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Research Article

Paediatric Primary Pulmonary Synovial Sarcoma: Report of Four Cases with Unusual Histology

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Abstract

Primary pulmonary synovial sarcoma is rare and poses a diagnostic challenge particularly when unusual histologic features are present and the pathognomonic translocation t(x;18) is negative or unknown. Four cases of paediatric primary pulmonary synovial sarcoma were evaluated noting unusual histologic features that may result in misdiagnosis. Histologically these tumors showed identical characteristics of typical adult pulmonary synovial sarcomas with dense cellularity, interlacing fascicles, hyalinized stroma, hemangiopericytoma-like vasculature, focal myxoid change, and entrapped benign pulmonary epithelium. They also showed unusual histologic features not usually seen with pulmonary synovial sarcoma but typical of other neoplasms. These included rosettes (2), papillary structures with fibrovascular cores (1), and adenomatoid change (1). Immunohistochemistry demonstrated typical expression of focal cytokeratins, vimentin, CD99, and Bcl-2, with focal immunoreactivity with smooth muscle actin. These tumours were positive with t(x;18) in 2 cases, while 2 had no tissue for testing. In conclusion, paediatric pulmonary synovial sarcoma are very similar to adult cases and awareness of focal unusual histology can prevent misdiagnosis, particularly when t(x;18) is negative or tissue is unavailable for testing.

Keywords: Paediatric; Pulmonary; Pleura; Mediastinum; Synovial Sarcoma

Introduction

Primary pulmonary synovial sarcoma is an aggressive tumor sharing common histologic features with soft tissue synovial sarcoma [1-5], has a mean age of 42 years at diagnosis, and rarely occurs in the paediatric population. Molecular testing for the pathognomonic t(x;18) chromosomal translocation has enabled diagnostic confirmation in over 90% of cases [6]. In t(x;18) negative cases, diagnosis must rely on histologic and immunophenotypic features. The differential diagnosis of primary pulmonary synovial sarcoma is particularly challenging when histologic features unusual to synovial sarcoma, but common to other neoplasms are present. This challenge is compounded with negative or unavailable t(x;18) findings. Four cases of paediatric primary pulmonary synovial sarcoma were evaluated here, including unusual histology, to bring awareness to this entity in the paediatric population.

Materials and Methods

Four cases of known pulmonary synovial sarcoma from 1980 to 2018 were retrieved from tissue archives. Radiology studies were not available. Follow-up 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. *SS18/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 SS18/SSX 1 and 2 fusion transcripts was performed using methods previously described [8].

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
Thyroid Transcription Factor-1	8G7G3/1’	1:25	Dako, Carpinteria, CA
Cytokeratin 5/6	D5/16B4	1:20	Dako, Carpinteria, CA
Bcl-2	124	1:20	Dako, Carpinteria, 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

Results and Discussion

Clinical findings

The study group included 4 females ranging from 10 to 17 years of age (mean, 15). The most common presenting symptoms were chest pain and shortness of breath. Tumors were distributed in the pleura (2), lung (1) and lung and mediastinum (1). Surgical procedures of primary tumour included pneumonectomy (2), lobectomy (1), and complete excision (1). Local recurrence, metastases, and survival data did not differ from typical adult pulmonary synovial sarcoma [9].

Gross and histologic findings

Tumors ranged in size from 8 to10 centimeters (mean, 9) and were well-circumscribed, soft, tan masses with foci of necrosis, hemorrhage, and cystic change. Histologically, tumors were monophasic (2) or biphasic (2). Tumors were grade 2 (2) and grade 3 (poorly differentiated, 2) according to French Federation of Cancer Centers (FNCLCC) grading. Tumor cell morphology included spindle cells or a combination of spindle and round/epithelioid cells. Mitoses ranged from 3 to 33 per 10 high power fields (mean, 16). Necrosis was present in three tumors and extensive in one. Histologic features typical of adult pulmonary synovial sarcoma were seen and included dense cellularity with interlacing fascicles, hyalinized or eosinophilic stroma and hemangiopericytoma-like vasculature (Figure 1).

Focal myxoid change, cystic change and benign entrapped pneumocytes 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 rosette formation (2), well -formed papillary structures (1), and adenomatoid areas (1) (Figure 2).

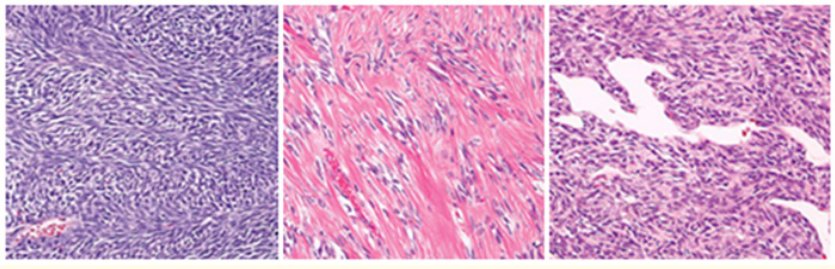

Figure 1: Typical histology of synovial sarcoma, left to right: dense spindle cells, hyalinized stroma, hemangiopericytoma-like vessels. H and E, medium power.

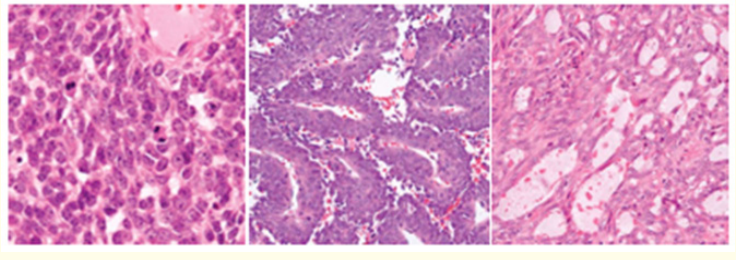

Figure 2: Unusual histology of synovial sarcoma, left to right: round cells with rosette-like areas, papillary structures and adenomatoid foci. H and E, medium power.

Immunohistochemical and molecular findings

Immunohistochemical studies showed focal positive membranous or cytoplasmic staining for epithelial markers including pancytokeratin (3), epithelial membrane antigen (2), and cytokeratin 5/6 (2), while no case showed immunoreactivity for all 3 epithelial markers. Diffuse immunoreactivity was seen in two cases with Bcl-2 and CD99. Focal immunoreactivity was present with S-100 (1) and smooth muscle actin (1). Entrapped benign pneumocytes, present in 2 cases, were immunoreactive with thyroid transcription factor-1 and epithelial markers. The chromosomal translocation t(x;18) was present in 2 cases studied in which 1 was fusion type SS18/SSX2. One case was reported as t(x;18) positive without information on the SSX fusion type. Tissue was unavailable in 2 cases.

Synovial sarcomas make up about 3-5% of sarcomas in the pediatric population [10]. Although rare, synovial sarcoma can be a primary pulmonary neoplasm with distinctive histology. While paediatric cases do not differ from adult cases clinically or pathologically, the presence of focal unusual histologic findings characteristic of more common epithelial and mesenchymal tumors may lead to misdiagnosis. This is particularly problematic in small biopsies or in tumour negative for the pathognomonic t(x;18) translocation, or where tissue is unavailable. We present four paediatric primary pulmonary synovial sarcoma cases with unusual histologic features.

An estimated 0.5 to 1 in 2 million children are affected by primary lung malignancies, including pulmonary sarcomas [11]. Pulmonary sarcomas make up 0.5% of primary lung malignancies, with primary pulmonary synovial sarcoma comprising approximately 16% of those cases [12]. Regarding treatment, surgical resection is the mainstay. Chemotherapy and radiation are also used; However, there is limited evidence supporting their long-term efficacy. Epigenetic therapies may hold future promise [13]. Primary pulmonary synovial sarcoma has an estimated 5-year survival rate of around 50%. This poor prognosis is primarily due to delayed detection along with common metastatic disease with initial presentation. As these tumours are extremely rare in paediatric populations, early detection remains a significant challenge [14]. This is compounded by non-specific symptoms that often mimic benign pulmonary conditions. Also making diagnosis difficult, is focal un-

usual histology in primary pulmonary synovial sarcoma that can erroneously suggest other primary and metastatic neoplasms, particularly on biopsy material.

Primary pulmonary synovial sarcoma with focal vague rosette formation can lead to misdiagnosis as Ewing sarcoma [6,15], Primary pulmonary synovial sarcoma may also be reminiscent of Ewing sarcoma when the former is poorly differentiated and displays round cell morphology. Unlike primary pulmonary synovial sarcoma, Ewing sarcoma typically has distinct cell borders, clear cytoplasm, scant stroma, and lacks hemangiopericytoma-like vasculature. Both tumors can express CD99, CD56, and cytokeratins [15,16], although expression of cytokeratin 7 makes a diagnosis of Ewing sarcoma less likely [16]. Chromosomal translocation t(11;22) is present in 85% of Ewing sarcoma [6].

Focal well-formed papillary or adenomatoid areas in primary pulmonary synovial sarcoma may be misinterpreted as carcinoma. Carcinomas can present with spindle cell and adenocarcinoma components. Carcinomas are more cytologically atypical with greater pleomorphism than primary pulmonary synovial sarcoma. Carcinomas may have areas of squamous differentiation or contain tumor giant cells, features not observed in primary pulmonary synovial sarcoma. While cytokeratins are focally expressed in primary pulmonary 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 are more likely to show an infiltrative growth pattern, regional lymph node involvement, and/or widespread metastases.

It should also be noted that one of the present cases showed focal immunoreactivity with S-100, similar to malignant peripheral nerve sheath tumor [15]. The stromal background of malignant peripheral nerve sheath tumor, however, typically lacks hyalinization and appears more basophilic. While focal immunoreactivity for S-100 can be present in both tumors [15], primary pulmonary synovial sarcoma is often immunoreactive for cytokeratin 7, a finding not generally seen in malignant peripheral nerve sheath tumor [17]. Clinically, malignant peripheral nerve sheath tumors arise from nerve or neurofibroma and are associated with neurofibromatosis type I in approximately two-thirds of cases [18]. Pleuropulmonary blastoma is also in the histologic differential diagnosis of monophasic synovial sarcoma as both can present with spindle or round cells, hyalinised stroma, and cystic change [7]. Nodules of cartilage can be seen with pleuropulmonary blastoma in contrast to synovial sarcoma. Also, cytokeratins, EMA, and CD99 are useful as these are not expressed in pleuropulmonary blastoma. Of course, the latter is also negative for t(x;18).

Conclusion

Presented here are four paediatric primary pulmonary synovial sarcoma cases with similar findings seen in adult cases, and with focal unusual histologic features that may erroneously suggest other primary and metastatic pulmonary neoplasms. This unusual histology may be particularly challenging in small biopsies or when t(x;18) is negative. Awareness of typical histology of pulmonary synovial sarcoma, their potential misleading unusual morphologic features, and prudent use of immunohistochemistry will prevent misdiagnosis, even in t(x;18)-negative cases.

Conflict of Interest

The author has no disclosures or conflicts of interest.

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