Case Report

Localized malignant pleural sarcomatoid mesothelioma misdiagnosed as benign localized fibrous tumor

Kwan-Chang Kim[1], Hong-Phuc Vo[2]

[1]Department of Thoracic and Caridiovascular Surgery, School of Medicine, Ewha Womans University, Seoul, Korea; [2]Department of Surgery, Windsor University, School of Medicine, St. Kitts Nevis, USA

Correspondence to: Kwan-Chang Kim, MD. Department of Thoracic and Cardiovascular Surgery, School of Medicine, Ewha Womans University, 1071 Anyangcheon-no, Yang Cheon-Gu, Seoul 158-710, Korea. Email: mdkkchang@ewha.ac.kr.

Abstract: Localized malignant pleural mesothelioma (LMPM) is a rare tumor with good prognosis by surgical resection. We report an atypical case of malignant pleural sarcomatoid mesothelioma (SM) in an asymptomatic 65-year-old woman, who had no history of exposure to asbestos. She presented with a small pleural mass without pleural effusion and was misdiagnosed as a benign localized fibrous tumor (BLFT) on pathologic examination through a surgical tumor specimen. However, seven months later, the patient returned with serious cancerous symptoms. A large recurrent tumor mass was found within the chest wall invading at the old surgical resection site. SM, a subtype of LMPM, was confirmed with histopathogy and immunohistochemisty. In conclusion, malignant pleural mesothelioma (MPM) can present with typical radiologic finding similar to a BLFT, and has a wide histopathologic presentation in biopsy specimen. A thorough pathologic investigation should be attempted even when a pleural mass resembles benign, localized, and small on radiologic studies.

Keywords: Pleura; mesothelioma; lobectomy; computed tomography (CT); pathology

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Introduction

Pleural mesothelioma is a cancer that typically starts in cells lining of the chest (1). Malignant mesothelioma is relatively rare (2-6). However, it is a highly malignant tumor, which arises from the mesothelial cells of the pleura, peritoneum, pericardium, and tunica vaginalis (1). More than 80% of malignant mesothelioma patients have histories of asbestos-exposure (1,7-9). Incubation period between the onset of malignant mesothelioma and asbestos exposure is about 30–40 years (7,8). The incidence of malignant mesothelioma would be expected to increase gradually in the world due to the asbestos exposures in each county after the World War II, mishandling of environmental carcinogens, ion radiation, viruses and genetic factors (1,8,10). Early detection of malignant pleural mesothelioma (MPM) is usually difficult due to its asymptomatic and non-specific presentation characters (5,7).

Typical radiologic studies, such as X-ray and CT scan, show unilateral pleural effusion and/or a diffuse pleural thickening or masses for typical MPM cases (11-14). However, it may manifests in a benign localized form such as benign localized fibrous tumor (BLFT) or solitary fibrous tumors of pleural (SFTP) (2,3,15-20). Furthermore, malignant mesothelioma has a wide histopathologic spectrum of various cell types (21). This makes it difficult to differentiate from other pleural tumors using only hematoxylin-eosin staining and immunohistochemistry to make diagnosis of malignant mesothelioma (7,21-23).

In this paper, we report a case of localized malignant pleural sarcomatoid mesothelioma (SM), which mimics as a BLFT of the pleura on the initial radiologic and pathologic examination.

Case report

A 65-year-old asymptomatic female presented with a mass

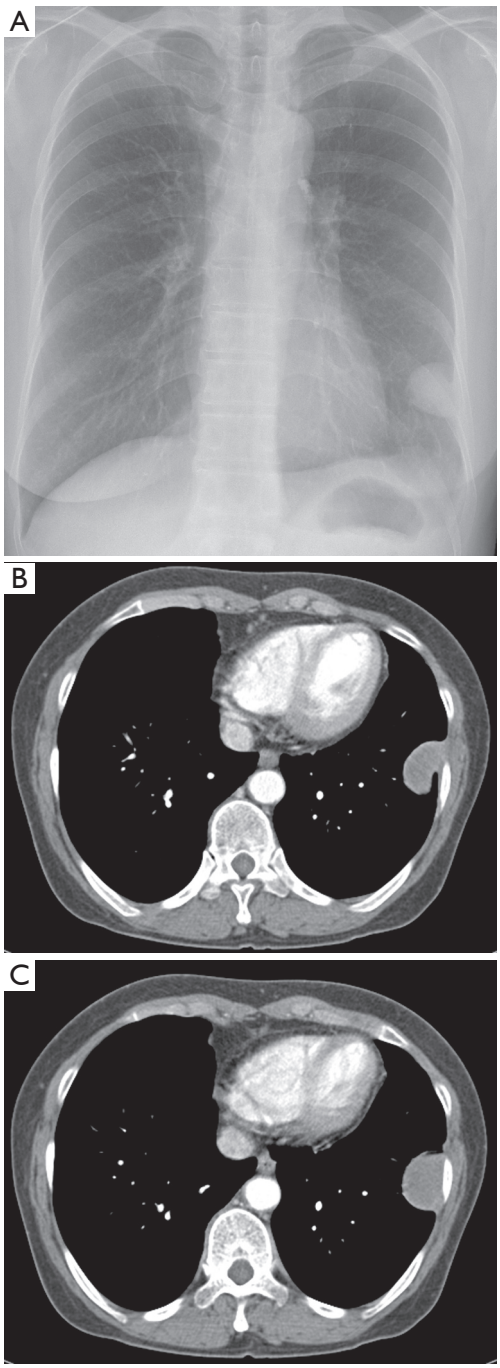

Figure 1 Initial chest X-ray and CT scan. (A) Chest X-ray shows a well-defined mass abutting the left lateral chest wall; (B,C) contrast-enhanced CT scan show a solitary sharp homogeneous oval enhancing mass abutting the pleura with diameter of 3.5 cm on the left lateral chest wall. The mass is pedunculated in the upper part of the left chest wall (B). Pleural effusion is not observed.

on chest X-ray. Patient had no past history of exposing to carcinogenic chemical known as asbestos. Her past medical history was unremarkable. There was no cancer history in her family. Her initial chest X-ray was taken and showed a sharp circumscribed mass in the left lower lung area abutting the lateral chest wall (*Figure 1A*). The contrast-enhanced CT scan performed and revealed a sharp homogenous oval enhancing mass with the diameter of 3.5 cm abutting the pleura in the upper left of the chest wall (*Figure 1B*,*C*). The tumor showed smooth margins and pedunculation. Pleural effusion and or other pleural abnormalities were not observed in the thorax. Percutaneous needle biopsy of the mass was performed with an 18-guage automated cutting needle. Pathologic examination revealed fibrocollagenous tissue with no evidence of malignancy. Then, the complete surgical excision of the mass was performed for histopathology analysis. The surgical specimen showed a benign fibroblast proliferation with collagenous fibrotic background. Plus, tumor cells were negative for calretinin, CD34, actin, and CK20 (Calretinin is a positive marker for malignant mesothelioma. CD 34 is a positive marker for solitary fibrous tumor. Actin is a positive marker for desmoid cyst). However, tumor cells had focal weak staining positive for TTF-1 and CK7 (TTF-1 is a negative marker for malignant mesothelioma). From the immunohistochemistry, differential diagnosis was a demoid and solitary fibrous tumor of the pleura (SFTP); specifically, it was rather a BLFT of the pleura.

Seven months after the surgery, patient visited our hospital with new complaints of progressive dyspnea and chest pain. A follow-up chest X-ray was taken and showed a large recurrent mass at the site of previous mass excision (*Figure 2A*). Contrast-enhanced CT scan was obtained and revealed a large homogeneously enhancing mass in the left lower hemi-thorax with invasion to its adjacent ribs and chest wall (*Figure 2B*). Large pleural effusion was observed. There was no evidence of metastasis to the thorax and upper abdomen. The second percutaneous needle biopsy was performed from the mass. Histopathologic examination revealed a diffuse spindle cell proliferation with mild pleomorphism and frequent appearance of mitosis in the collangenous background (*Figure 3A*,*B*). In addition, tumor cells showed positive for D2-40, which is a novel mesothelial positive marker for malignant mesothelioma (*Figure 3C*). Therefore, this confirmed the

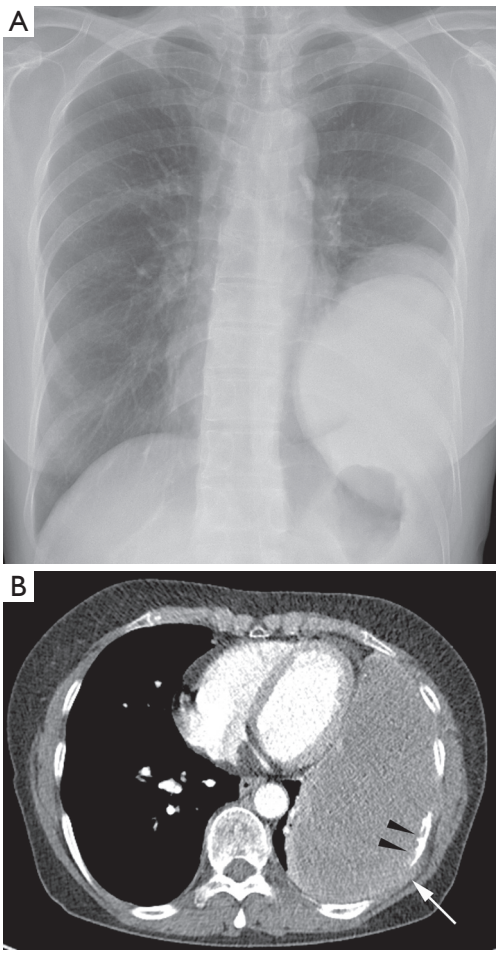

Figure 2 Follow-up chest X-ray and CT scan obtained seven months after surgical resection of pleural mass. (A) Chest X-ray shows a large recurrent mass at the site of previous mass excision; (B) contrast-enhanced CT scan shows a solitary large well-defined homogeneous enhancing mass in the left lower hemithorax. There are sign of bony destruction of adjacent rib (arrowheads) and chest wall invasion (white arrow). Image noise in the mass was owing to the low radiation dose CT scanning with iterative reconstruction algorithm. A 100 kVp and dose modulation of mAs was used.

diagnosis of SM, a subtype of MPM. A second surgery was done to remove the mass. Pleurectomy and left lower lobectomy were performed with partial removal of affect adjacent ribs and a part of affect diaphragm, which were invaded by the tumor. Patient was also treated with chemotherapy and radiation therapy. Treatment was successful without mortality. Patient was discharged home and returned to normal life.

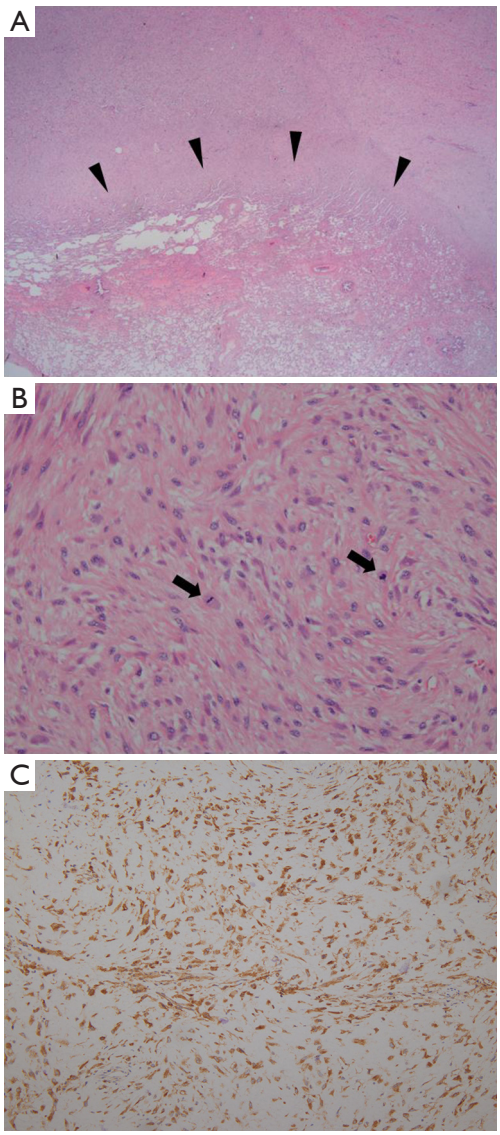

Figure 3 Histopathologic examination of pleural mass. (A) The 12× magnification on a light microscopy shows pleural mass infiltrating into the parenchyma of the lung (arrowheads); (B) the 200× magnification on a light microscopy shows spindle cell proliferation with mild pleomorphism and frequent mitosis (black arrows) in the collagenous background; (C) the 100× magnification on a light microscopy shows D2-40, a novel mesothelial marker, indicates strong positive for malignant mesothelioma.

Discussion

Malignant mesothelioma is a common pleural neoplasm due to asbestos exposure for 80% of cases (1,7,8). Its prognosis

is poor (5,7). Localized malignant pleural mesothelioma (LMPM) is a rare tumor (2-6). The incidence is 1.25/100,000 in Great Britain and 1.1/100,000 in Germany (4). In the United States, about 3,000 new mesothelioma cases have been diagnosed each year (1,24). Only a small number of case reports have been published in English literature (2) since Crotty *et al*. first described a series of six localized malignant mesotheliomas in 1994 (3). Most, but not all localized malignant mesotheliomas, were of pleural origin (21). LMPMs appeared as solitary circumscribed nodule or mass attached, either in a sessile or pedunculated manner to the surface of the pleura (25). This type of tumor should be distinguished from diffuse MPMs, because a good prognosis may be obtained by surgical resection (2,15,16).

Malignant mesothelioma has a wide histopathologic spectrum of various cell types. Although it has three typical cell types, which are epithelioid, sarcomatoid, and biphasic, epithelioid are common and tend to have better prognosis than the other types (1). About 10% of mesotheliomas are sarcomatoid (1), which has worse outcome (7). In the past few years, an accurate differentiation between subtypes of MPM has been challenging due to differences in chemosensitivity and clinical presentation (5,7). There are atypical variations, from lymphohistocytoid, small cell, deciduoid, clear cell, to other benign pleomorphic types such as localized fibrous tumor of the pleura (LFTP) and solitary fibrous of tumor of the pleura (SFTP). LFTP is also a rare benign tumor and is asymptomatic in half the patients (17). The diagnosis is difficult to establish before operation (17). Also, it is difficult to diagnose solely on immunohistochemistry and microscopic examination, which are the gold standard tools to diagnosis malignant mesothelioma (4,7). Today, there are positive and negative markers in immunohistochemistry to help make differential diagnosis of mesothelioma (22,23,26). Main positive markers are as calretinin, CK5/6, Wilms tumor 1 protein (WT1), D2-40, podoplanin, and mesothelin (21,26). Main negative markers are TTF-1, CEA, MOC-31, B72.3, and Ber-EP4 (21).

In the presented case, the initial radiologic finding was a single 3.5cm diameter pleural mass. Microscopic study found spindle cell proliferation favored fibrous tumor, such as solitary fibrous tumor, localized fibrous tumor, or desmoid tumor, which commonly occurs in the pleura. Therefore, pathologist performed immunohistochemistry for only calretinin, which is the most commonly used marker for malignant mesothelioma. Unfortunately, tumor cells were negative for calretinin. Plus, the patient was asymptomatic. Overall, this supported the initial differential diagnosis of LFTP (17). However, seven months later patient returned with worse progress, which displayed mesothelioma symptoms such as progressive dyspnea and chest pain. Now, radiographic studies showed a solitary large well-defined homogeneous re-current mass in the left lower hemithorax at the old resection sites seven months ago. There were sign of bony destruction of adjacent rib and chest wall due to tumor invasion. Pleural malignancy was highly suspected. Immunohistochemistry of tumor markers for malignant mesothelioma were scanned. Tumor cells were positive for D2-40, which confirmed the diagnosis for malignant pleural SM (26).

Malignant pleural SM usually presents with unilateral pleural effusion or diffuse pleural thickening or masses (27). However, atypical presentation, such as LMPM, would be expected to be frequent, along with an increase of the overall incidence of malignant mesothelioma (10). This would be expected to increase until the predicted peak year; 2015–2020 in Europe, 2025 in Japan, and 2015 in Australia (10,28). The important fact is most LMPM can be resolved by surgical excision (29-33). Therefore, physicians should attempt pathological examination as early as possible to prevent tumor invasion, even when the mass is localized and tiny. A careful pathologic examination should be performed with immunohistochemistry using more than two positive markers for malignant mesothelioma. The combination of CAM5.2, WT1, and AE1/AE3 are recommended for routine pathological diagnosis (22). A Japanese study by Kushitani *et al*. in 2008 showed that CAM5.2 had the highest sensitivity and specificity for differentiating SM (22).

The presented case showed a huge recurrent mass, several months after a surgical resection; whereas, some previously reported LMPM were cured by a surgical resection (2,15,16). Subtype of the presented case was sarcomatoid cell type (7,8). It is the least common of the three mesothelioma cell types. It can be challenging to diagnose (8) because it tends to resemble fibrosarcomas, or malignant soft tissue tumors in the fibrous connective tissue. SM cells are more resistant than the other cell types to most treatments, including surgery, chemotherapy (34-36) and radiation therapy, which has the poorest prognosis (37,38).

In conclusion, localized malignant pleural SM may radiologically and pathologically mimic benign fibrous tumors arising from the pleura, such as solitary fibrous tumor or localized fibrous tumors. As the incidence of malignant mesothelioma gradually increase in the world, a careful pathological examination should be performed to

differentiate malignant mesothelioma from benign tumor of the mesothelium. This should be done even when a mass is localized and small on the radiologic studies even when patient is asymptomatic.

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Footnote

Conflict of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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