Thymoma with Pseudosarcomatous Stroma - an Unusual Variant of a Slowly Progressing Thymic Neoplasm

The authors present the first Polish case of an extremely rare thymoma in a 70-year old female surgical patient with 15-year observation before surgery.

Introduction

Thymomas are rare mediastinal tumors; their assessment is based on the classification developed by Müller-Hermelink or else on the WHO classification; the two systems differ mainly as to the terminology [1, 3]. Nevertheless, as it appears, these two classifications do not include all the morphological types of thymomas [2]. Recently, the authors have observed the first Polish case of a thymoma with a pseudosarcomatous stroma, similar to the cases described by Suster et al. [5] and Shimosato and Mukai [4].

A Case Description

A 69-year old woman reported for surgical treatment due to a tumor situated in the anterior-inferior and middle mediastinium. The tumor had been originally detected radiologically 15 years earlier, but at that time the patient refused her consent to surgical treatment. Over the 15-year period, the tumor was slowly but steadily increasing, reaching finally the diameter of approximately 10cm. The patient was asymptomatic, and in particular showed no myasthenia or other autoimmune disease symptoms. A core biopsy of the tumor allowed solely for determining that the neoplasm was characterized by a low malignancy grade and should be excised surgically (specimen No. 1525718). Computed tomography revealed that the tumor was adjacent to the anterior chest wall, right atrium, superior vena cava and ascending aorta (Fig. 1). A tumorectomy was performed in November 2003, during which a solid tumor, 10 x 10 x 7cm, was totally resected. The tumor did not infiltrate any mediastinal structures and had a vascular pedicle, by which it was connected to the descending aorta and superior vena cava. The postoperative course was uneventful.

The formalin-fixed material constituted a solid tumor with the diameter up to 10cm (Fig. 2), whose sections were collected and embedded in paraffin. The sections were stained with HE, silver-stained using the Gomori and Grimelius methods, as well as used in immunohistochemistry employing sera supplied by DAKO, and appropriate controls to assess the presence of EMA, cytokeratin, chromogranin, synaptophysin, smooth muscle actin, S-100, calretinin, vimentin, CD3, CD5, CD57, CD99, Ki-67.

Histologically, the tumor was composed of two components with a relative abundance of cells; however, the components were clearly separated and did not mix. One component was composed of tightly packed, medium-sized epithelial cells with oval or round nuclei and scant, pink cytoplasm; the cells have distinct borders, no atypia and mitotic figures. The structure of the other component was more loose, mesenchymal in character. The component consisted of less abundant spindle cells with elongated nuclei, which also showed no atypia and mitotic figures (Fig. 3). This part of the tumor focally demonstrated slight hyalinization. Within the mesenchymal structures, infrequent oval, psammomatous calcifications were seen (Fig. 4). No necrosis or hemorrhages were observed within the tumor. The tumor showed scarce, scattered T lymphocytes (CD3+), situated mainly within the spindle-like structures. In the peripheral part of the tumor, small thymic remnants were noted, with small cysts located either within such remnants or in the peripheral part of the neoplasm. The cysts were lined with a single layer of flattened cells or tumor cells. The Gomori staining was negative in the epithelial structures, but demonstrated the presence of numerous small fibrils in the spindle cell structures (Fig. 5).

In immunohistochemistry, the epithelial cells were cytokeratin-positive (Fig. 6); fewer cells reacted to the EMA antigen. Single cells and small cell clusters were S-100 and CD57 antigen-positive. The spindle cells showed no presence of cytokeratin, but were strongly EMA-positive.
Chromogranin and synaptophysin, as well as calretinin were not present in the tumor cells. The Grimelius silver staining was negative. The spindle cells were strongly positive for vimentin, which was also present in some epithelial cells. The Ki-67 antigen was observed solely in isolated tumor cells, but was clearly visible in the lymphocytes within the tumor and in thymic remnants. The CD5 and CD3 antigens were present in approximately 10% of tumor cells, both in the epithelial and mesenchymal zones. Smooth muscle actin was found in some spindle cells and in the walls of capillaries that were abundant within the tumor. The CD99 antigen was not observed throughout the tumor.

Discussion

Thymomas with a biphasic histological structure, similar to the above-described tumor, are extremely rare [4, 5]. They should be distinguished from highly malignant neo-
plasms termed "carcinosarcoma" (sarcomatoid carcinoma), where marked atypia and numerous mitotic figures involve both the epithelial and mesenchymal components. They also should not be mistaken for the so-called low-grade metaplastic carcinoma (biphasic thymic epithelial tumors with mesenchymal metaplasia), which have been recently described by Yoneda et al. [6]. These tumors show transitory structures, placed between the epithelial and spindle cell forms, as well as the CD5 antigen present in the solid epithelial component. Both the tumors described by Yoneda et al. and thymomas with pseudosarcomatous stroma are associated with a good prognosis [2, 6]. Yoneda et al. classify them as atypical thymomas, avoiding terming them "carcinomas". It should be borne in mind, however, that in the case of thymomas, typical or very atypical histology does not always correlate with a good or poor prognosis [5]. A decisive factor in the further development seen in the patient is the surgical excision of the entire tumor, including the capsule. In our case, a total tumorectomy was performed and the capsule was completely excised. The prolonged course of the disease, with the patient followed-up for 15 years, combined with the slow growth rate of the tumor definitely confirm its non-malignant character and speak against using the term "carcinoma".

The question whether the spindle cell component is a stromal reaction to an epithelial tumor, or else it constitutes another element of the tumor cannot be decided at the present stage. It also appears that - based on the literature - it is presently impossible to firmly differentiate between a thymoma with pseudosarcomatous stroma and the tumors described by Yoneda et al. [6]. According to Yoneda and his colleagues, these are different thymic tumors.

While differentiating biphasic thymic tumors, one should also consider mixed, biphasic mesotheliomas. In our case, the absence of calretinin expression, which is often present in mesotheliomas, the location of the tumor, the
presence of thymic remnants on the periphery, as well as no pleural effusion constitute the case against such a diagnosis.

References


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