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Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case Report

Pulmonary spindle cell carcinoma presenting with hemothorax

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ARTICLE INFO

Keywords:

Lung cancer

Hemothorax

Nontuberculous mycobacteriosis

ABSTRACT

Spontaneous hemothorax is less common. We report the case of an 83-year-old woman with spontaneous hemothorax caused by lung cancer with nontuberculous mycobacteriosis. She presented with chest pain and hemoptysis. Computed tomography revealed a tumor in the right middle lobe with middle syndrome and pleural effusion. Hemothorax was confirmed, and the right middle lobe was resected to control bleeding. The lung tumor invaded the mediastinal tissue, and tumor rupture was observed. Histological examination revealed pulmonary spindle cell carcinoma and epithelioid granulomas with caseous necrosis. Rapid tumor growth and mediastinal invasion could have led to intratumoral hemorrhage and tumor rupture.

1. Introduction

Spontaneous hemothorax is a condition in which blood accumulates within the pleural space, excluding that caused by trauma or iatrogenicity [1]. Previous studies have reported neoplasia leading to hemothorax. The most common neoplasias that cause spontaneous hemothorax are pulmonary angiosarcoma and mesothelioma, metastases of the lung or pleura from hepatocellular carcinoma, and sarcoma [1]. However, there have been few reports of spontaneous hemothorax caused by lung cancer. Therefore, little is known about the actual clinical course, test results, and potential cause of hemothorax. We report a patient with pulmonary spindle cell carcinoma, who eventually developed hemothorax.

2. Case presentation

An 83-year-old woman was admitted to our hospital with right chest pain and hemoptysis. She had a history of hypothyroidism with no history of smoking. Computed tomography (CT) revealed a 9-cm mass shadow in the middle lobe of the right lung and right pleural effusion (Fig. 1A and B). There was no obvious neoplastic lesion. Contrast-enhanced CT could not be performed because the patient was allergic to iodinated contrast agents. She had been referred to our hospital 5 months before this admission with abnormal findings following routine chest radiography. CT indicated middle lobe syndrome and exacerbation of the right middle lobe infiltrative shadow (Fig. 1C) compared with findings 5 years prior. Serum anti-mycobacterium avium complex antibody was positive. At that time, a nodule shadow was also observed in the right middle lobe (Fig. 1D). Thoracentesis was conducted, confirming hemothorax. Her vital signs were stable, and surgery was selected to control the bleeding.

Open antero-axillary thoracotomy was performed. A tumor was located in the right middle lobe with adhesion to the mediastinal adipose tissues. The site of the tumor rupture with bleeding was confirmed in the vicinity of the adhesion detachment (Fig. 2A). A right middle lobectomy was performed. Histological examination revealed that the tumor comprised round-to-short spindle tumor

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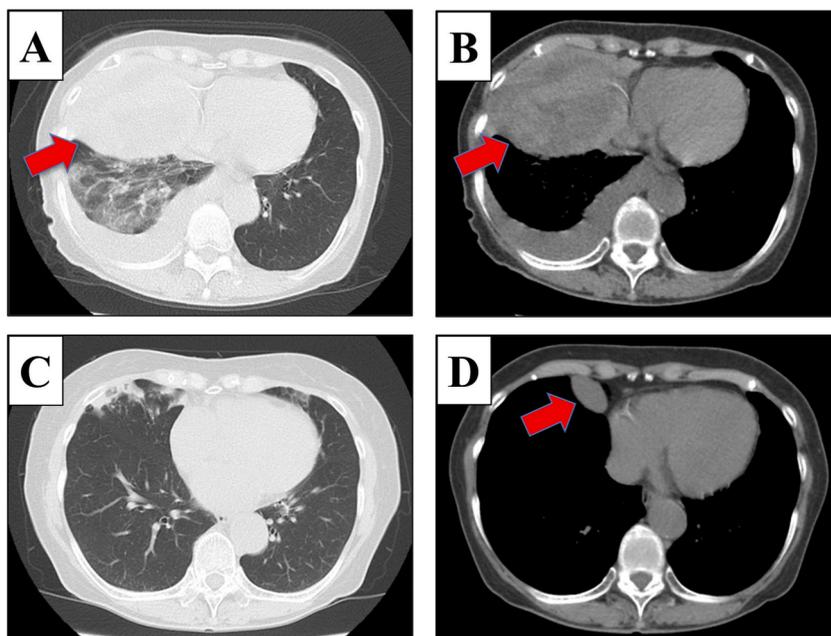


Fig. 1. Computed tomography (CT) shows a 9-cm mass shadow in the middle lobe of the right lung (arrow) and right pleural effusion (A, B). CT at 5 months before admission shows an infiltrative shadow (C) and a 2.5-cm nodule shadow in the middle lobe (arrow) (D).

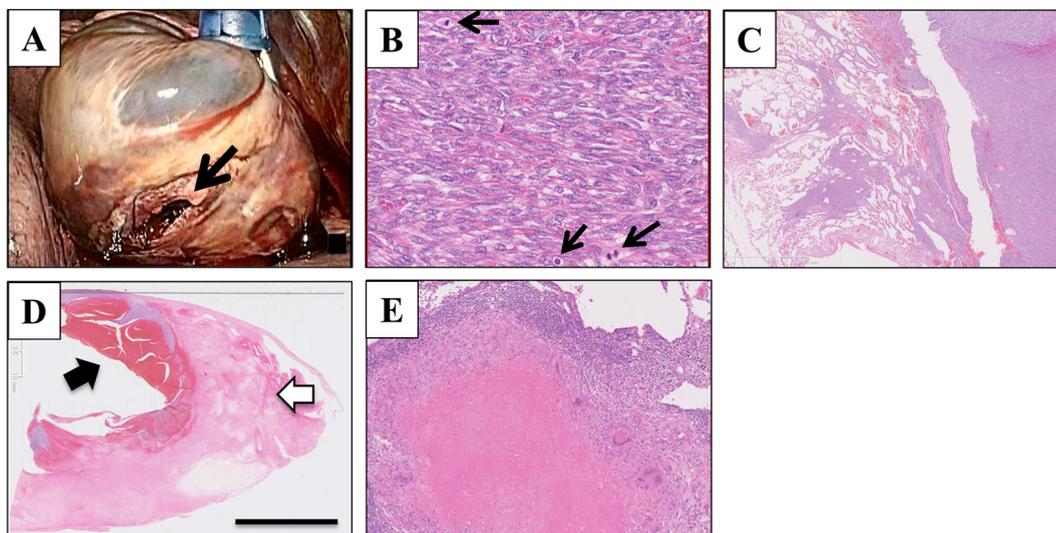


Fig. 2. Surgical view showing the middle lobe tumor and rupture site (arrow) (A). Photomicrograph of hematoxylin and eosin stained tissue (B–E). The tumor is comprised of round-to-short spindle tumor cells with eosinophilic cytoplasm and frequent mitoses (arrow) ($\times 400$) (B). The tumor is in the lung parenchyma and has infiltrated into the peripheral alveolar walls ($\times 40$) (C). Intratumoral hemorrhage (black arrow) and ischemic necrosis lesions (white arrow) are shown. (scale bar: 10 mm) (D). Epithelioid granulomas with caseous necrosis are present near the tumor ($\times 100$) (E).

cells with fascicular and storiform patterns (Fig. 2B). The tumor cells exhibited eosinophilic cytoplasm with prominent nucleoli and frequent mitoses. Epithelial-like components and rhabdoid cells were not seen. The tumor was present in the lung parenchyma (Fig. 2C) and was considered a lung tumor. There was no obvious indication that the tumor cells originated from the bronchus. Squamous precursor lesions were not found in the surgical specimen. Intratumoral hemorrhage (Fig. 2D) as well as vessel and mediastinal adipose tissue invasion were confirmed. Ischemic necrosis caused by intratumoral hemorrhage was observed. At the ruptured site, tumor cells had invaded the visceral pleura and were exposed to the surface. Immunohistochemical staining showed that the lung tumor cells were strongly positive for vimentin, weakly positive for AE1/AE3 and calretinin, and negative for TTF-1, CEA, p40, CK5/6, D2-40, and CD34 (Fig. 3A–D). Based on the clinical and pathological findings, the lung tumor was diagnosed as pulmonary spindle cell carcinoma, measuring 90 mm in diameter, with the following features: pT4N0, pI2, V1, and Ly1. Epithelioid cell granulomas with caseating necrosis were found near the tumor (Fig. 2E). Mycobacterial cultures of the lung tissue and sputum were negative, but imag-

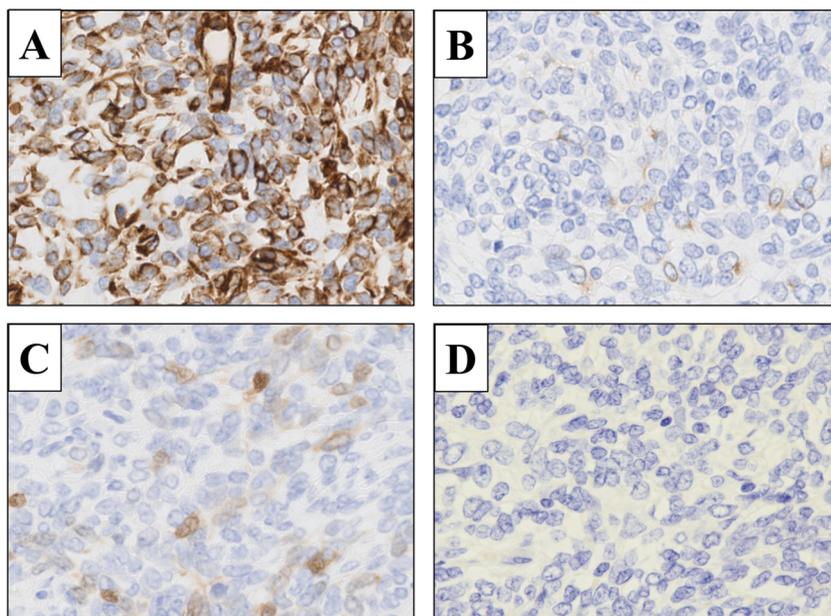


Fig. 3. Photomicrograph of an immunohistochemically stained section showing that a lung tumor positive for vimentin (A), weakly positive for AE1/AE3 (B) and calretinin (C), and negative for CK5/6 (D) ($\times 400$).

ing and pathological findings suggested pulmonary nontuberculous mycobacteriosis. Additional tests or treatments were not performed because the patient did not provide consent. The patient was doing well 12 months postoperatively, with no evidence of recurrence.

3. Discussion

Spontaneous hemothorax is rare except when it is associated with spontaneous pneumothorax. Previous studies have reported neoplasia leading to hemothorax. The most common neoplasias that cause spontaneous hemothorax are pulmonary angiosarcoma and mesothelioma, metastases of the lung or pleura from hepatocellular carcinoma, and sarcoma [1]. However, there have been few reports of spontaneous hemothorax caused by primary lung cancer. Kazawa et al. reported the case of a patient with hemothorax caused by the rupture of a pulmonary pleomorphic carcinoma with pleural invasion [2]. Sangani et al. reported that hemothorax from hemorrhage ulcerations infiltrated by parietal pleura was present in a pseudomesotheliomatous-type sarcomatoid squamous cell carcinoma [3]. In both cases, surgery was selected as a treatment for hemothorax. Yamamoto et al. reported that bronchial artery embolization was effective in a case of poorly differentiated adenocarcinoma showing hemothorax and hemoptysis caused by tumor rupture with pleural invasion [4]. The putative etiology of hemothorax in lung cancer, excluding bleeding from pleural metastases, is rupture caused by the pleural infiltration of tumor cells, bleeding from the pulmonary artery invaded by tumor cells, and intratumoral bleeding [5]. In this case, CT showed the rapid growth of a lung tumor over 5 months. Pathological examination of the surgical tissue specimen revealed a large hematoma surrounded by tumor cells and vessel invasion, indicating intratumoral hemorrhage, which was assumed to be the cause of hemoptysis. Furthermore, in the presence of the intratumoral hemorrhage, tumor cells had invaded the visceral pleura and mediastinal adipose tissue, and the location of the tumor rupture was confirmed. It was considered that intratumoral bleeding overflowed into the thoracic cavity from the location where the tumor was ruptured, leading to hemothorax.

Currently, whether performing surgery to treat spontaneous hemothorax caused by neoplasia is of oncological benefit is controversial. Most neoplasias that cause hemothorax are aggressive and progressive malignant tumors and thoracotomy is a heavy burden for patients with such tumors. A previous report recommended that catheter arterial embolization, a less invasive procedure, should be selected first [4]. However, in our case, the estimated amount of hemothorax was large, and increased hemothorax and anemia progression were confirmed within 4 h after admission. We determined that the risk of delayed bleeding with catheter arterial embolization was high and might eventually require tumor resection. Her vital signs were stable and her original performance status was good; therefore, we opted for surgery. Spontaneous hemothorax caused by lung cancer could lead to life-threatening complications. Therefore, treatment should be selected from a comprehensive perspective, including differential diagnosis and management specific to its etiology and patient condition.

CT showed middle lobe syndrome and pathological examination of the surgical specimen revealed epithelioid granulomas with caseating necrosis near the tumor cells in the middle lung tumor. Mycobacterial cultures of the lung tissue and sputum were negative, but serum anti-mycobacterium avium complex antibody was positive, indicating the possibility of pulmonary nontuberculous mycobacteriosis. The association between mycobacterial infection and lung cancer was previously highlighted. Approximately 6.5% of lung cancer cases are accompanied by pulmonary nontuberculous mycobacterial disease [6]. Lande et al. showed that patients with mycobacterium avium complex had a higher rate of squamous cell carcinoma in the periphery of the lung than those with non-

mycobacterium avium complex regardless of smoking history [6]. In a mouse model, squamous cell metaplasia developed in the lungs of 80% of mice chronically infected with mycobacterium, with some lesions showing squamous cell carcinoma transformation [7]. Mycobacterial infection typically can affect the small bronchi and bronchioles in peripheral tissues, which is one of the causes of increased peripheral pulmonary squamous cell carcinoma in mycobacterium avium complex [6]. Pulmonary spindle cell carcinoma was previously categorized as a subtype of squamous cell carcinoma; however, it is now classified as a sarcomatoid carcinoma of the lungs in the 5th edition of the WHO Classification of Thoracic Tumors [8]. In our case, the middle lobe tumor comprised only spindle-shaped tumor cells and did not contain a non-small cell lung cancer component. Immunohistochemical analysis of operative tissue specimens revealed that some tumor cells were strongly positive for vimentin, weakly positive for AE1/AE3 and calretinin, and negative for TTF-1, p40, CK5/6, and D2-40. Based on the results of immunohistochemistry, it was difficult to distinguish it from mesothelioma and sarcoma such as sarcomatoid mesothelioma and monophasic fibrous synovial sarcoma. However, the primary lesion of the tumor was in the lung rather than the mesothelium. The tumor had fascicular and storiform growth patterns and was composed of spindle cells with eosinophilic cytoplasm and prominent nucleoli. From the location and pathological morphology of the tumor, it is unlikely to originate from a mesothelioma or sarcoma. The possibility of a metastatic tumor was also considered, but preoperative and postoperative CT showed no other lesions. Therefore, taken together, this conclusively led to a diagnosis of primary pulmonary spindle cell carcinoma. In this case, the immunohistochemical analysis of p40 and CK5/6, and pathological findings did not indicate involvement with the bronchus. These findings indicate that the tumor showed no obvious squamous cell carcinoma differentiation. However, CT showed the progression of middle lobe syndrome compared with that 5 years before. It remains possible that nontuberculous mycobacterial infection contributed to the development of her pulmonary spindle cell carcinoma. Further studies are warranted to examine the possible association between chronic infection with pulmonary nontuberculous mycobacteriosis and lung cancer.

4. Conclusion

- We present a case of spontaneous hemothorax caused by pulmonary spindle cell carcinoma with nontuberculous mycobacteriosis.
- The right middle lobe was resected because of increased hemothorax over a short period and tumor resection was required to control bleeding.
- Treatment for spontaneous hemothorax caused by a neoplasm should be selected after comprehensive evaluation including general condition and examination.

Statement of ethics

Written informed consent was obtained from the patient to publish the information, including radiological and pathological images.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not -for-profit sectors.

Author contributions

Yoko Kataoka: Conceptualization, Data Curation, Writing - Original Draft. Takuya Fujita: Conceptualization, Data Curation, Writing - Review and Editing. Yuto Kato: Writing - Original Draft. Kentaro Fukunaga: Writing - Original Draft. Jun Hanaoka: Conceptualization, Writing – Review and Editing, Supervision.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgement

We thank Dr Hiroyuki Sugihara and Dr Yasushi Itoh for their advice on the pathological diagnosis.

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