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Primary Pulmonary Sarcoma with Morphologic Features of Biphasic Synovial Sarcoma: A Case Report

We report an unusual primary case of pulmonary sarcoma that developed in the lung of a 36-year-old woman. The tumor had histologic, immunologic and ultrastructural features identical to those of biphasic synovial sarcoma of the soft tissue. It consisted of an intimate admixture of cytokeratin and epithelial membrane antigen (EMA)-positive neoplastic epithelial cells and vimentin-positive fibroblast-like spindle cells with areas of hyalinization. The patient had a lobectomy and showed no evidence of recurrence or tumor at other sites 15 months after surgery. This case is an useful addition to the small number of published reports on pulmonary synovial sarcoma. The distinctive features of this neoplasm allow it to be different from other types of primary and metastatic malignancies in the lung.

Key Words : *Lung tumor, Biphasic synovial sarcoma, EMA*

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INTRODUCTION

Although the histogenesis of synovial sarcoma is unknown, synovial sarcoma has been recognized as a soft tissue tumor with a distinctive morphology for many years (1). Synovial sarcoma may account for up to 10% of all soft tissue sarcomas (2) and occurs especially in young adults, primarily in the periarticular regions, usually in association with tendon sheaths, bursa and joint capsules (3, 4). The tumor generally occurs as a deep-seated palpable swelling in the mentioned sites (3). Although most of these tumors develop in the extremities, they rarely arise in the lung and pleura which are other possible sites of origin (5, 6, 7). In this report, we present the light microscopic, immunohistochemical, and ultrastructural features of an unique primary synovial sarcoma that arose in the lung. We discuss the histologic differential diagnosis and briefly review its pathogenesis.

MATERIALS AND METHODS

Sections of the tumor were fixed in 10% neutral buffered formalin and processed for light microscopic examination. Immunohistochemical studies were performed on formalin-fixed, paraffin-embedded tissue, using the avidin-biotin-peroxidase complex method, with antibodies to broad-spectrum cytokeratin (Dako, Glaustrup, Denmark), epithelial membrane antigen (Dako, Glaustrup, Denmark), vimentin (Dako, Glaustrup, Denmark), S100-protein (Dako, Glaustrup, Denmark), CEA (Dako, Glaustrup, Denmark), Factor VIII-related antigen (Dako, Glaustrup, Denmark), desmin (Dako, Glaustrup, Denmark), and alpha-smooth muscle actin (Dako, Glaustrup, Denmark). Additional formalin-fixed tumor tissue was fixed in glutaraldehyde for ultrastructural study and processed using standard techniques with post-fixation in osmium tetroxide and plastic epoxy embedding. Thin sections were stained with uranyl acetate and lead citrate and examined with an electron microscope (JoeL 1200EXII).

CASE HISTORY

A 36-year-old woman was admitted to the hospital in October, 1995 because of intermittent mild dyspnea of 6 months' duration. There was no significant past medical history. A chest radiograph revealed a 3.5 cm-sized solitary mass in the left upper lobe of the lung. The involved lobe of the lung was surgically resected. No extrapulmonary neoplasm was found on the subsequent clinical evaluation. The patient showed no evidence of recurrence or tumor at other sites after 15 months' follow-up with repeated chest CT scans.

PATHOLOGIC FINDINGS

A round well circumscribed, lobulated, firm, grayish yellow tumor mass, measuring 3.5 cm at maximum diameter, was observed within the subpleural parenchyma of the left upper lobe (Fig. 1). It was focally attached to the bronchial wall. The cut surface was finely trabeculated and showed neither hemorrhage nor necrosis. Microscopically, the neoplasm revealed varying arrangements of epithelial cells with fibroblast-like spindle cells, which showed a biphasic pattern (Fig. 2). The neoplastic epithelial cells, comprising approximately 80% of the tumor volume, were arranged in the nests or solid cords, or infrequently bordered pseudoglandular spaces which contained granular or homogeneous eosinophilic secretion. The epithelial cells were characterized by large, round or oval, vesicular nuclei and moderate amount of pale-staining cytoplasm with distinctly outlined cellular borders. Mitotic activity was 2/10HPF, but no atypical mitosis was seen in the epithelial cell area. The fibroblast-like spindle cells around epithelial cell nests showed moderate cellularity of well oriented, rather plump, spindle-shaped cells with small amounts of indistinct cytoplasm and oval to spindle vesicular nuclei. These fibroblast-like spindle cells are not so cellular and anaplastic. Nests of epithelial cells frequently demonstrated intercellular focal hyalinization. A few foci of indistinct

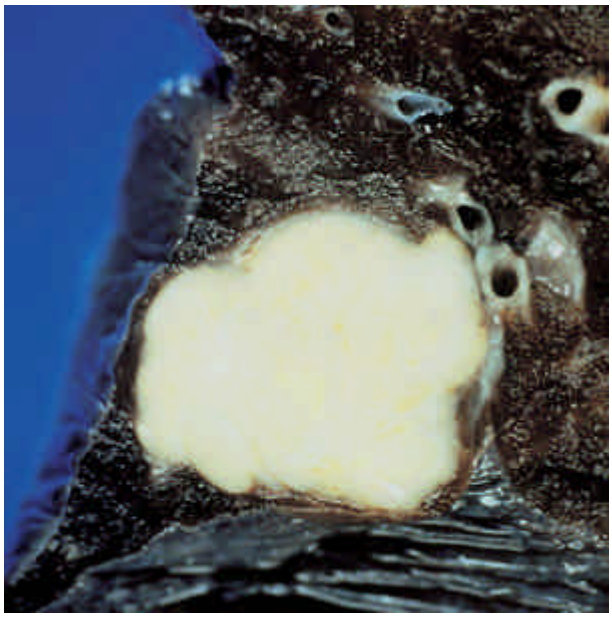

Fig. 1. Gross photograph of the lung showing a round well circumscribed, lobulated, firm, graysh yellow 3.5 cm mass in the subpleural parenchyma.

margin between nests of pale-staining epithelial cells and stromal cells were observed. The tumor infiltrated the adjacent respiratory bronchioles, involving the mucosa. No blood or lymphatic vessel invasion was noted. A mild

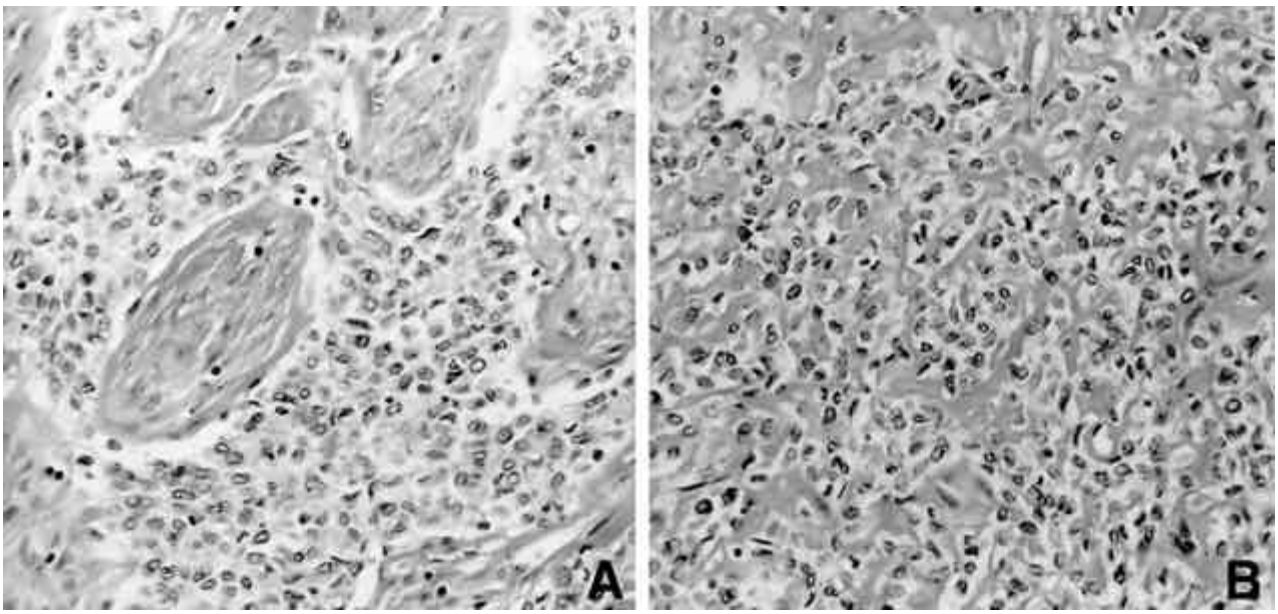

Fig. 2. Photomicrograph of the pulmonary synovial sarcoma showing a biphasic pattern, which consists of an intimate admixture of neoplastic epithelial cells and fibroblast-like spindle cells. The epithelial cells are characterized by large, round or oval, vesicular nuclei and moderate amount of pale-staining cytoplasm with distinctly outlined cellular borders (A). Some areas show hyalinization throughout tumor cell nests seperating individual or a few neoplastic cells, representing transitional area between epithelial component and fibrous component (B).

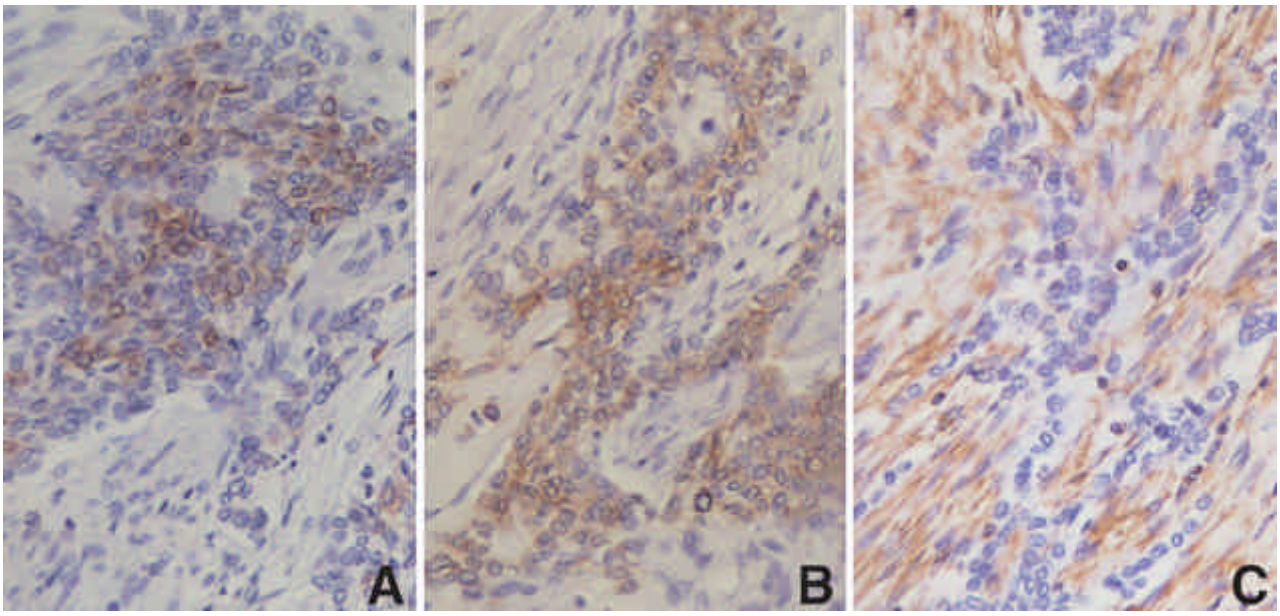

Fig. 3. Immunohistochemical staining for EMA (A), cytokeratin (B), and vimentin (C) in the pulmonary synovial sarcoma. The malignant epithelial cells stain positively for EMA and are rather weakly positive for cytokeratin, but negative for vimentin. The surrounding fibroblast-like spindle cells stain positively for vimentin, but negatively for EMA and cytokeratin.

inflammatory infiltrate was present with lymphoplasma cells and scattered mast cells in the spindle cell portion rather than in the epithelial portion of the neoplasm.

On the immunohistochemical studies, the malignant epithelial cells stained weakly positive for EMA and for cytokeratin. However, they were negative for vimentin

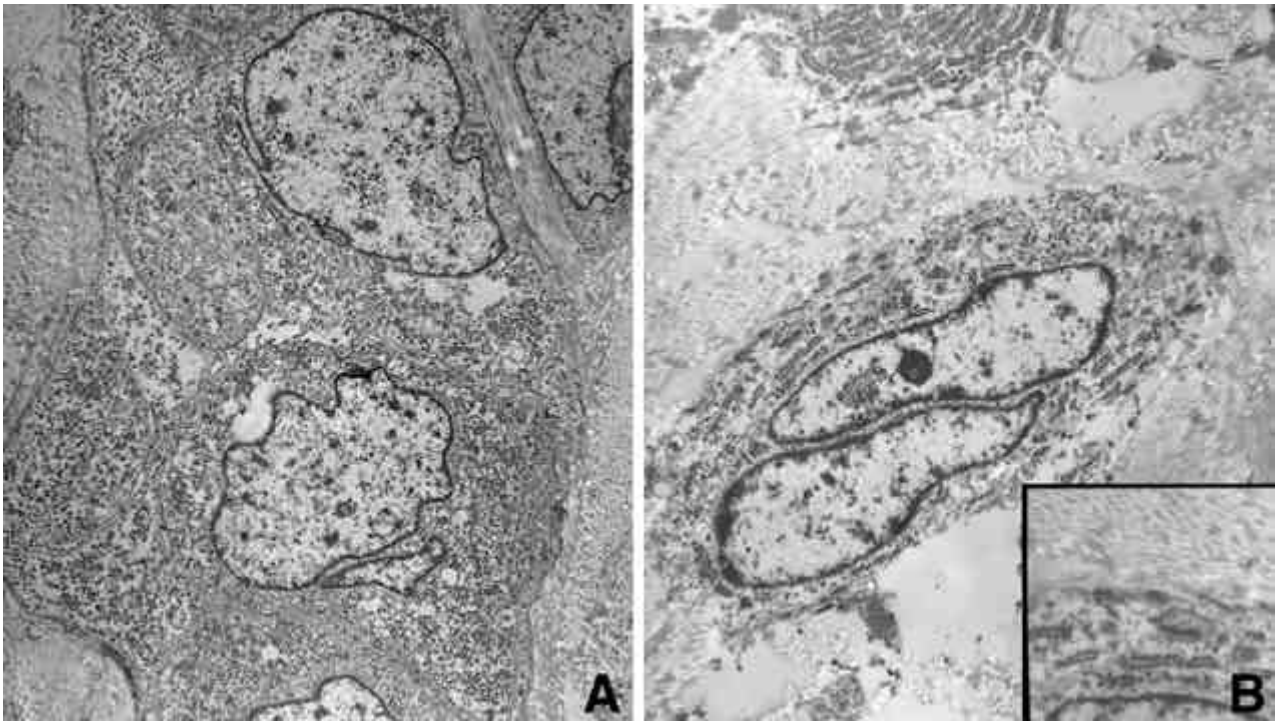

Fig. 4. Ultrastructural study of pulmonary synovial sarcoma. (A) Epithelial cell component within discontinuous basal lamina, showing microvilli-like cytoplasmic processes protruding into luminal glandular spaces, and intercellular junction formation (×3,000). (B) Extracellular space rich in densely packed fibrillar collagen shows scattered spindle cells which contain stacked arrays of rough endoplasmic reticulum and subplasmalemmal dense plaques (Inset), indicating features of myofibroblasts (×4,000).

(Fig. 3). The pseudoglandular pattern of the epithelial component was highlighted by the strong stain of cytokeratin and EMA in the cytoplasm of the tumor cells. The surrounding fibroblast-like spindle cells or fibrous stromal area stained positively for vimentin, but negatively for cytokeratin and EMA. The staining results for S100, desmin, alpha-smooth muscle actin, factor VIII-related antigen and CEA were negative (8, 9).

Ultrastructural study showed that sheets and cords of epithelial cells were enclosed within continuous or discontinuous basal lamina, with interdigitation of cell membranes; they were joined by desmosome-like junctions. Some of the epithelial cell aggregates had small glandular lumina into which microvilli protruded (Fig. 4A). The glandular lumina contained amorphous material, but no intracellular mucin was seen. The abundant cytoplasm contained mitochondria and rough endoplasmic reticulum, and scattered intermediate filaments. Extracellular space was rich in densely packed fibrillar collagen with which intimately arranged were spindle cells containing stacked arrays of rough endoplasmic reticulum and subplasmalemmal dense plaques, indicating features of myofibroblasts (Fig. 4B). The ultrastructural features of the epithelial component considered to be of diagnostic value were microvilli-like cytoplasmic processes protruding into the luminal spaces, and intercellular junction formation. The tumor in which these features were found was regarded as showing good epithelial differentiation (1, 10).

DISCUSSION

Synovial sarcomas are morphologically well defined sarcomas which are commonly found in soft tissue (5). Histologically, these tumors have been divided into three subtypes: 1) biphasic, 2) monophasic fibrous, and 3) monophasic epithelial type. Among these subtypes, monophasic epithelial type rarely occurs and can be recognized by the predominance of epithelial differentiation and minute foci of spindle cell differentiation (3). Although at least 90% of synovial sarcomas occur in periarticular soft tissue, several unusual anatomic locations have been documented in the literature for their occurrence. The locations include the neck (11), soft palate (12), intravascular space (13), abdominal wall (2), and mediastinum (14). Recent descriptions of other cases arising in the lung and pleura establish the thoracic cavity as another possible area of origin (5, 6, 7).

Despite its unusual location, the case we have presented herein had the light microscopic, immunohistochemical, and ultrastructural features that are similar to their counterparts in soft tissue. The clinical, radiological, and surgical findings of our case showed no evidence of primary extrapulmonary involvement, supporting the claim that it was a primary pulmonary neoplasm. We classified the tumor as a primary biphasic type of synovial sarcoma. To our knowledge, this is an useful addition to the small number of published reports on a primary synovial sarcoma of biphasic type (15, 16, 17).

The histogenesis of "primary pulmonary" synovial sarcoma is unknown as in the case of soft tissue synovial sarcoma (5). Potential sources of synovial sarcoma are the so-called arthrogenous or primitive mesenchyme (7). The predilection of synovial sarcomas for the vicinity of large joints and the microscopic resemblance between tumor tissue and normal and hyperplastic synovium favor origin from the so-called arthrogenous mesenchyme. However, the presence of synovial sarcomas in deep-seated locations with no connections to synovial tissue such as upper aerodigestive tract and abdominal wall, and the difference between normal synovium and synovial sarcoma on histochemical and ultrastructural grounds favor their origin from primitive mesenchyme (1). Recently reported cases of synovial sarcomas in the lung or pleura reflect the ubiquitous occurrence of synovial sarcoma (5, 6, 7). Gaertner et al. (7) described pleural synovial sarcomas and suggested that the origin of pleural synovial sarcomas might lie in the submesothelial mesenchyme.

The histologic differential diagnosis of our case includes a wide variety of primary and metastatic neoplasms of 1) pseudobiphasic pattern showing an epithelial tumor component with an intervening reactive spindle cell stromal component, such as intrapulmonary thymoma, and 2) true biphasic pattern, such as malignant mesothelioma, pulmonary blastoma, carcinosarcoma and malignant glandular schwannoma. Intrapulmonary thymoma consists of epithelial lobules of tumor tissue separated by fibrous bands of stroma and scattered small lymphocytes. The lobules are composed of epithelial cells with uniform nuclei, pale or clear cytoplasm. Perivascular spaces are present. The tumor nuclei are vesicular with small nucleoli. Scattered lymphocytes are present particularly towards the periphery of the tumor where distinct remnants of thymic tissue are found. Ultrastructural study shows characteristics of thymic epithelium (cells with interdigitating cell processes, numerous desmosomes, and tonofilament bundles). Because of their lobular architectural pattern with hyalinized septa, perivascular spaces, cysts and 'benign' nuclei, it is difficult to differentiate between intrapulmonary thymomas and synovial sarcomas. Immunohistochemical and ultrastructural studies may be useful (18, 19, 20).

Malignant mesothelioma represents another entity to be discriminated from synovial sarcoma. This distinction is especially important because their prognoses are dif-

ferent. In contrast to malignant mesotheliomas, the secretions seen in synovial sarcomas stain with mucicarmine and PAS, and resist hyaluronidase or diastase digestion, respectively. In about 5% of mesotheliomas, the secretions may show mucicarmine and PAS staining, but these stainings will be eliminated with digestion. Ultrastructural studies can be useful in distinguishing between these entities. Malignant mesotheliomas show long, thin, often branched microvilli, intracytoplasmic glycogen, and abundant intermediate filaments (7). Pulmonary blastoma is a biphasic tumor composed of malignant glands and malignant mesenchyme that are primitive or embryonal in appearance. The epithelial component of blastomas is distinctive in its endometrioid gland-like appearance (7). Malignant glandular schwannoma is a very rare tumor, often associated histologically with rhabdomyoblastic elements and clinically neurofibromatosis, and it has characteristic intestinal-type epithelial elements (7).

Carcinosarcoma of the lung is another important consideration in differential diagnosis. By definition, the tumors are biphasic and composed of an intimate admixture of carcinomatous and sarcomatous elements. Unlike synovial sarcoma, carcinosarcoma of the lung generally tends to demonstrate a more pronounced cytological atypia and infiltrative growth pattern with high mitotic rate, marked nuclear pleomorphism, and frequent areas of transition with either adenocarcinoma or squamous cell carcinoma. The tumor also reveals aggressive behavior with infiltrative borders and early metastatic spread (5).

In Zeren et al's report (5) which described the results of follow-up ranging from 2 to 20 years in 18 cases of pulmonary monophasic fibrous synovial sarcoma, six patients died of their tumors, whereas four patients died of unrelated causes without evidence of recurrence or metastases. Four patients were alive with disease (recurrence and/or metastases) from 1 to 7 years after diagnosis and four patients were alive and well without evidence of disease after surgery, 2 to 20 years after diagnosis of their lung tumor. The behavior of synovial sarcomas in intrapulmonary location appears to be similar to that described for their counterparts in soft tissue (11, 21).

As with its soft tissue counterparts, surgical resection appears to be the common treatment for these tumors. However, the use of chemotherapy or radiation therapy for the treatment would have to be considered in particular cases (i.e., in patients with advanced disease) (5).

In conclusion, this case, histologically, immunohistochemically, and ultrastructurally, resembles a biphasic type of synovial sarcoma of the soft tissue and is the counterpart of biphasic synovial sarcoma of the soft tissue and thus should be distinguished from other primary and metastatic pulmonary neoplasms.

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