommon underlying cause of pneumothorax, we should look for the presence of a malignant pathology if a pneumothorax persists despite appropriate management.

In general for MPM, CT scan findings include pleural thickening, homogeneous mass with inhomogeneous contrast enhancement, deviation of the mediastinum toward the side of the lesion due to contraction of the hemithorax caused by tumor, and invasion of nearby structures with rib destruction or below the diaphragm into the retroperitoneum. CT scan is superior in evaluating tumor invasion of nearby structures compared with X-ray. However, here, it was relatively difficult to detect pleural lesion even in CT scanning as well as chest X-ray, especially in our second case. Therefore, pleural biopsy might be needed in older patients presenting with a spontaneous hydropneumothorax and/or with a history of asbestos exposure.

With an expected rise in the incidence of MPM, it would be reasonable to assume that the number of atypical presentations including pneumothorax will also increase. Suspicion should increase in older patients with occupational or environmental exposure of asbestos and with initial presentations of a hydropneumothorax on chest X-rays. It is nec-

essary to rule out malignant mesothelioma based on past history of asbestos exposure, analysis of the value of hyaluronic acid in the pleural effusion, and CT scan findings revealing pleural thickening, plaques, and nodules. Pathological pleural examination through video-assisted thoracic surgery or endoscopic thoracoscopy should be routinely considered in those patients undergoing management of pneumothorax.

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### Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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