Pathology – Research and Practice 212 (2016) 1076–1080

Contents lists available at ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp

Case report

Ectopic pleural thymoma in a 49-year-old woman: A case report

Borislav A. Alexiev (MD) (Associate Professor)*, Anjana V. Yeldandi (MD)

Department of Pathology, Northwestern University Feinberg School of Medicine, Northwestern Memorial Hospital, United States

ARTICLE INFO

Article history:
Received 20 June 2016
Received in revised form 13 July 2016
Accepted 30 August 2016

Keywords:
Pleural thymoma
Pathology
Differential diagnosis

ABSTRACT

Ectopic pleural thymoma is an exceedingly uncommon clinical entity that has only been described sporadically. Because of their peculiar location and variety of histologic patterns manifested, pleural thymomas may be confused with other neoplasms and may cause diagnostic problems clinically, radiologically, and morphologically. We describe the case of a giant left-sided ectopic pleural thymoma, preoperatively suspected to be a solitary fibrous tumor. A complete surgical resection was achieved and a postoperative diagnosis of WHO Type AB, modified Masaoka stage I tumor was attained. Subsequent thymectomy demonstrated unremarkable thymic tissue. The possibility of ectopic thymoma should be considered when the morphology of the lesion reveals a dual population of epithelial cells without significant nuclear atypia and lymphoid cells. Immunohistochemical studies are helpful in supporting the morphologic impression, both by characterizing the epithelial component as thymic in origin and by demonstrating the immature T-cell phenotype of the admixed reactive lymphocytes.

1. Introduction

Thymomas are rare tumors originating from the thymic epithelium. They account for the 1% of the adult neoplasms and are the most frequent anterior mediastinal tumors [4,12]. Ectopic tumors have been described, accounting only for 4% of all thymomas [2,5]. Ectopic thymomas originate from aberrant embryological migration of thymic tissue [2–7,9–14,17,18]. The most common locations for ectopic thymomas are the neck, middle, posterior mediastinum, and lung [2,10,17]. The pleural location is extremely rare and has been documented only a few times [3–7,9,11–14,18].

The occurrence of ectopic thymomas can cause substantial diagnostic difficulty as the entity is almost never included in the differential diagnosis and its biphasic morphology can cause further complications during the diagnostic process. We describe the case of a giant pleural thymoma, preoperatively suspected to be a solitary fibrous tumor.

2. Clinical history

A 49-year-old woman presented with chronic cough and rhinitis. A chest X-ray was obtained for rhonchi and showed a large shadow left of heart. A computed tomography (CT) scan was performed, demonstrating a large (10+ cm) left-sided left mediastinal pleura based mass abutting the pericardium and left chest wall. No signs of local invasion were identified. The differential diagnoses included solitary fibrous tumor vs more aggressive (malignant) neoplasm.

Complete surgical resection was performed with general anesthesia and single lung ventilation via a left anterolateral thoracotomy. A large mass was found on the left lower chest cavity arising from the mediastinal pleura. No continuity with the thymic gland was observed. The frozen section was reported as suspicious for lymphoproliferative disease. A transcervical thymectomy was performed a month following the resection of the mediastinal mass and showed no evidence of tumor. The patient is still alive and disease-free 54 months after surgery

3. Material and method

Representative tissue sections from the pleural mass and thymectomy were fixed in 10% buffered formalin and embedded in paraffin. Representative tissue blocks were submitted for frozen section, flow cytometry and permanent sections. Eight air-dried and alcohol-fixed touch imprint cytology slides from a freshly cut tumor surface were prepared during frozen section and stained with Diff-Quick and hematoxylin–eosin (H&E). For routine microscopy, 4-μm-thick sections were stained with H&E. Immunohistochemical staining was performed using an automated immunostainer (Leica Bond-III, Leica Biosystems, Buffao

* Corresponding author at: Department of Pathology, Northwestern University Feinberg School of Medicine, Northwestern Memorial Hospital, 251 East Huron St, Feinberg 7–342A, Chicago, Illinois 60611, United States.
E-mail address: Borislav.Alexiev@northwestern.edu (B.A. Alexiev).

http://dx.doi.org/10.1016/j.prp.2016.08.011
0344-0338/

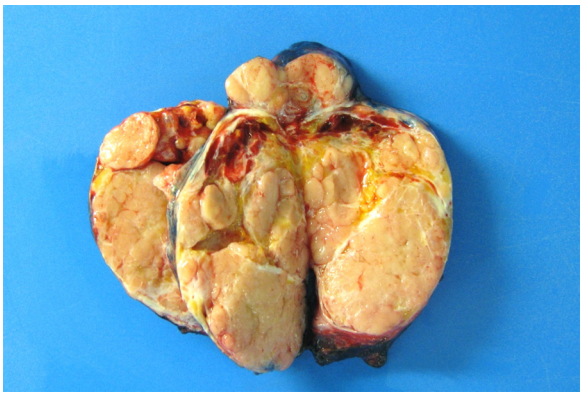

Fig. 1. Pleural thymoma. Note lobulated cut surface with multiple tan-colored nodules of various sizes separated by fibrous bands.

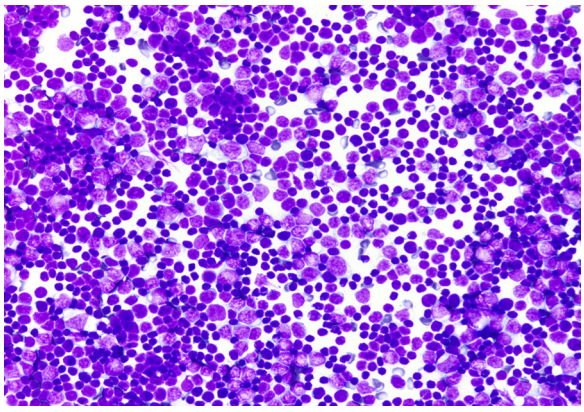

Fig. 2. Pleural thymoma. Note dual population of oval epithelial cells and small lymphocytes. Diff-Quick stain, 400×.

Grove, Il) and BondRefinePolymerTM biotin-free DAB detection kit. The following antibodies were used: CD20, CD34, EMA, CK5/6, CD99 (prediluted, mouse monoclonal, Dako); CD3, CD5, TdT (prediluted, mouse monoclonal, Leica); calretinin (prediluted, rabbit monoclonal, Cell Marque), OCT4 (prediluted, mouse monoclonal, Cell Marque). A positive nuclear, cytoplasmic and/or membranous expression in 10% or more of neoplastic cells qualified as "positive (+)".

4. Results

4.1. Gross pathology

Grossly, the specimen was received fresh labeled with patient's name and designated as "pleural mass". The mass weighted 378 g and measured 12.5 × 11 × 5.5 cm. Serial sections revealed a lobulated cut surface with multiple tan-colored nodules of various sizes separated by white fibrous bands (Fig. 1).

Cytologic findings Diff-Quick and H&E stained touch imprint cytology slides were moderately cellular and consisted of a dual population of oval or elongate epithelial cells and small lymphocytes (Fig. 2). The neoplastic epithelial cells contained round, oval or spindle pale nuclei with dispersed chromatin and inconspicuous nucleoli. The cytoplasm was scant, and the cell borders were ill-defined. The nuclear/cytoplasmic ratio was moderate to high. Nuclear pleomorphism was minimal. Mitoses were not seen in the epithelial cell component.

4.2. Histologic and immunohistochemical findings

Histologically, the pleural tumor was encapsulated and showed a nodular growth pattern with areas composed of a variable mixture of a lymphocyte-poor WHO Type A thymoma and lymphocyte-rich WHO Type B thymoma components (Figs. 3A and B). The WHO Type A thymoma component formed bundles of elongated fibroblast-like spindle cells (Fig. 3C). The WHO Type B thymoma component was composed predominantly of polygonal epithelial cells with small round, oval, or spindle pale nuclei showing dispersed chromatin and inconspicuous nucleoli admixed with numerous lymphocytes (Fig. 3D). Large epithelial cells with prominent nucleoli and vesicular nuclei and nucleoli were uncommon. Subsequent thymectomy found no evidence of a thymic tumor.

Immunohistochemically, WHO Type A thymoma component showed strong EMA expression and was negative for CK5/6 (Fig. 4A). WHO Type B thymoma component stained strongly positive for CK5/6 and was negative for EMA (Fig. 4B). In WHO Type B component, stromal lymphocytes demonstrated strong CD3, TdT and CD99 expression consistent with an immature phenotype (Fig. 4C). Numerous CD20 positive tumor cells were also noted in WHO Type B thymomal component (Fig. 4D). No immature lymphocytes were identified in WHO Type A thymomal stroma. Tumor cells in both WHO Type A and Type B components were negative for CD5, CD34, OCT4 and calretinin.

4.3. Flow cytometry

Flow cytometric findings were consistent with thymic T cells at various stages of maturation.

5. Discussion

Embryologically, the thymic epithelium originates in the third or fourth branchial pouches and descends caudally with the third parathyroid into the anterior mediastinum by the fifth or sixth week of gestation [2,4]. Aberrant migration may occur anywhere along this pathway and it is believed that ectopic thymomas originate from this aberrant thymic tissue [4]. Because of their ectopic site and variety of histologic patterns, diagnosis of primary pleural thymomas by fine needle aspiration cytology, pleural biopsy or frozen section can be very difficult, especially if the pathologist is not aware of this entity or if the more typical features of thymoma are lacking. In the present case, a frozen section misdiagnosis of "lymphoproliferative disease" was rendered. The cytologic features of ectopic thymomas are identical to those of mediastinal/thymic thymoma [1], but a correct diagnosis is extremely challenging because of the unusual location and its rare incidence. Critical to the cytologic diagnosis of most WHO Type B thymomas is the recognition of a distinct population of epithelial cells mixed with lymphocytes. Failure to do so can lead to the erroneous interpretation of thymoma as benign or malignant lymphoid lesions. WHO Type A thymoma may contain only epithelial cells and thus mimic a spindle cell neoplasm, or a reactive or neoplastic mesothelial lesion. Moreover, an epithelial predominant thymoma may be incorrectly diagnosed as carcinoma or seminoma. Several cytologic clues were helpful after retrospectively reviewing the present case. A dual population of neoplastic epithelial cells and non-neoplastic small lymphocytes, the absence of nuclear atypia, mitosis, and necrosis can exclude malignancy. A careful search and a precise interpretation of the epithelial cell and lymphocytic components could lead to an accurate diagnosis. The diagnosis of ectopic pleural thymoma requires extensive clinical, histological and immunohistochemical work-up, in particular to exclude (1) solitary fibrous tumor (SFT), (2) malignant mesothelioma, (3) lymphoma, (4) metastatic carcinoma with lymphoepithelioma-like features, (5) metastatic seminoma, and (6)