Mediastinal Epithelioid Solitary Fibrous Tumor

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We describe the case of a 74-year-old man with a mediastinal tumor composed predominantly of epithelioid cells exhibiting histopathologic and immunohistochemical features intermediate between those of a solitary fibrous tumor and those of a cellular adenomatoid tumor. We discuss the differential diagnosis and possible histogenesis of this unusual neoplasm, and we propose the term epithelioid solitary fibrous tumor for this entity.

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Klemperer and Rabin first described neoplasms that are currently classified as solitary fibrous tumors (SFTs) as a localized form of mesothelioma in 1931 and proposed a derivation from submesothelial fibroblasts. These neoplasms frequently develop in the pleura and other serosal surfaces but can also arise from a variety of sites including the lung, mediastinum, nasal cavity, meninges, tongue, liver, kidney, abdominal wall, breast, inguinal region, retroperitoneum, and others. Solitary fibrous tumors are usually well-circumscribed neoplasms characterized histopathologically by the presence of spindle-shaped or oval cells that have bland nuclear features and that are scattered haphazardly among a collagenized stroma (so-called patternless pattern). Histopathologic features that are frequently present but not specific for SFT include dense collagenization, variable cellularity with hypocellular and hypercellular areas, myxoid changes, prominent vascularity that resembles the features of hemangiopericytomas, and others. The cells of SFT usually exhibit strong intracytoplasmic immunoreactivity for CD34, vimentin, and Bcl-2, and do not react with antibodies to cytokeratin. To our knowledge, the presence of epithelioid cells has not been described as a prominent feature of benign SFT. Okike et al described malignant SFT with tubulopapillary and bimorphic patterns, before the advent of immunostains for CD34 and calretinin. Their report illustrates a lesion with a bimorphic growth pattern that appears to be considerably more cellular and atypical than the tumor of our patient.

The peritoneum and other mesothelial surfaces can be the site of origin of adenomatoid tumors, benign lesions composed of bland mesothelial cells organized in tubules and cords. Adenomatoid neoplasms are usually present on the mesothelial surfaces of the testis or the female genital tract, adjacent to the fallopian tubes, the broad ligament, and the serosal surface of the uterus. Rare examples of adenomatoid tumors of the pleura and the heart have been described. We report the clinical, pathologic, and immunohistochemical findings of an unusual mediastinal neoplasm with a prominent epithelioid cell component and histopathologic and immunophenotypic features intermediate between those of SFT and those of adenomatoid tumor. We also discuss this lesion’s probable histogenesis.

REPORT OF A CASE

The patient was a 74-year-old black man with multiple medical problems, including hypertension, diabetes mellitus, and carcinoma of the prostate that had been treated with leuprolide and radiation therapy. A routine chest radiograph showed an ill-defined left intrathoracic density. The patient remained asymptomatic. He underwent follow-up chest radiographs and computed tomography scans 6 months later. The repeated chest radiographs revealed an area of superior mediastinal widening on the left that appeared on the computed tomography scan as a round, sharply circumscribed mediastinal mass located anterior to the spine at the apex of the chest. A comprehensive clinical workup revealed no evidence of residual prostate cancer. The patient underwent resection of the mediastinal mass by a left video-assisted thoracoscopy. At surgery, the tumor was well encapsulated and located in the posterior aspect of the superior mediastinum, adjacent to the base of the subclavian artery. No tumor attachment to the pleura or to the intrathoracic nerves was identified.

MATERIALS AND METHODS

Sections 4 μm in thickness were cut from paraffin blocks and stained with hematoxylin-eosin. Additional sections were cut from selected paraffin blocks for immunohistochemical studies with a standard Dako Envision peroxidase method (Dako, Carpinteria, Calif) and the primary antibodies and dilutions listed in the Table.

PATHOLOGIC FINDINGS

The tumor consisted of a 22-g well-circumscribed, firm, tan-pink, partially lobulated mass with a homogenous surface. It measured 4.7 × 3.8 × 2.6 cm. No hemorrhage or necrosis was present. Microscopically, the lesion was partially encapsulated and was composed of epithelioid cells and scanty spindle cells dispersed in a collagenized stroma. The majority of the neoplastic cells had epithelioid features with central round to oval nuclei and abundant, slightly eosinophilic cytoplasm (Figure 1). The epithelioid cells were arranged in solid sheets and cords, without overt tubular formation (Figure 2). Some of the epithelioid cells had central intranuclear pseudoinclusions and/or small nucleoli, but the cells exhibited no significant nucle-
The epithelioid cells and the spindle cells had a similar immunophenotype (Table). They exhibited strong cytoplasmic immunoreactivity for cytokeratin AE1/AE3, vimentin, calretinin (Figure 5), Bcl-2, and CD34 (Figure 6). The tumor cells were not immunoreactive for epithelial membrane antigen (EMA), cytokeratin 5/6, S100 protein, factor VIII, CD31, collagen IV, HMB-45, CD117, chromogranin, and synaptophysin (Table).

**COMMENT**

Witkin and Rosai described 14 cases of SFT composed of spindle cells that had variable immunoreactivity for vimentin but not for keratin. Unlike the neoplasm in our patient, these lesions did not exhibit epithelioid cell features and lacked ultrastructural evidence of mesothelial or epithelial differentiation. Recent studies have shown that the cells of SFT exhibit cytoplasmic CD34 immunoreactivity but lack reactivity for calretinin. The unusual mediastinal tumor in our patient was composed of epithelioid cells organized in solid sheets, cords, and tubules, admixed with a collagenized stroma.

**IMMUNOHISTOCHEMICAL FINDINGS**

The epithelioid cells of adenomatoid tumors usually exhibit cytoplasmic immunoreactivity for keratin, EMA, and calretinin in but lack CD34 and Bcl-2 immunoreactivity. Our neoplasm shares with cellular adenomatoid tumors certain histopathologic features, such as the presence of epithelioid cells arranged in cords, but it lacks the tubular formation usually seen in these neoplasms, and it has a spindle cell component that is usually not seen in these neoplasms. The neoplastic cells exhibited immunoreactivity for keratin and mesothelial markers as well as for CD34 and Bcl-2; EMA immunoreactivity, usually observed in adenomatoid tumors, was absent. We propose the term epithelioid solitary fibrous tumor for this unusual epithelioid neoplasm, although it would be difficult to argue against other possible nomenclatures such as SFT-like adenomatoid tumor or cellular adenomatoid tumor with CD34- and Bcl-2-immunoreactive cells. We excluded the diagnosis of malignant mesothelioma because of the presence of a well-circumscribed extrapleural mass composed of epithelioid cells that lacked cytologic atypia, necrosis, and increased mitotic activity.

The pathologic features of this unusual tumor raise interesting questions regarding its possible histogenesis. Indeed, the cell of origin of SFT in extracelomic locations remains elusive, and there has been some controversy regarding whether adenomatoid tumors are of mesothelial or mesenchymal derivation. Mai and colleagues described 20 adenomatoid tumors of the genital tract that were characterized by glandlike structures with a pseudoinfiltrative pattern, and they identified reactive subserosal stromal cells in some of these lesions. They postulated that adenomatoid tumors arise from pluripotent mesenchymal cells that differentiate toward submesothelial stromal cells and eventually to mesothelial cells. In contrast, Delahunt and colleagues favor an exclusive mesothelial origin of adenomatoid tumors, based on a study of paratesticular lesions with immunohistochemistry. All of their 12 adenomatoid tumors exhibited immunoreactivity for cytokeratin AE1/AE3, EMA, and vimentin, and had no immunoreactivity for factor VIII and CD34. The histologic and immunohistochemical features of our neoplasm probably support a histogenesis from pluripotent mesenchymal cells that can differentiate toward mesothelial and SFT lines of differentiation. The neoplasm had no direct relationship to the pleura and exhibited at least some histopathologic and immunohistochemical features that can be seen in adenomatoid tumors and SFT, a neoplasm of mesenchymal origin. Perhaps epithelioid SFT is an unusual manifestation of a spectrum of neoplasms that includes SFT, adenomatoid tumors, and adenomatoid tumors with reactive subserosal stromal cells.

Because this type of neoplasm has not been previously

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**Table: Immunohistochemical Stains and Results**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Results</th>
<th>Dilution</th>
<th>Source*</th>
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<tr>
<td>Cytokeratin AE1/AE3</td>
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<td>Dako</td>
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<tr>
<td>Calretinin</td>
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<td>1:800</td>
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<td>BioGenex</td>
</tr>
</tbody>
</table>

* Antibodies were from Chemicon, Pittsburgh, Pa; Dako Corporation, Carpinteria, Calif; Zymed, San Francisco, Calif; Becton Dickinson, Franklin Lakes, NJ; Biocare, Hsinchu, Taiwan; and BioGenex, San Ramon, Calif.
† EMA indicates epithelial membrane antigen.
Figure 1. The tumor is composed of epithelioid cells with round nuclei and slightly eosinophilic cytoplasm, forming solid sheets and cords. No necrosis is present (hematoxylin-eosin, original magnification ×100).

Figure 2. The epithelioid tumor cells are arranged in cords and lack significant cytologic atypia or increased mitotic activity (hematoxylin-eosin, original magnification ×200).

Figure 3. The tumor has less cellular areas and a small number of spindle-shaped cells admixed with the epithelioid cells. The spindle cells are difficult to distinguish from stromal fibroblasts, but they exhibited CD34 immunoreactivity (hematoxylin-eosin, original magnification ×100).

Figure 4. The spindle-shaped cells and the epithelioid cells lack cytologic atypia (hematoxylin-eosin, original magnification ×200).

Figure 5. The neoplastic cells exhibit cytoplasmic and nuclear calretinin immunoreactivity (immunoperoxidase, original magnification ×200).

Figure 6. The neoplastic cells exhibit membrane and cytoplasmic CD34 immunoreactivity. Cytoplasmic immunoreactivity for Bcl-2 was also present (not shown in this photograph) (immunoperoxidase, original magnification ×200).
described, to our knowledge, it is difficult to determine its biologic potential. The prognosis of individual patients with SFT is difficult to determine with certainty. Malignant SFT usually exhibits infiltrating margins, larger tumor size, variable nuclear atypia, necrosis, and increased mitotic activity. The lack of cytologic atypia, necrosis, and increased mitotic activity in our neoplasm does not favor the diagnoses of malignant SFT or of early malignant mesothelioma, mixed epithelial and sarcomatous type.

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References