Primary pleural thymoma: A mimic in thoracic pathology

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Abstract: We report a case of ectopic thymoma of the pleura with a growth pattern mimicking diffuse pleural mesothelioma. Diagnostic imaging showed that the pleural tumour encased the entire left lung. The specimen biopsied from the tumour was composed of lymphocytes and epithelial cells, consistent with the B1 type of thymoma. The surgical exploration of the anterosuperior mediastinum found no evidence of a thymic tumour. The thymoma was thought to originate from an ectopic thymic tissue in the pleura, as a lesion independent from the primary mediastinal thymoma, and it spreads along the pleura like a diffuse mesothelioma. Owing to their peculiar location and a variety of manifested histologic patterns, pleural thymomas may be confused with other neoplasms and may cause diagnostic problems clinically, radiologically, and morphologically. A combination of clinical information, histopathological appearance of the tumour, and immunohistochemical studies will often help to distinguish a primary pleural thymoma from other neoplasms.

Keywords: thymoma; ectopic thymus; pleura


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Introduction

The occurrence of thymoma outside the mediastinum is a rare event[1]. Thymomas are neoplasms arising from the epithelial elements of the thymus and are commonly located in the anterosuperior mediastinum. Occasionally, thymomas growing at ectopic sites have been described, including the neck[2,3], trachea[4], lung[5,6], and thyroid[7]. Primary pleural thymomas are rarely reported, with the largest series published by the Armed Forces Institute of Pathology (AFIP)[8] and by Attanoos et al.[9], each comprising eight cases. This report describes a case of primary thymoma of the parietal pleura simulating diffuse mesothelioma.

Case report

A 43-year-old woman was referred to our hospital with dyspnoea and right chest pain. A chest roentgenogram revealed pleural thickening and encasement of the lung. Right pleural effusion was present. Computed tomography of the chest confirmed several polilobated masses covering the whole right pleural surface, mediastinal, diaphragmatic, and parietal pleura, along with encasement of the lung. The lower right lobe of the lung was atelectatic and a massive effusion was seen in the right pleural cavity. CA125 was slightly elevated. A mediastinoscopy was performed and a pleural mass was aspored for histological examination. The anterior-superior mediastinum was completely free from masses or disease. The provisional radiological and clinical diagnosis was mesothelioma.

Materials and methods

A surgical pleural biopsy was performed and the specimen was sent to the Pathology Department. A firm, greyish-white-coloured nodule (2.5 cm in diameter) was observed. The tissue was routinely processed in a formalin-fixed, paraffin-embedded material. Representative sec-
tions were cut for morphological examination and tissue blocks submitted for immunohistochemistry. Immunohistochemistry methods were used to confirm the diagnosis, with the avidin-biotin-peroxidase complex (ABC) method being chosen for our investigation. Immunohistochemical markers included CK AE1/AE3 (Ventana Medical System; polyclonal, prediluted, trypsin treatment), CK 5/6 (Cell Marque; polyclonal [D5 e 16B4], prediluted, heat treatment), calretinin (Cell Marque; polyclonal, prediluted, heat treatment), CD3 (DakoCytomation [F7.2.38]; concentrated, heat treatment), CD5 (DakoCytomation [4/F6]; concentrated, heat treatment), CD20 (DakoCytomation [L26]; concentrated, heat treatment), CD1a (Cell Marque [MT B1]; prediluted, heat treatment), CD99 (Cell Marque [HO36.1]; prediluted, heat treatment), TdT (Cell Marque; polyclonal, prediluted, heat treatment), P53 (Neomarkers [DO7]; concentrated, heat treatment), and Ki67 (Ventana Medical System [K-2]; prediluted, heat treatment).

**Results**

Microscope images showed a pattern closely resembling normal functional thymic cortex, with scant neoplastic epithelial-like cells surrounded by a consistent lymphoid component. The epithelial-like cells showed large nuclei with a slight atypia and sometimes prominent nucleoli. The tumour had a lobular architecture with lobules of varying sizes, separated by thin and thick acellular fibrous bands. The neoplastic epithelial-like component was relatively inconspicuous and the cells were dispersed without forming cellular groupings. The lymphoid component was a densely packed population of small lymphocytes (Fig. 1).

The tumour cells were positive with broad spectrum cytokeratin AE1/AE3 and CK 5/6. Calretinin did not demonstrate any defined nuclear expression in the epithelial cells. CD5 was negative in the epithelial cells. The lymphoid component predominantly consisted of T-cells (CD3+, CD5+) and showed an immature phenotype (CD1a+, CD99+, and TdT+). Ki67 showed a low proliferative activity in the epithelial cells (<5%) (Fig. 2).

The diagnosis was Type B1 thymoma (in accordance to WHO classification). P53 was expressed in the neoplastic cells, at a level that was more than expected in a classic B1 thymoma. Surgical treatment was not possible and cisplatin/cyclophosphamide/epirubicin (PCE) chemotherapy was prescribed. Patient refused treatment and died three years later.

**Discussion**

The widely accepted explanation for unusually positioned thymomas is the neoplastic transformation of ectopic tissue secondary to the aberrant descent of thymic tissue from the third or fourth branchial arches. Pathological studies on myasthenia gravis patients have shown that thymic tissue can be widely distributed not only in the mediastinum, but also at other sites that include the thoracic cavity.
of thymic epithelial tumours is illustrated by the WHO classification\[^7\]. Thymic epithelial tumours may range from a pure spindle cell proliferation (Type A thymoma) to an epithelial polygonal cell neoplasm with a variable lymphoid component (Type AB, B1, B2, and B3). Type C thymoma is a carcinoma, generally with squamous or glandular differentiation. When observed via light microscopy, a pleural-based thymoma may morphologically mimic sarcomatoid, biphasic, and epithelioid malignant mesothelioma, depending on the histological type. In immunohistochemical examination of thymoma, the neoplastic cells have an arboring network of cytokeratin-positive cells, emphasizing the presence of interconnecting cytoplasmic processes\[^18\]. The epithelial component also shows immunoreactivity for cytokeratin subtype 5/6\[^9\].

Calretinin is variably expressed in different tumour subtypes within stromal cells, some defined as mast cells and neural components. Unequivocal nuclear expression in thymic epithelial cells was not seen\[^9\]. An awareness of these findings is important to prevent misdiagnosis. The T lymphocytes in the thymic tumour coexpress CD1a, terminal deoxynucleotidyl transferase, and CD99\[^20\]\. CD5 is expressed by neoplastic cells only in carcinoma of the thymus and not in thymoma, but lymphocytes within the tumour may exhibit CD5 immunoreactivity\[^21\]. The presence of an immature T-cell phenotype in an epithelial neoplasm strongly suggests the diagnosis of thymic epithelial tumour, regardless of anatomical site\[^9\]. An immature T-cell phenotype is not seen in lymphohistiocytoid mesothelioma or other forms of undifferentiated epithelial malignancy\[^9\].

**Conclusion**

Because of their ectopic site and various histologic patterns, as well as the occurrence of an “invasive” border, the diagnosis of primary pleural thymomas via pleural biopsy can be very difficult, especially if the pathologist is not aware of this entity or if the typical features of thymoma are lacking\[^15\]\. A combination of clinical information, histopathologic appearance of the tumour, and immunohistochemical studies will often help to distinguish primary pleural thymoma from other neoplasms.

**Table 1. Immunoreactivity of some markers in primary pleural thymoma and mesothelioma**

<table>
<thead>
<tr>
<th></th>
<th>CK AE1/AE3</th>
<th>CK 5/6</th>
<th>P63</th>
<th>Calretinin</th>
<th>CD 3</th>
<th>CD1a</th>
<th>CD99</th>
<th>TdT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymoma</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (SC) − (EC)</td>
<td>+ (LC)</td>
<td>+ (LC)</td>
<td>+ (LC)</td>
<td>+ (LC)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td>+ (LC) − (LC)</td>
<td>− (LC)</td>
<td>− (LC)</td>
<td>− (LC)</td>
</tr>
</tbody>
</table>

SC = Stromal cells; EC = Epithelial cells; LC = Lymphoid cells
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References


