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Epithelioid Angiosarcoma of the Pleura
: A Case Report

Angiosarcomas of the pleura are very rare tumors and it is difficult to differentiate them from other common pleural tumors such as mesothelioma and metastasic carcinoma clinically and pathologically. We report a case of a young Korean woman with angiosarcoma arising in the pleura. A 34-yr-old woman presented with dyspnea and chest tightness and pain for several months. A computed tomographic scan of the chest showed diffuse thickening of the left pleura and effusion with passive atelectasis. At thoracotomy the left pleura was thick and indurated. Histologically, the decorticated pleura revealed infiltration of sheets or cords of polygonal and epithelioid tumor cells showing rudimentary vascular differentiation. Immunohistochemically, the tumor cells were strongly positive for CD31, CD34, and vimentin, whereas weakly positive for factor VIII, and negative for cytokeratin, which are characteristic and specific findings of angiosarcoma.

Key Words : *Pleura; Hemangiosarcoma*

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INTRODUCTION

Malignant vascular tumors rarely occur in pleura or other serous membranes such as pericardium and peritoneum. Many of these serous membrane-related angiosarcomas show histologically epithelioid feature, and the distinction from other common tumors such as mesothelioma and metastatic carcinoma is difficult (1, 2). A total of 31 cases of primary malignant pleural vascular tumors were identified in the English literature (1-10). We report a case of epithelioid angiosarcoma of the left pleura, which was pathologically proven on decorticated pleural specimen.

CASE REPORT

A 34-yr-old woman was admitted due to dyspnea and chest tightness and pain for several months. She had been clinically diagnosed as tuberculosis for the same symptoms, 4 months before, and had been under medical treatment accordingly. However, her symptoms did not improve and even aggravated recently. She had no history of smoking or occupational exposure to asbestos. A computed tomographic scan of the chest showed diffuse left pleural thickening and effusion with passive atelectasis and air space nodules at right lung field suggesting an endobronchial spread of tuberculosis (Fig. 1). The sputum culture showed no acid-fast bacilli. There was no evidence of tumor lesion in other organs on preoperative radiologic studies. At thoracotomy the lesion grew along the entire medial and lateral parietal pleural surface and was characterized by variably thick rinds of tissue encasing the lung. The visceral pleura was adhered with the lesion. The lung parenchyma underneath the pleura showed areas of dark red and friable consolidation. She underwent pleural decortication. The resected pleural tissues were leath-

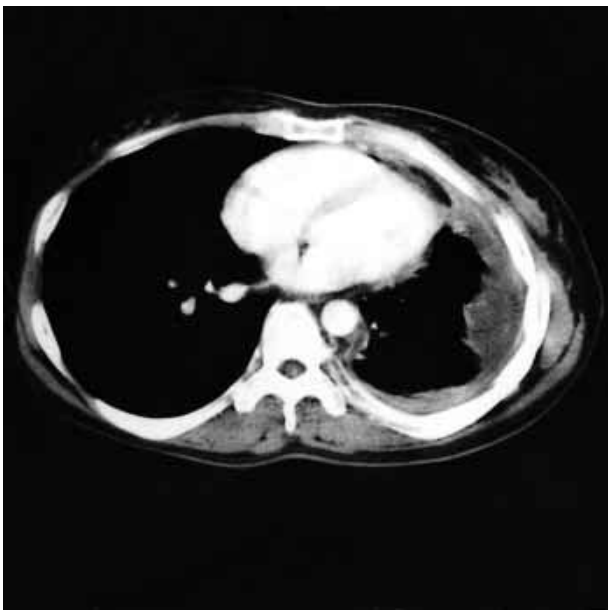

Fig. 1. Chest CT revealed diffuse thickening of the left pleura with effusion.

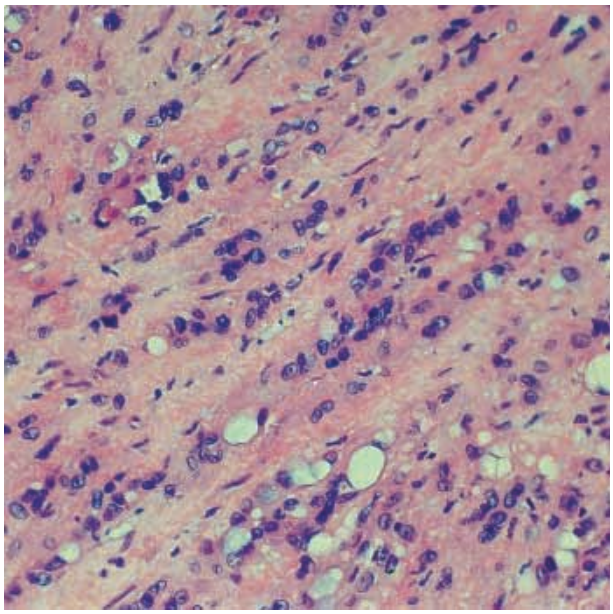

Fig. 2. The pleura showed diffuse infiltration with sheets, nests or cords of large epithelioid tumor cells (H&E, ×200).

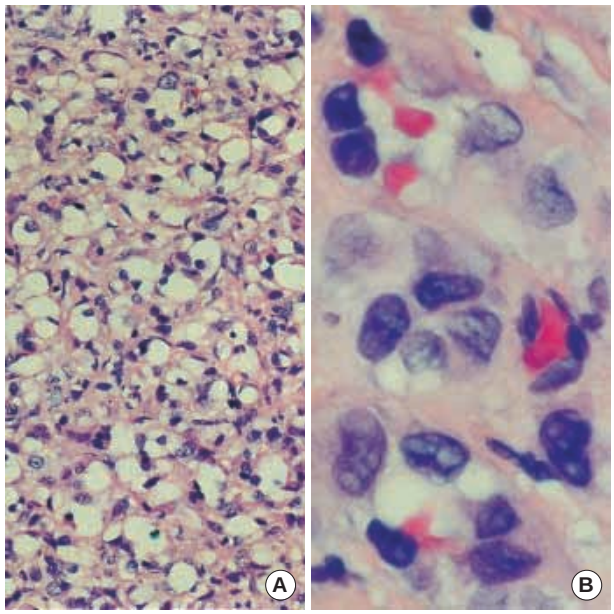

Fig. 3. (A) Some tumor cells had delimited intracytoplasmic vacuoles or clear cytoplasms (H&E, ×200). (B) The tumor cells form rudimentary channels containing RBCs (H&E, ×1,000).

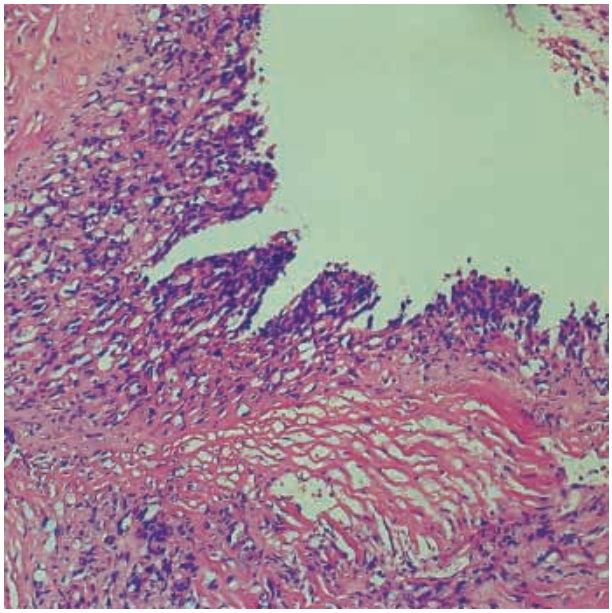

Fig. 4. Cystic space was lined with micropapillary tumor projections (H&E, ×100).

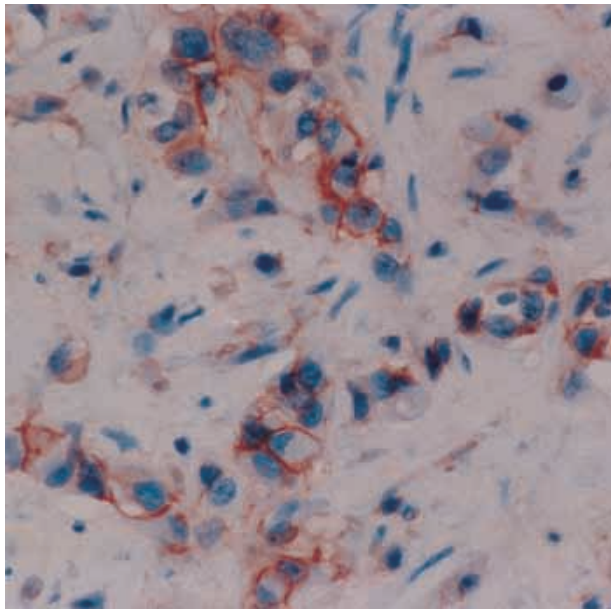

Fig. 5. Immunohistochemically, the tumor cells were strongly positive for CD31 (×400).

ery, thickened, and covered by a fibrinous exudate. Histologically, the pleura was thickened with fibrosis and showed infiltration of sheets, nests or cords of large epithelioid tumor cells (Fig. 2). The tumor cells were polygonal and had round to oval nuclei with vesicular chromatin pattern and prominent nucleoli, and rather abundant amphophilic or eosinophilic cytoplasms, giving an epithelioid appearance. Strands of tumor cells in hyaline stroma were present, which were reminiscent of indian file appearance of breast carcinoma. In area, aggregations of tumor cells with clear cytoplasms were also present, which was confused with metastatic renal cell carcinoma (Fig. 3A). Focally cystic spaces lined by micropapillary tumor projections and endothelial-lined spaces with tumor cells forming grape-like clusters were noted (Fig. 4).

However, unlike in mesothelioma, there were sharply delimited intracytoplasmic vacuoles, part of which contained entrapped intact and degenerating RBCs (Fig. 3B). Extensive hemorrhage and multifocal necrosis were also noted. Immunohistochemically, the tumor cells were strongly positive for CD31 (Fig. 5), CD34, and vimentin, while weakly positive for factor VIII, and negative for cytokerain, EMA, S100 protein and smooth muscle actin. The patient received two cycles of adjuvant chemotherapy with adriamycin and ifosfamide after surgery. No evidence of tumor recurrence or metastasis is noted and the patient is alive for 5 months. But she is in a serious condition with severe chest pain at present.

DISCUSSION

Angiosarcoma is a rare soft tissue sarcoma that usually occurs in the skin, deep soft tissue, breast, spleen, and liver. Rarely it can arise in the pleura as well as in other serous membranes. A total of 31 cases of primary malignant pleural vascular tumors were identified in the English literature (1-10). The age of the patients ranged from 22 to 79 yr (mean, 57 yr) and the male to female ratio was 9:1. Thus it is uncommon to occur in young female as in this case. The most frequent clinical presentation is pleural thickening and effusion, simulating mesothelioma clinically. Distinct mass formation is very unusual. Most of the patients die of the disease shortly after diagnosis.

The pathogenesis and etiologic factor are still obscure. Some authors have speculated that serosal angiosarcoma could represent a peculiar malignant mesothelioma differentiating along an abnormal angioblastic pathway or, alternatively, a lesion arising from the native subpleural vessels or a vascular malformation (11). Although all reported Japanese patients with pleural angiosarcoma had a history of chronic pyothorax caused by pulmonary or pleural tuberculosis for a long period before development of pleural angiosarcoma (9), Zhang et al. (10) documented no strong causative linkage in cases reported in the West. Aozasa et al. (9) reported the frequency of chronic tuberculous pyothorax-associated angiosarcoma to be supposedly over 3600-fold higher than that in normal population and suggested an important role of chronic inflammation as a source of physiological mediators such as nitric oxide and cytokines. In a review of 22 cases from Western countries, prior radiation and asbestos exposure might be etiologically responsible in a few cases: radiation-related in 2 cases (2.9%) and asbestos-related in 3 cases (14%) (10). Interestingly, among the Western cases, there were only 2 female patients with a history of radiation therapy for ovarian cancer and both developed concurrent peritoneal and pleural involvements. Although the patient in our case had been under medication for tuberculosis, it is possible that the diagnosis might not be correct. In this regard, no specific etiologic factor is found in our case.

In our case, some area of the tumor showed a relatively low-grade histological appearance simulating that of epithelioid hemangioendothelioma of soft tissue. In soft tissues, epithelioid hemangioendothelioma is conventionally considered to be a low-grade or borderline-grade vascular tumor. However, the distinction and relationship between epithelioid angiosarcoma and epithelioid hemangioendothelioma of the pleura have not been well defined in the literature. And all previously reported pleural angiosarcomas and all but one of the previously reported pleural epithelioid hemangioendothelioma were rapidly fatal (1-10). In our case, although the tumor had histological appearance of epithelioid hemangioendothelioma, obvious histological features of angiosarcoma including atypical nuclear feature, miotosis, vascular differentiation, and necrosis were present. So we diagnosed this tumor as epithelioid angiosarcoma rather than epithelioid hemangioendothelioma.

Pleural angiosarcomas are often epithelioid (74%) (10) and can be easily mistaken for mesothelioma or carcinoma both clinically and histologically (1, 2, 8). In our case, focal histologic findings suggested an involvement of carcinoma. In an area, strands of tumor cells infiltrated in hyalinized stroma had an indian file appearance of breast carcinoma. In addition, some tumor cells with clear cytoplasm were confused with metastatic renal cell carcinoma. But the results of immunohistochemical study suggested sarcoma rather than carcinoma. The possibility of liposarcoma was considered since the tumor cells having abundant vacuolar cytoplasm were reminiscent of lipoblast. Possibility of this rare tumor prompted us to use the endothelial markers when faced with a questionable mesothelioma. The immunohistochemical stains for intermediate filament prove to be informative, as these tumors show strong reactivity for vimentin and either absence or weak to moderate level of cytokeratin expression. When the immunostains are optimally performed with adequate fixation, all mesotheliomas and adenocarcinomas are strongly positive for cytokeratin. In epithelial mesothelioma and adenocarcinoma, the vimentin staining is usually less intense than that of the cytokeratin (1). When cytokeratin is negative or focally positive with vimentin reactivity, a vascular tumor should be suspected and confirmed with vascular markers. Epithelioid vascular tumors of the pleura always react with at least one of three endothelial markers, i.e., CD31, CD34, and factor VIII (1, 2). These are the endothelial-specific immunologic markers with variable specificity and sensitivity. Factor VIII-related antigen, in spite of its high specificity, is believed to be relatively insensitive, particularly in malignant vascular tumors (12). CD34 was reported to be a specific and sensitive endothelial marker, but it also reacts with nonvascular soft tissue neoplasm, including epithelioid sarcoma, malignant peripheral nerve sheath tumor, leiomyosarcoma, and clear cell sarcoma (13). CD31 has been shown to be a highly specific and sensitive endothelial marker that reacts rarely and only weakly with nonvascular tumors (12).

In conclusion, angiosarcoma may rarely present with exclusive involvement of the pleura and we report a case of epithelioid angiosarcoma of the pleura in a young Korean woman proven by histological and immunohistochemical stains on decorticated pleural specimen. Angiosarcoma of the pleura frequently shows epithelioid feature and the distinction from other common tumors such as mesothelioma and metastatic carcinoma is very important.

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