Primary Pleural Synovial Sarcoma: Clinicopathologic Evaluation of 19 Cases with Focal Unusual Histology and Diagnostic Pearls

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Abstract

Primary pleural synovial sarcoma is rare and poses a diagnostic challenge particularly when unusual histologic features are present. Nineteen cases of primary pleural synovial sarcoma were evaluated to define clinicopathologic features including unusual histology that may result in misdiagnosis. Clinically, compared with pulmonary synovial sarcomas, pleural synovial sarcomas were similar in age and gender distribution. Radiology images were available in three cases. Histologically, tumors showed many identical characteristics of typical pulmonary and soft tissue synovial sarcomas with dense cellularity, interlacing fascicles, hyalinized stroma, mast cell influx, focal hemangiopericytoma-like vasculature, focal myxoid change and entrapped pulmonary epithelium. In contrast to soft tissue synovial sarcomas, they showed less calcification and focal unusual histology typical of other neoplasms. These included neuroendocrine-like rossettes (n = 4), Verocay bodies (n = 2), papillary structures with fibrovascular cores (n = 1), adenomatoid change (n = 1), and rhabdoid morphology (n = 1). Immunohistochemistry demonstrated expected expression of focal cytokeratins, Bcl-2, and focally, CD99 and smooth muscle actin. Where tissue was available for testing, 15 cases were positive for t(x;18), and one was negative. In conclusion, this series of pleural synovial sarcomas occurred with similar clinical, radiologic and pathologic findings compared with pulmonary synovial sarcoma, and, compared with soft tissue synovial sarcomas, had less calcification and showed focal histology typical of other neoplasms. Awareness of focal unusual histology can prevent misdiagnosis particularly in the event of t(x;18) negative tumors.

Keywords: Pleura; Synovial Sarcoma; Histology; Molecular Translocation; Lung Sarcomas

Introduction

Primary pleural synovial sarcoma is an aggressive tumor sharing common clinical and 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 pathologic differential diagnosis of primary pleural 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 potential negative t(x;18) findings. We evaluated 19 cases of primary pleural 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.

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Materials and Methods

Nineteen cases of known primary pleural 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].

	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 1: *Antibodies.*

Results

Clinical findings

Pertinent clinical features are presented in table 2. The study group included 11 males and 8 females ranging from 17 to 64 years of age (mean, 41). The most common presenting symptoms were chest pain and shortness of breath. Surgical procedures of primary tumour included excision (n = 13), and open biopsy (n = 6). Local recurrence, metastases, and survival data were not different from pulmonary synovial sarcoma [9].

Mean age, years	41
Gender	
Male	11
Female	8
Common symptoms	
Chest pain	8
Dyspnea	6
Cough	3
Pleural effusion	2
Surgical Procedure	
Excision of mass	13
Open biopsy	6

Table 2: *Clinical findings.*

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Radiology was available in three cases. On computed tomography, these tumors showed homogeneous or heterogeneous enhancement without evidence of bone destruction or chest wall invasion. On magnetic resonance, T1-weighted and T2-weighted images showed a well-circumscribed mass without evidence of spiculation or satellite nodules. T2-weighted images included nodular areas of intermediate signal intensity combined with discreet or cystic areas of high signal intensity most consistent with necrosis or hemorrhage (Figure 1).
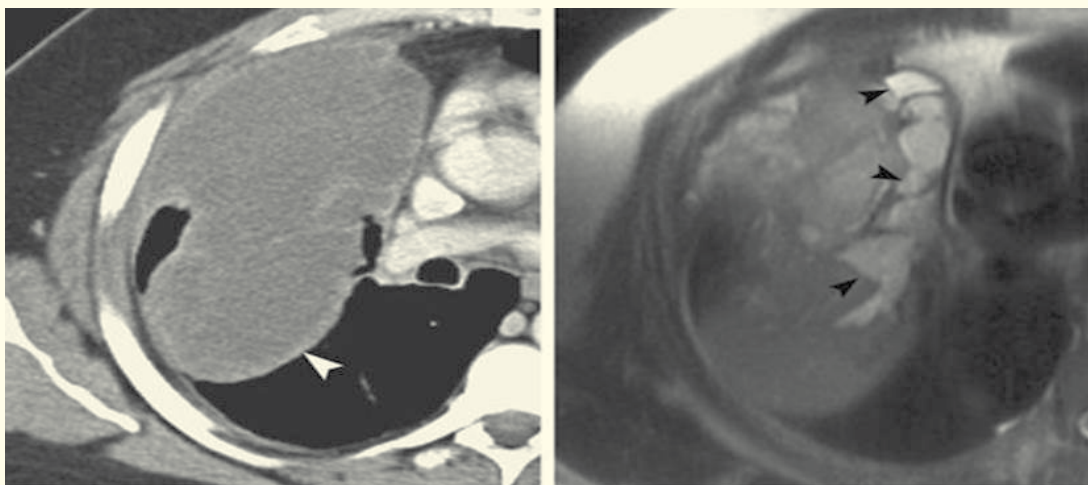

Figure 1: Contrast-enhanced CT scan demonstrates a large low attenuation mass with rim enhancement (arrowhead) and internal septations. Axial T2-weighted (2110/57.6) magnetic resonance image shows greater contrast among internal components, with well-demarcated spaces (arrowheads) which suggest cysts.

Gross and Histologic findings

Histologic findings are presented in table 3 and shown in figures 2 and 3. Tumor size averaged 9 cm (range = 2-16 cm) and were grossly described as soft, tan-gray masses with foci of necrosis. Histologically, tumors were monophasic (n = 16) or biphasic (n = 3). Tumors were grade 2 (n = 15) and grade 3 (poorly differentiated, n = 4) according to French Federation of Cancer Centers (FNCLCC) grading. Tumor cell morphology included spindle cells (n = 13), a combination of spindle and round/epithelioid cells (n = 5), or round/epithelioid cells only (n = 1). Mitoses ranged from 1 to 95 per 10 high power fields (mean, 17). Necrosis was present in less than 50% of the lesion in 14 tumors, and extensive (> 50%) in one case.

Subtypes	
Monophasic	16
Biphasic	3
Typical histology	
Dense interlacing fascicles	19
Eosinophilic stroma	19
Mast cell influx	19
HPC-like vasculature	16
Myxoid change	12
Unusual histology (common to other neoplasms, focally present)	
Neuroendocrine-like rosettes	4
Verocay body-like areas	3
Papillary structures	1
Adenomatoid areas	1
Rhabdoid morphology	1

Table 3: Histologic findings.

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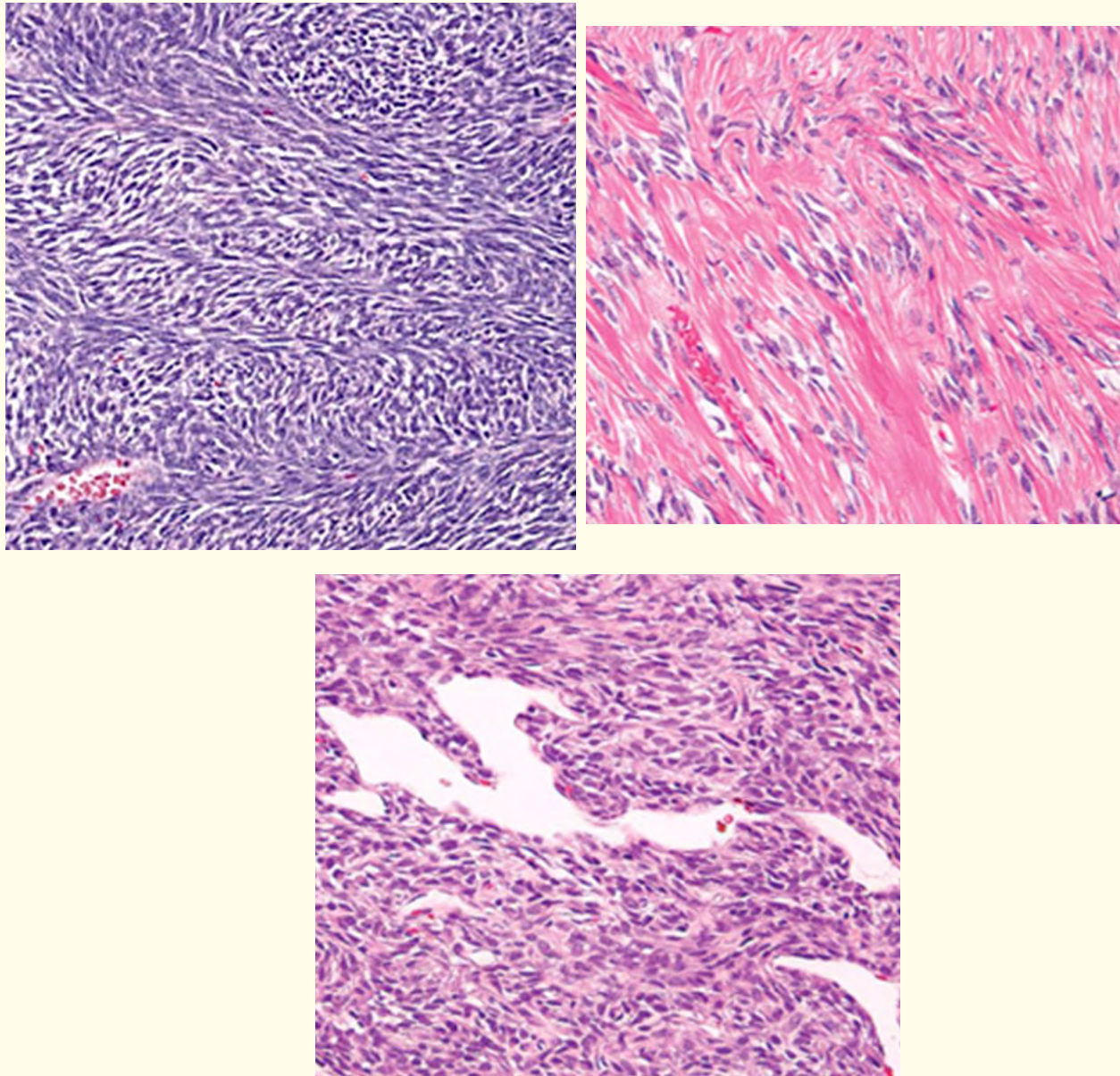
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Figure 2: *Typical histologic features of pleural synovial sarcoma, characteristically composed of densely cellular interlacing fascicles (a), eosinophilic stroma (b), and hemangiopericytoma-like vasculature (c).*
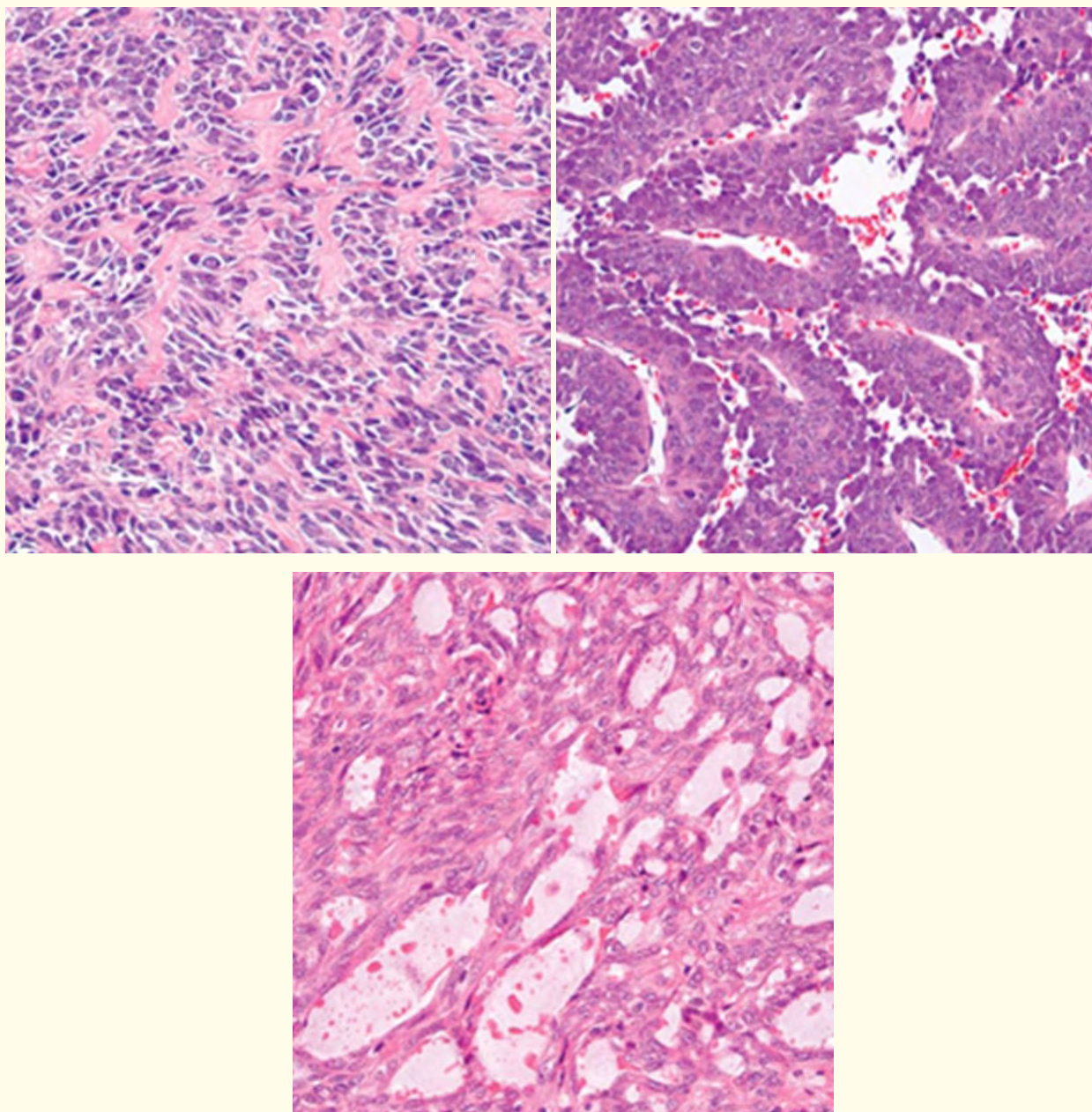
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Figure 3: *Unusual histology that may lead to misdiagnosis include Verocay body-like areas (a), papillary formations (b), and adenomatoid appearance (c).*

Histologic features typical of pulmonary and soft tissue synovial sarcoma were seen and included dense cellularity (n = 19), interlacing fascicles (n = 19), and hyalinized or eosinophilic stroma (n = 19). Mast cell influx (n = 19), hemangiopericytoma-like vasculature (n = 16), and focal myxoid change (n = 12) were also seen (Figure 2). 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 neuroendocrine-like rosettes (n = 4), Verocay body-like areas (n = 3), well-formed papillary structures (n = 1), adenomatoid areas (n = 1), and rhabdoid morphology (n = 1) (Figure 3).

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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 (12/18), epithelial membrane antigen (13/18), cytokeratin 7 (8/15), and cytokeratin 5/6 (1/2). Three tumours showed immunoreactivity with three cytokeratin markers. Diffuse immunoreactivity was seen with Bcl-2 in 10/10 cases, and CD99 in five of six cases. Focal immunoreactivity was present with CD56 (5/5), S-100 (5/19) and smooth muscle actin (2/9).

Antibody	+/tested	%
Pancytokeratin	12/18	67
Epithelial Membrane Antigen	13/18	72
Cytokeratin -7	8/15	53
Calretinin	5/6	83
Cytokeratin 5/6	1/2	50
CD99	5/6	83
Bcl-2	10/10	100
CD56	5/5	100
S-100	5/19	26
Smooth Muscle Actin	2/9	22

***Table 4:** Immunohistochemical findings.*

Total t(x;18) positive	15
Total SYT/SSX1	9
Total SYT/SSX2	4
Total t(x;18) positive, SSX unknown	2
Total t(x;18) negative	1
No tissue available	3

***Table 5:** Molecular findings.*

The chromosomal translocation t(x;18) was present in 15 cases in which nine were fusion type SYT/SSX1 and four fusion type SYT/SSX2. Two cases were reported as t(x;18) positive without information on the SSX fusion type. One case was negative.

Discussion and Conclusion

Synovial sarcoma, although rare, is a primary pleural neoplasm sharing distinctive clinical and pathologic features with synovial sarcomas of lung 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 pleural synovial sarcomas that are negative for the pathognomonic t(x;18) translocation. We present 19 primary pleural synovial sarcoma cases for clinicopathologic characterization and comparison with pulmonary and soft tissue synovial sarcomas, including focal unusual histology.

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Clinically, compared with pulmonary synovial sarcomas, this series of pleural synovial sarcomas occurred with similar age and gender distribution. Histologically, tumors showed many identical characteristics of typical pulmonary and soft tissue synovial sarcomas with dense cellularity, interlacing fascicles, hyalinized stroma, mast cell influx, focal hemangiopericytoma-like vasculature, and focal myxoid change. In contrast, they showed less calcification than soft tissue synovial sarcomas, and focal unusual histology more typical of other neoplasms. The focal unusual histology in primary pleural synovial sarcoma can erroneously suggest more common primary and metastatic pulmonary neoplasms. Pleural synovial sarcoma with focal vague rosette formation can lead to misdiagnosis as primitive neuroectodermal tumor [6,10]. Pleural synovial sarcoma may also be reminiscent of primitive neuroectodermal tumor when the former is poorly differentiated and displays round cell morphology. Unlike pleural synovial sarcoma, primitive neuroectodermal tumor typically has distinct cell borders, clear cytoplasm, scant stroma, and lacks hemangiopericytoma-like vasculature. Both tumors can express CD99, CD56, and cytokeratins [10,12,13] although expression of cytokeratin 7 makes a diagnosis of primitive neuroectodermal tumor less likely [12]. Chromosomal translocation t(11;22) is present in 85% of primitive neuroectodermal tumors [6].

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 pleural synovial sarcoma is often immunoreactive for cytokeratin 7 and negative with S-100, findings not generally seen in malignant peripheral nerve sheath tumor [11,12]. 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 pleural 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 pleural synovial sarcoma. Carcinomas may have areas of squamous differentiation or contain tumor giant cells, features not observed in pleural synovial sarcoma. While cytokeratins are focally expressed in pleural 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 often show regional lymph node involvement, and/or widespread metastases not seen with pleural synovial sarcomas. While pleural synovial sarcomas may express CK5/6 and calretinin, mesotheliomas are usually more diffusely positive for cytokeratin and negative with t(x;18).

We present 19 primary pleural synovial sarcoma cases occurring in similar age and gender distribution compared with pulmonary synovial sarcoma, and less calcification and focal unusual histologic features not seen in soft tissue synovial sarcomas that may erroneously suggest more common primary and metastatic pleuropulmonary, mediastinal, or other primary-site neoplasms. This unusual histology may be particularly challenging in small biopsies or when t(x;18) is negative. Awareness of typical histology of pleural synovial sarcoma, their potential misleading unusual morphologic features, and prudent use of immunohistochemistry will prevent misdiagnosis, even in t(x;18)-negative cases.

Disclosure/Conflict of Interest

The author has no disclosures or conflicts of interest.

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