Presence of Malignant Mesothelial Cells in the Sputum

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Abstract

Malignant pleural mesothelioma and peripheral adenocarcinoma, of the lung, also known as pseudomesotheliomatous adenocarcinoma, have similar clinical and radiological characteristics and even similar microscopic findings, and this makes it difficult to differentiate them. Malignant pleural mesothelioma rarely invades the bronchial lamina or bronchioloalveolar spaces, and tumor cells are not usually found in the sputum. Therefore, the appearance of tumor cells in sputum more likely supports the diagnosis of peripheral lung cancer. We report a rare case in which malignant pleural mesothelioma cells were found in the sputum. For the differential diagnosis of a mass involving both the pleura and lung, physicians should consider that malignant mesothelial cells can be found in the sputum, although this is very rare.

Key words: malignant pleural mesothelioma, sputum, peripheral adenocarcinoma

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Introduction

Malignant pleural mesothelioma (MPM) is a rare malignant neoplasm that affects both the parietal and visceral pleural surfaces. It progresses to encase the lung and eventually invades the lung, mediastinum and chest wall (1-3). However, mesothelioma cells are not usually found in sputum because the tumor rarely invades the bronchial lumina or bronchioloalveolar spaces (4). For this reason, the appearance of malignant cells in the sputum from the tumor displaying both pleural and lung lesions may favor the diagnosis of peripheral lung cancer with the pleural invasion rather than MPM. Here, we report a rare case in which malignant pleural mesothelioma cells were found in the sputum.

Case Report

A 58-year-old female patient was admitted to our hospital for evaluation of right-sided chest pain. She also complained of exertional dyspnea, cough and blood tinged sputum. The patient denied any history of exposure to asbestos or smoking.

On a chest X-ray, there was an apical pleural thickening in the right thorax and a mediastinal contour bulging into the right suprahilar area (Fig. 1A). The chest CT showed diffuse irregular thickening of the right upper pleura and a poorly defined mass opacity in the right upper lobe, which was inseparable from the pleural lesion (Fig. 1B). A diffuse thickening of the right mediastinal pleura and enlarged lymph nodes in the bilateral lower paratracheal chains were also found (Fig. 1C). Fusion PET images were taken for further evaluation. There was intensively diffuse and nodular uptake of 18F-FDG along the right pleural thickening. The images also revealed increased uptake in the pleura-based mass of the right upper lobe and enlargement of the right paratracheal lymph nodes (Fig. 2).

A few malignant tumor cells were detected in the sputum cytology, indicating that this tumor had more likely originated from the lung (Fig. 3A). Percutaneous biopsy was done and histologic examination including some immunohistochemical markers was performed. There were many large pleomorphic cells, which had large hyperchromatic nuclei and plump eosinophilic cytoplasm. They had an arranged tubular, solid and isolated infiltrative pattern suggesting the epithelioid type of mesothelioma. Alveolar space invasion of tumor cells was not examined because lung tissue was not included in the biopsy specimen (Fig. 3B). Immunohistochemical staining was performed using the ABC method according to the manufacturers’ guide. The tumor cells were

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Figure 1. Chest X-ray revealed apical pleural thickening in the right thorax and a mediastinal contour bulging into the right suprahilar area (A). The chest CT showed diffuse irregular thickening of the right upper pleura and poorly defined mass opacity in the right upper lobe, which was inseparable from the pleural lesion (B). It also showed diffuse thickening of the right mediastinal pleura and enlarged lymph nodes in the bilateral lower paratracheal chains (C).

Figure 2. The fusion PET images showed intensively diffuse and nodular uptake of 18F-FDG (SUV of 11.4) along the right pleural thickening.

positive for cytokeratin (Zymed Laboratories, San Francisco, CA, 1:100), vimentin (Zymed, 1:100), calretinin (Neo-marker, Lab Vision Corporation, Fremont, CA 1:100), CK5/6 (Cell Marque Corp., Hot Springs, AR, 1:50), and WT-1 (Cell Marque, 1:20), and negative for CEA (DAKO, 1:25), TTF-1 (Neomarker, 1:100) and podoplanin (Zymed, 1:100); these findings were compatible with malignant mesothelioma (Fig. 4).

Discussion

Peripheral lung cancer may invade into the pleura and spread along its surface, while MPM can infiltrate into the lung parenchyma and mediastinum; this can make it difficult to differentiate the two. Especially when the type of lung cancer is adenocarcinoma, the differentiation can be more difficult, even with performing histologic examinations (5, 6). MPM is a rare malignant neoplasm with a poor prognosis, and it typically affects individuals who are occupationally exposed to asbestos in a variety of industries (7). Therefore, making the accurate diagnosis is very important for the therapeutic and medicolegal aspects.

The adenocarcinoma cells are more commonly detected in the sputum because they are easily shed in the alveolar lumen, and especially when tumor cells produce a large amount of mucin (8). In contrast to this, mesothelioma cells are rarely found in the sputum (4). Frost and colleagues (9) suggested that detecting tumor cells in the sputum may be helpful to make a diagnosis of peripheral adenocarcinoma, also known as pseudomesotheliomatous adenocarcinoma, which clinically and pathologically mimicks MPM and was first described by Harwood et al in 1976 (10). A review of the English medical literature revealed only three case reports on the appearance of mesothelioma cells in sputum (11-13). Therefore, this is thought to be either extremely rare or it is generally unrecognized. Whitaker et al reported that malignant cells, presumably derived from intrapulmonary deposits, were found in sputum specimens of patients suffering with diagnosed mesothelioma (11). Wada et al reviewed their cases of malignant mesothelioma but only briefly mentioned the presence of mesothelioma cells in the sputum (12). Nakajima et al suggested that invasion into the lung along the alveolar walls was responsible for shedding tumor cells in the sputum (13).

For the present patient, considering the tumor cells in the sputum and the mediastinal lymphadenopathy seen on the CT and PET images, we preliminarily diagnosed the lesion as peripheral lung cancer rather than MPM. However, the tumor was confirmed to be MPM based on the results of the biopsy and immunohistochemical staining. Malignant mesothelioma can be distinguished from adenocarcinoma by the use of specific antibodies. Malignant mesothelioma is characterized by the presence of positive staining for podoplanin, calretinin, cytokeratin 5/6, WT1 protein and thrombomodulin (5, 14, 15). Our case disclosed positive staining
Figure 3. (A) Malignant tumor cells with hyperchromatic nuclei and distinct large nucleoli were detected in liquid-based sputum cytology. This cytologic feature was similar to pleural tumor (Papanicolaou stain, ×1,000). (B) Pleural biopsy revealed many large pleomorphic cells with hyperchromatic nuclei, which arranged nested glandular and solid features and individually infiltrative patterns (A, Hematoxylin and Eosin staining, ×200).

Figure 4. Immunohistochemical staining of the tumor was positive for WT-1 (A) and calectinin (B), and negative for CEA (C) and podoplanin (D).

results for cytokeratin, calretinin, cytokeratin 5/6 and WT1 protein. WT1 protein is one of the recently recognized and very useful markers distinguishing mesothelioma from lung adenocarcinoma (15). However, the signal of WT1 immunostaining in this case was observed in the cytoplasm of tumor cells in contrast with previous reports that showed nuclear positivity. The explanation for this finding is unclear. However, considering there were previous studies showing cytoplasmic WT-1 positivity in rhabdomyosarcoma and endometrial stroma tumors (16), it would be possible in MPM although further investigations are necessary to confirm this. Physicians should remember that for making the differential diagnosis of a mass involving both the pleura and lung, malignant mesothelial cells can be found in the sputum, although this is very rare.

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