A rare case of monophasic pleuropulmonary synovial sarcoma [v1; ref status: not approved 2, http://f1000r.es/URdbBv]

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Abstract Pleuropulmonary synovial sarcoma is a diagnostic challenge. Synovial sarcoma is a soft tissue tumor of joints and extremities and are rarely seen in the mediastinum. We report this tumor at a very unusual location – the mediastinum in a 40-year-old female. The histopathology picture along with the location suggested a differential diagnosis of solitary fibrous tumor or mesothelioma, but immunohistochemistry helped in reaching the diagnosis of synovial sarcoma.

Introduction

Primary synovial sarcoma arising in the lung is very rarely seen in clinical practice¹². Before 2005, only 60 cases of synovial sarcoma in the pleuropulmonary region were reported in the English-language scientific literature³. It is normally a tumor found in adolescents and young adults between 15 and 40 years of age. Males are affected more than females¹. The use of molecular techniques like immunohistochemistry (IHC), polymerase chain reaction (PCR) and fluorescence in situ hybridization (FISH) is required for confirmation of diagnosis. They include detection of translocation T(x; 18) (p11.2; q11.2) is a highly specific gene mutation for synovial sarcoma⁴.

Classically, synovial sarcoma has a biphasic pattern and is composed of sheets of spindle cells and sharply segregated epithelial cells forming gland-like areas⁵. Diagnosis of monophasic synovial sarcoma, particularly at an unusual location like the mediastinum, is a challenge as it is often misdiagnosed as primary pulmonary spindle cell sarcoma/carcoma or metastatic carcinoma⁶⁷. Further work-up including clinical, histopathological and immunohistochemical findings are core when the diagnosis is uncertain and molecular testing is necessary⁸. This is particularly important for cases like ours from developing countries where financial and infrastructural constraints are major drawbacks.

Case

A 40-year-old female presented with complaints of cough, chest pain and shortness of breath with progressive weight loss for the past year. The past medical history was unremarkable. The radiological study x-ray (PA view, Figure 1) showed a large round opacity in the lower zone of the right lung with small nodules in the middle and lower zones of the left lung. Bronchoscopy revealed a right-sided growth involving the middle and lower pulmonary lobes. The computed tomography (CT) of the thorax (Figure 2) showed a well-defined mass measuring 8x7x6 cm on the right lung, infiltrating the diaphragm with small nodules of 1–2 cm in the left upper and lower lung lobes. The origin of mass from lung substance or pleura could not be identified with certainty.

CT-guided fine-needle aspiration cytology and bronchoalveolar lavage was inconclusive. Finally, a right side partial lobectomy
The cut surface of the tumor was fleshy, homogenous gray-white with areas of calcification. The other two pieces comprised of lung tissue measuring 7cm x 6cm x 2cm and tumor measuring 6cm x 6cm x 4cm.

Microscopy examination showed a spindle cell tumor with a varied pattern of cellularity, with areas of high cellularity mixed with low cellularity areas (Figures 4 and 5). The tumor cells were arranged in random, fasciculate and at places storiform pattern. Cytologically the cells had varying degrees of anaplasia with fusiform to plump cells having hyperchromatic nuclei and mild to moderate pink eosinophilic cytoplasm. Necrosis was minimal, there were occasional mitotic figures seen and metastatic calcification was also noted. It was therefore interpreted as a low-grade spindle-cell neoplasm of uncertain histogenesis. The tumor on immunohistochemical analysis was Epithelial membrane antigen cytokeratin5/6, mic-2, bci-2 and calponin was performed. On histopathology, we received three soft tissue pieces, the largest one measuring 19cm x 15cm x 10cm and consisting of part of the lung tissue with the tumor. A well circumscribed tumor measuring 19cm x 9cm x 9cm was seen.
with sharply segregated epithelial cells forming gland-like areas\textsuperscript{2,5}. Primary pulmonary monophasic synovial sarcoma is mainly of monophasic subtype and is difficult to diagnose due to its uniform spindle cell pattern. The differential diagnosis includes malignant peripheral nerve sheath tumor, fibrosarcoma, leiomyosarcoma, sarcomatoid variant of mesothelioma, Ewing's sarcoma, hemangiopericytoma, spindle cell lymphoma, desmoplastic small round cell tumor and metastatic carcinoma\textsuperscript{6}. Based on morphology, our first differential diagnosis was solitary fibrous tumor followed by mesothelioma. Ancillary immunohistochemical techniques helped to reach the final diagnosis. The immunohistochemical features of pleuropulmonary sarcoma are similar to those of soft tissue synovial sarcoma\textsuperscript{10}. EMA, cytokeratin, and vimentin positivity in combination with CD-34 negativity are the most useful and sensitive biomarkers for diagnosis of monophasic synovial sarcoma. In our case, immunostaining was strongly positive for EMA, vimentin, bcl-2 and focally for cytokeratin. It was negative for thyroid transcription factor (TTF)-1, calretinin, WT-1, CD34, S-100 and CD-99. Theses markers ruled out the possibility of malignant peripheral nerve sheath tumor (S 100 Positive), primitive nerve sheath tumor (CD99 Positive), germ cell tumor (PLAP, Alpha AFP, HCG Positive) and leiomyosarcoma (SMA Positive). P63 and CD34 were negative, which further ruled out thymoma and solitary fibrous tumor. Bcl-2 was positive, but it was not specific, as it could be seen in solitary fibrous tumor and monophasic synovial sarcoma. The diagnosis of pleuropulmonary synovial sarcoma was based on an absence of tumor at any other primary site. Brain metastasis was not seen in our case as it is uncommon in soft tissue sarcoma with only a single reported brain metastasis in the literature\textsuperscript{11}.

The overall prognosis is poor in pleuropulmonary synovial sarcoma\textsuperscript{12}. Tumor size more than 5 cm, male gender, advanced age >20 years, high mitotic activity >10 mitosis/10 HPF, presence of tumor necrosis and SYT-SSX1 gene variant are the main poor prognostic factors\textsuperscript{13}. To conclude, pleuropulmonary synovial sarcoma is a rare tumor. The diagnosis of this tumor requires meticulous clinical and pathological correlation, immunohistochemistry and molecular techniques. Familiarity with this entity is essential as it carries poor prognosis.

**Table 1** IHC Profile of tumors\textsuperscript{10,12}.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Cytokeratin</th>
<th>Vimentin</th>
<th>EMA</th>
<th>S-100</th>
<th>bcl-2</th>
<th>Calretinin</th>
<th>CD34</th>
<th>Desmin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial sarcoma</td>
<td>P</td>
<td>P</td>
<td>V</td>
<td>P</td>
<td>P</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>P</td>
<td>P</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>P</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td>N</td>
<td>P</td>
<td></td>
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<tr>
<td>MNPS</td>
<td>P</td>
<td>P</td>
<td></td>
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<td></td>
<td>N</td>
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<td></td>
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<tr>
<td>Fibrosarcoma</td>
<td>P</td>
<td>V</td>
<td>V</td>
<td>N</td>
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<tr>
<td>Angiosarcoma</td>
<td>P</td>
<td>P</td>
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</tbody>
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P-Positive, N-Negative, V-Variable, MPNST-Malignant Peripheral Nerve sheath tumor.
Author contributions
Rateesh Sareen wrote the article and contributed to the conception and design. Chandra lekha Pandey aided in the design and final approval of the manuscript. Akanksha Dutt contributed in manuscript writing. Mohit Sareen helped in gathering images and literature search.

Competing interests
No competing interests were disclosed.

References


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Matteo Giaj Levra
Department of Oncology, University of Torino, Torino, Italy

The authors spoke about a diagnosis of synovial sarcoma but there is no evidence of the research of the t(x; 18)(p11.2; q11.2) translocation for this case.

I'm sorry, but to establish a diagnosis of synovial sarcoma the positivity of the translocation is needed. Without the presence of this test I couldn't judge the rest of the paper.

If the authors forgot to write in the paper the execution of the test, they have to write it; otherwise I do not approve the paper.

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Competing Interests: No competing interests were disclosed.

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This short case report does not add any interesting information on monophasic pleural synovialosarcoma. Furthermore to establish a definitive diagnosis of synovialosarcoma we need to have the presence of the translocation t(X; 18).

In this case report the presence of the translocation is not mentioned. The global treatment of the patient is not reported.

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Competing Interests: No competing interests were disclosed.