

Primary mediastinal synovial sarcoma: Clinicopathologic evaluation of 5 cases

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Abstract

Primary mediastinal synovial sarcoma is rare and poses a diagnostic challenge particularly when unusual histologic features are present and $t(x;18)$ is negative. Five cases of primary mediastinal synovial sarcoma were evaluated to define clinicopathologic features including unusual histology that may result in misdiagnosis. Clinically, compared with pulmonary synovial sarcomas, mediastinal synovial sarcomas occurred in younger patients and showed male predominance. Histologically, tumors showed many identical characteristics of typical pulmonary and soft tissue synovial sarcomas with dense cellularity, interlacing fascicles, hyalinized stroma, and mast cell influx with focal hemangiopericytoma-like vasculature and calcification. In contrast, they showed no myxoid change, more infiltrative growth, and focal unusual histology not usually seen with soft tissue synovial sarcoma but typical of other neoplasms. These included Verocay bodies [1], papillary structures with fibrovascular cores [1], and adenomatoid change [1]. Immunohistochemistry demonstrated typical expression of focal cytokeratins, CD99, Bcl-2, and smooth muscle actin. Three of 5 tumors were positive for $t(x;18)$, with one having no tissue remaining for testing. In conclusion, this small case series of mediastinal synovial sarcomas occurred in younger patients with male predominance compared with pulmonary synovial sarcoma, and had more infiltrative growth, less myxoid change and focal histology typical of other neoplasms. Awareness of focal unusual histology can prevent misdiagnosis particularly in $t(x;18)$ negative tumors.

Introduction

Primary mediastinal synovial sarcoma is an aggressive tumor sharing common histologic features with pulmonary and soft tissue synovial sarcoma [1-5]. Molecular testing for the pathognomonic $t(x;18)$ chromosomal translocation has enabled diagnostic confirmation in the vast majority of cases [6]. In $t(x;18)$ negative cases, diagnosis must rely on histologic and immunophenotypic features. The differential diagnosis of primary mediastinal synovial sarcoma is particularly challenging when histologic features unusual to synovial sarcoma, but common to other neoplasms are focally present. This challenge is compounded with negative $t(x;18)$ findings. We evaluated 5 cases of primary mediastinal synovial sarcoma to compare clinicopathologic findings with those reported for pulmonary and soft tissue synovial sarcoma and bring awareness of unusual histology in this entity.

Materials and methods

Five cases of known mediastinal synovial sarcoma from 1981 to 2006 were retrieved from tissue archives. Clinical data were obtained from patient records. Hematoxylin and eosin stained sections were available for each case. Tumors were subtyped as monophasic or biphasic according to World Health Organization criteria [7]. Grading by tumor cell differentiation, mitotic rate, and necrosis was performed following the French Federation of Cancer Centers (FNCLCC) scheme. Unusual histologic features were noted and immunohistochemistry was performed on paraffin embedded sections using commercially available antibodies (Table 1). Molecular analysis was performed on RNA extracted from paraffin embedded samples. *SYT/SSX* RNA fusion transcripts resulting from $t(x;18)$ (p11;q11) translocation were detected using real-time reverse transcriptase-polymerase chain reaction [8]. Subtyping of *SYT/SSX 1* and *2* fusion transcripts was performed using methods previously described [8].

Results

Clinical findings

Pertinent clinical features are presented in Table 2. The study group included 4 males and one female ranging from 10 to 71 years of age (mean, 36). The most common presenting symptoms were chest pain and shortness of breath. Surgical procedures of primary tumour included excision (n=2), and open biopsy (n=3). Local recurrence, metastases, and survival data were similar to pulmonary synovial sarcoma [9]. Radiology was not available in any of the cases.

Histologic findings

Histologic findings are presented in Table 3. Tumor size was not available, but tumors were described as soft, tan-gray masses with foci of necrosis. Histologically, tumors were monophasic (n=4) or biphasic (n=1). Tumors were grade 2 (n=5) with no grade 3 (poorly differentiated) tumors according to French Federation of Cancer Centers (FNCLCC) grading. Tumor cell morphology included spindle cells (n=3) or a combination of spindle and round/epithelioid cells (n=2). Mitoses ranged from 1 to 15 per 10 high power fields (mean, 7). Necrosis was present in 4 tumors (<50%).

Histologic features typical of pulmonary and soft tissue synovial sarcoma were seen and included dense cellularity, interlacing fascicles, and hyalinized or eosinophilic stroma. Mast cell influx (n=5), hemangiopericytoma-like vasculature (n=3), focal myxoid change

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(n=1) were also seen. Unusual histologic features were focal, noted in at least 1 but no more than 4 slides per case, varying from 4 to 90 high power fields and included Verocay body-like areas (n=1), well-formed papillary structures (n=1), and adenomatoid areas (n=1) (Figure 1).

Immunohistochemical and molecular findings

Immunohistochemical findings are presented in Table 4 and molecular findings in Table 5. Immunohistochemical studies showed focal positive membranous or cytoplasmic staining for epithelial markers including pancytokeratin (n=5), cytokeratin 7 (n=3), epithelial membrane antigen (n=1), and cytokeratin 5/6 (n=1). No tumours showed immunoreactivity for more than two cytokeratin markers. Diffuse immunoreactivity was seen with CD99 in three cases and Bcl-2 in two cases. Focal immunoreactivity was present with CD56 (n=2) and smooth muscle actin (n=2).

Table 1. Antibodies

	Clone	Titer	Source
Pancytokeratin	AE1/AE3	1:200	Roche, Mannheim, Germany
Cytokeratin-7	OV TL12/30	1:160	Dako, Carpinteria, CA
Epithelial membrane antigen	E29	1:100	Dako, Carpinteria, CA
Cytokeratin 5/6	D5/16B4	1:20	Dako, Carpinteria, CA
Calretinin	CAL 3F5	1:50	Zymed, San Francisco, CA
Bcl-2	124	1:20	Dako, Carpinteria, CA
CD56	123C3	1:100	Caltag, Burlingame, CA
CD99	12E7	1:80	Dako, Carpinteria, CA
S-100	Polyclonal	1:800	Dako, Carpinteria, CA
Smooth Muscle Actin	1A4	1:800	Sigma, St. Louis, MO

Table 2. Clinical findings

Mean age, years	36
Gender	
Male	4
Female	1
Common symptoms	
Chest pain	2
Dyspnea	1
Surgical Procedure	
Excision of mass	2
Open biopsy	3

Table 3 Histologic findings

Subtypes	
Monophasic	4
Biphasic	1
Infiltrative growth	3
Unusual (common to other neoplasms, focally present)	
Verocay body-like areas	1
Papillary structures	1
Adenomatoid areas	1

Table 4. Immunohistochemical findings

Pancytokeratin	5
Epithelial Membrane Antigen	1
Cytokeratin -7	3
Calretinin	0
Cytokeratin 5/6	2
CD99	3
Bcl-2	2
CD56	2
S-100	0
Smooth Muscle Actin	2

Table 5. Molecular findings

Total t(x;18) positive	4
Total SYT/SSX1	1
Total SYT/SSX2	2
Total t(x;18) positive, SSX unknown	1
Total t(x;18) negative	1

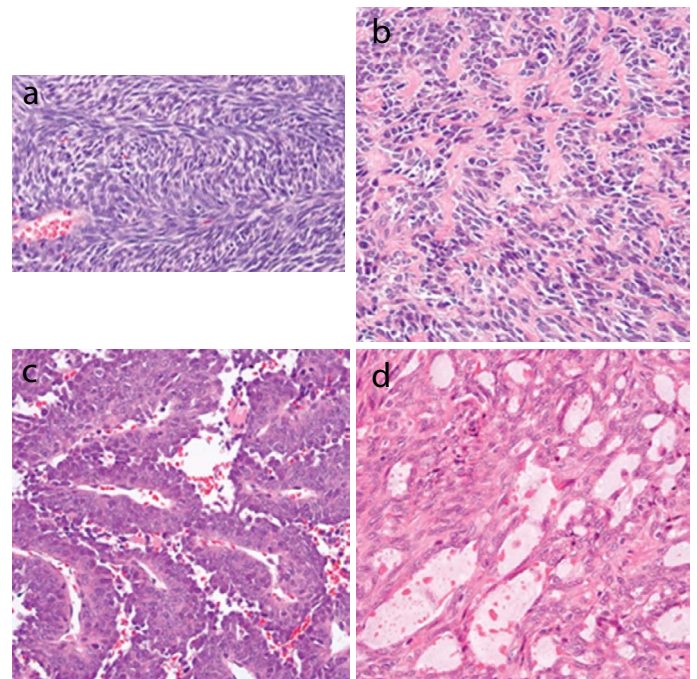


Figure 1. (a) Typical histologic features of mediastinal synovial sarcoma, characteristically composed of densely cellular interlacing fascicles. (b) Unusual features that may lead to misdiagnosis include Verocay body-like areas. (c) Papillary formations (d) Adenomatoid appearance

The chromosomal translocation t(x;18) was present in three cases studied in which two were fusion type SYT/SSX2 and one fusion type SYT/SSX1. One case was reported as t(x;18) positive without information on the SSX fusion type.

Discussion

Synovial sarcoma, although rare, is a primary mediastinal neoplasm sharing distinctive histology of synovial sarcomas of lung, pleura, and soft tissue. The presence of focal unusual histology characteristic of more common epithelial and mesenchymal tumors may lead to misdiagnosis. This is particularly problematic in small biopsies or in primary mediastinal synovial sarcomas that are negative for the pathognomonic t(x;18) translocation. We present five primary mediastinal synovial sarcoma cases for clinicopathologic characterization and comparison with pulmonary and soft tissue synovial sarcomas, including focal unusual histologic features.

Clinically, compared with pulmonary synovial sarcomas, this small series of mediastinal synovial sarcomas occurred in younger patients and showed male predominance. Histologically, tumors showed many identical characteristics of typical pulmonary and soft tissue synovial sarcomas with dense cellularity, interlacing fascicles, hyalinized stroma, and mast cell influx with focal hemangiopericytoma-like vasculature and calcification. In contrast, they showed less myxoid change, more infiltrative growth, and focal unusual histology not usually seen with soft tissue synovial sarcoma but typical of other neoplasms. The

focal unusual histology in primary mediastinal synovial sarcoma can erroneously suggest more common primary and metastatic pulmonary neoplasms. Verocay body-like areas can occur which are similar to those seen in malignant peripheral nerve sheath tumor [10]. The stromal background of malignant peripheral nerve sheath tumor, however, typically lacks hyalinization and appears more basophilic. Primary mediastinal synovial sarcoma is often immunoreactive for cytokeratin 7, a finding not generally seen in malignant peripheral nerve sheath tumor, [11, 12] and negative with S-100. Clinically, malignant peripheral nerve sheath tumors arise from nerve or neurofibroma and are associated with neurofibromatosis type I in approximately two-thirds of cases [13].

Focal well-formed papillary or adenomatoid areas in primary mediastinal synovial sarcoma may be misinterpreted as carcinoma or malignant mesothelioma. In particular, pleomorphic carcinoma can present with spindle cell and adenocarcinoma components. Carcinomas are more cytologically atypical with greater pleomorphism than primary mediastinal synovial sarcoma. Carcinomas may have areas of squamous differentiation or contain tumor giant cells, features not observed in primary mediastinal synovial sarcoma. While cytokeratins are focally expressed in primary mediastinal synovial sarcoma, diffuse positivity for epithelial markers is not characteristic. However, it should be kept in mind that spindle cell carcinomas may also be only focally positive for cytokeratins. Carcinomas share an infiltrative growth pattern with this series of mediastinal synovial sarcomas, but in contrast show regional lymph node involvement, and/or widespread metastases. While mediastinal synovial sarcomas may express CK5/6, calretinin was negative in our cases.

We present five primary mediastinal synovial sarcoma cases occurring in younger patients with male predominance compared with pulmonary synovial sarcoma, and more infiltrative growth, less myxoid change and focal unusual histologic features that may erroneously suggest more common primary and metastatic pulmonary or mediastinal neoplasms. This unusual histology may be particularly challenging in small biopsies or when t(x;18) is negative. Awareness of typical histology of mediastinal synovial sarcoma, their potential misleading unusual morphologic features, and prudent use of immunohistochemistry will prevent misdiagnosis, even in t(x;18)-negative cases.

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