Case Report

A Case of Pulmonary Metastasis of Epithelioid Sarcoma Presenting as Pulmonary Cysts with CA125 Expression

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Running Title: Epithelioid sarcoma with pulmonary cysts

ABSTRACT

A 39-year-old Japanese woman presented with swelling in the right hand and right-sided pneumothorax. Chest computed tomography revealed bilateral multiple pulmonary thin-walled cysts measuring ≤1 cm in diameter and small nodules. Initial skin biopsy lead to a misdiagnosis of metastatic adenocarcinoma, as tumor cells were positive for cytokeratin, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), and cancer antigen 125 (CA125). However, chemotherapy proved ineffective, and skin biopsy was performed again. A final diagnosis of epithelioid sarcoma (ES) was made. Open lung biopsy showed that pulmonary nodules represented metastasis of ES. Although pulmonary cyst walls did not contain tumor cells, bronchiolar wall adjacent to the cyst had been infiltrated by tumor cells. These findings suggest that pulmonary cysts, a rare form of pulmonary metastasis from soft tissue sarcomas, developed through the ball-valve effect of metastatic tumor in small airways. However, presence of CA125 represented an obstacle to diagnosis of ES in the present case.

KEY WORDS

epithelioid sarcoma; pulmonary metastasis; pulmonary cyst; pneumothorax; immunohistochemistry; CA125

SHORT TITLE

Epithelioid sarcoma with pulmonary cysts

ABBREVIATIONS

CEA, carcinoembryonic antigen; CT, computed tomography; EMA, epithelial membrane antigen; ES, epithelioid sarcoma

INTRODUCTION

Epithelioid sarcoma (ES) is a rare soft-tissue sarcoma simulating necrotizing granuloma or carcinoma histologically and immunohistochemically. We describe a case of ES with pulmonary metastasis presenting as multiple pulmonary cysts with positive immunohistochemistry for cancer antigen 125 (CA125), leading to a misdiagnosis of adenocarcinoma of unknown primary site. Histopathological studies revealed the possible mechanism by which cystic pulmonary metastasis may have developed.

CASE REPORT

A 39-year-old Japanese woman presented with swelling in the right hand that had gradually progressed to the forearm over the course of 15 months. Initial biopsy of skin from the right hand revealed nodular aggregates of epithelioid atypical cells. These displayed revealed positive staining for cytokeratin, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA) and CA125. Metastatic carcinoma was suspected from pathological examination. At the same time, the patient experienced right-sided pneumothorax that required placement of a chest tube. After the completion of treatment for pneumothorax, chest radiographs were normal, but computed tomography (CT) of the chest revealed bilateral multiple thin-walled pulmonary cysts ≤1 cm in diameter and multiple small nodules ≤5 mm in diameter, which were interpreted as pulmonary metastasis (Fig. 1). Laboratory

examination revealed that serum chemistry and tumor markers were within normal limits except for elevated serum CA125 at 42.3 U/ml (normal: <35 U/ml), which led to suspicion of adenocarcinoma. However, systemic examination showed no primary site. Chemotherapy with carboplatin and paclitaxel was administered intravenously based on a diagnosis of metastatic adenocarcinoma of unknown primary site. After chemotherapy, swelling in the right hand revealed no change and chest CT showed no marked changes in pulmonary cysts or nodules.

Biopsy from the skin of the right forearm was performed again in our hospital 6 months after chemotherapy. Histopathological analysis showed epithelioid cells arranged in nodular aggregates around areas of central necrosis, which were typical for ES (Fig. 2A, B). Immunohistochemical studies were performed again, revealing cells positive for vimentin in addition to cytokeratin, EMA, CEA, and CA125 (Fig. 2C). ES of the right forearm was finally diagnosed. Open lung biopsy was performed to diagnose whether pulmonary cysts and nodules represented metastatic lesions. Pulmonary nodules consisting of epithelioid cells were also positive for cytokeratin, EMA, CEA, CA125 and vimentin, and were thus diagnosed as metastases of ES. Pulmonary cysts contained air and were surrounded by normal lung parenchyma with no identifiable neoplastic cell component. However, the wall of a small airway next to a cyst contained malignant cells, suggesting that cysts developed by the ball-valve effect of the metastatic tumor (Fig. 3).

She underwent chemotherapy for soft tissue sarcoma with

ifosfamide, doxorubicin and cyclophosphamide in combination, resulting no significant change. She thereafter suffered from repeated bilateral pneumothorax, and died 53 months after she first felt swelling in the right hand.

DISCUSSION

ES is a distinctive soft tissue neoplasm with a predilection for the distal extremities of young adults (1). Typical examples contain admixtures of epithelioid and spindle cells that are often arranged in nodular aggregates around areas of central necrosis, simulating necrotizing granuloma or carcinoma. Metastases to the lymph nodes, lungs and skin reportedly occur in about 50% of patients with ES (2, 3). Pulmonary metastases of soft tissue sarcomas commonly take the form of solid nodules. Although some tumors occasionally present as cystic pulmonary metastases, few cases of cystic pulmonary metastases of soft tissue sarcomas have been described (4, 5). Three possible mechanisms have been proposed for the development of malignant cysts (4-6): 1) excavation of a nodular tumor through discharge of the necrotic material inside; 2) infiltration of malignant cells into the walls of a pre-existing benign pulmonary bulla; or 3) distension of alveoli and small airways by partial bronchial obstruction through the ball-valve effect of the tumor. Involvement of the first and second mechanisms in the present case was ruled out due to the absence of identifiable neoplastic cells around cysts. The presence of malignant cells in

the bronchiolar wall next to a cyst would suggest that the mechanism of development of the cyst in the present case was the ball-valve effect. Pneumothorax may therefore have also been caused by distension of alveoli through the ball-valve effect, permitting passage of air along the interlobular septa to the pleura, where blebs may have formed and eventually ruptured.

Immunohistochemical analyses of ES typically reveal positive results for vimentin, keratins, EMA and occasionally CEA and CD34 (7). In the present case, tumor cells were positive for CA125 in addition to vimentin, keratin, EMA and CEA. CA125 is a large glycoprotein expressed on the epithelium of the fallopian tubes, endometrium, endocervix and ovary, in addition to mesothelial cells of the pleura, pericardium and peritoneum (8). CA125 is a differentiation antigen associated with coelomic epithelium and both normal and neoplastic derivatives. Serum CA125 concentration has been found to represent a marker for epithelial ovarian carcinoma. CA125 is also reportedly elevated in other cancers, including endometrial, pancreatic, lung, breast and colon cancer. Elevated serum levels of CA125 have occasionally been reported in mesenchymal tumors such as leiomyosarcoma (9), alveolar rhabdomyosarcoma (10) and desmoplastic small round cell tumor (11). Kato *et al.* recently reported elevated levels of serum CA125 in 3 patients with ES, and immunohistochemical expression in 10 of 11 ES patients (12, 13). These cases in addition to the present case suggest that CA125 might prove useful as an immunohistochemical and serum marker for diagnosing ES.

Clinicians and pathologists should be aware of the possibility of ES when encountering cases with nodular aggregates of epithelioid atypical cells that are positive for CA125.

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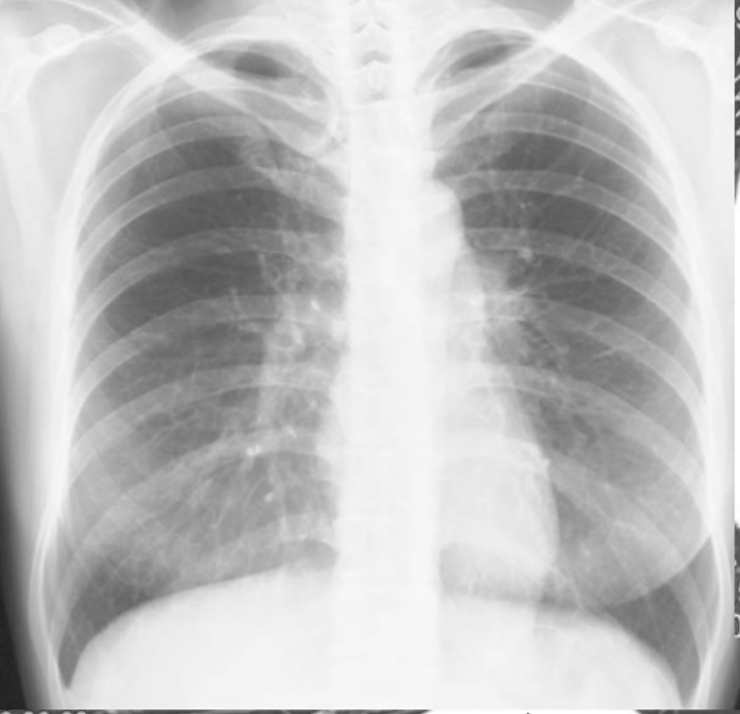
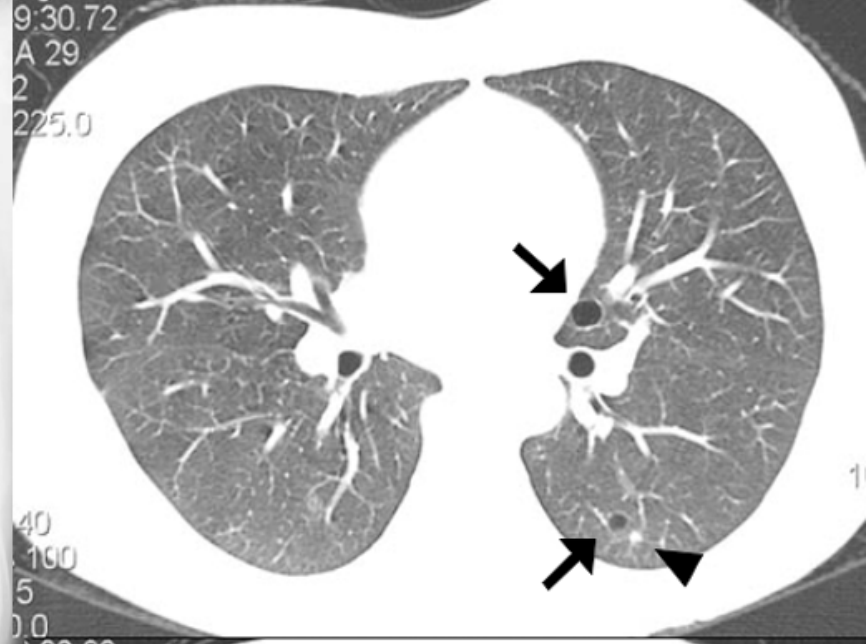
FIGURE LEGENDS

Figure 1: A) Chest radiograph showing no abnormalities. B-D) Computed tomography (CT) of the chest showing bilateral multiple pulmonary thin-walled cysts ≤1 cm in diameter (arrows) and multiple small nodules ≤5 mm in diameter (arrowheads).

Figure 2: A) Skin biopsy specimen. The tumor was located in the lower dermis, showing geographic necrosis surrounded by epithelioid tumor cells with eosinophilic cytoplasm. These findings are typical for epithelioid sarcoma (×4, HE). B) Epithelioid cells surrounded by collagenous stroma in a tumor with necrosis (×20, HE). C) Tumor cells were strongly positive for CA125 (×40).

Figure 3: Microscopic findings from the lung biopsy specimen showing that the cyst wall (arrows) contains no neoplastic cell component, but the wall of a small airway next to a cyst (arrowheads) contains malignant cells (×4, HE).

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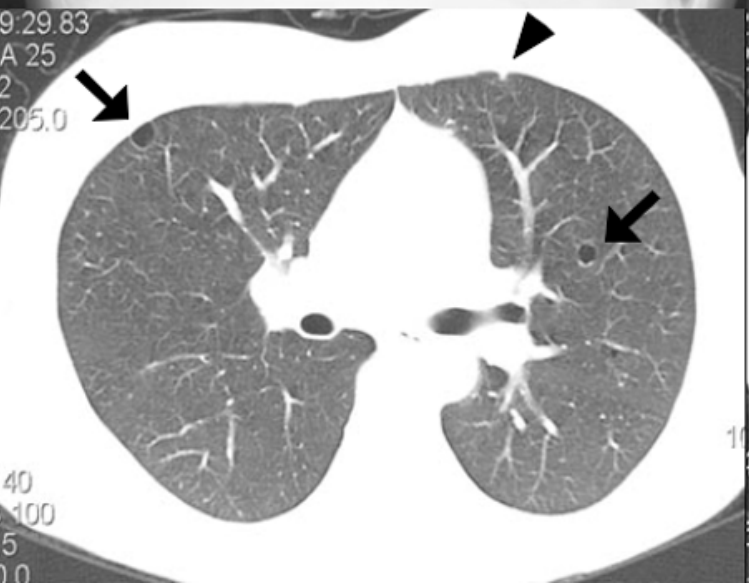
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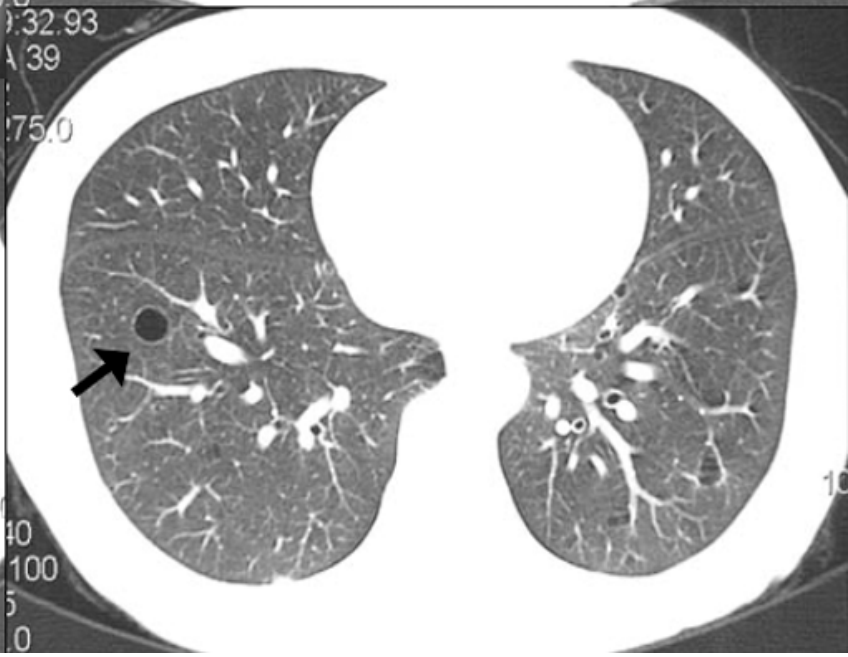
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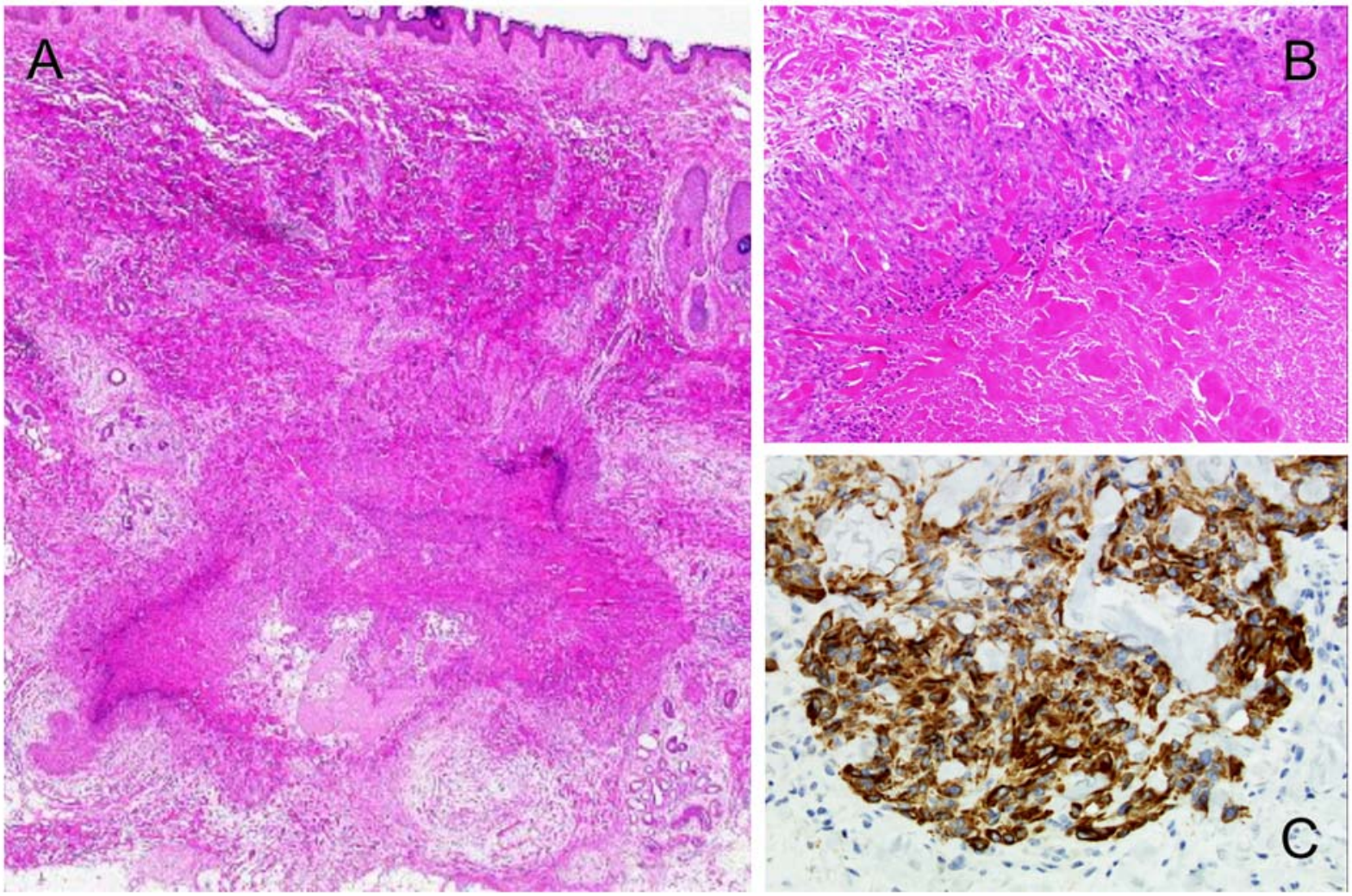
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