Case Report

Type B3 Thymic Epithelial Tumor in an Adolescent Detected by Immunohistochemical Staining for CD5, CD99, and KIT (CD117): A Case Report

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A 16-year-old male patient was admitted to the hospital for a medical workup to examine an anterior mediastinal tumor in April 2000. A tumor excision and a right lower lung lobe nodule resection were performed in June 2000. The tumor tissue showed a cobblestone-like proliferation of atypical cells containing a discrete nucleolus that were aligned in an epithelial fashion against mainly lymphocytic inflammatory cells in the background; also shown were undifferentiated tumor cells with epithelioid characteristics. Immunohistochemical staining for CD5, CD99, and KIT (CD117) revealed that the tumor cells were CD5-negative and that some of the lymphocytes infiltrating the tumor tissue stained positive for CD99 and negative for KIT. The lesion was therefore diagnosed to be a type B3 thymic epithelial tumor. (Ann Thorac Cardiovasc Surg 2009; 15: 324–327)

Key words: thymoma, thymic epithelial tumor, immunohistochemical staining, KIT, adolescent

Introduction

Thymomas rarely occur in juveniles or adolescents,[1)] and there have been few reports of this type of tumor since the introduction of the new World Health Organization (WHO) classification of thymic epithelial tumors (TETs) in 1999. In recent years, the new WHO histological classification has been investigated for its validity and prognostic significance.[2–6)] Several reports demonstrated that immunohistochemical staining may be effective in differentiation between type B3 and type C TETs, which is frequently difficult, according to the new classification.[7,8)] A case of TET that had developed in an adolescent was diagnosed using immunohistochemical staining for diagnostic typing of the neoplasm according to the WHO classification.

Case

The patient was a 16-year-old male adolescent who initially presented with symptoms of cough, backache, and neck pain in January 2000. He was admitted to this hospital in April 2000 for a medical workup and treatment. The only positive finding noted in the hematological and blood-chemical tests was a slight increase in serum C-reacting protein. A chest radiograph revealed a mass measuring 18 × 11 cm protruding rightward from the mediastinal shadow. A chest computed tomography (CT) scan showed a heterogeneous mass measuring 10 × 5 cm in the anterior mediastinum displacing the superior vena cava and ascending aorta (Fig. 1). A biopsy of the mediastinum indicated a germ cell tumor (seminoma) (Fig. 2); a thymoma was also suspected because the neoplastic tissue specimen was negative for placental alkaline phosphatase staining. A urological examination revealed no problematic findings. Radiation was administered to the lesion, but it had to be discontinued because leukopenia was noted after a cumulative irradiation dose of 14.4 Gy. In May

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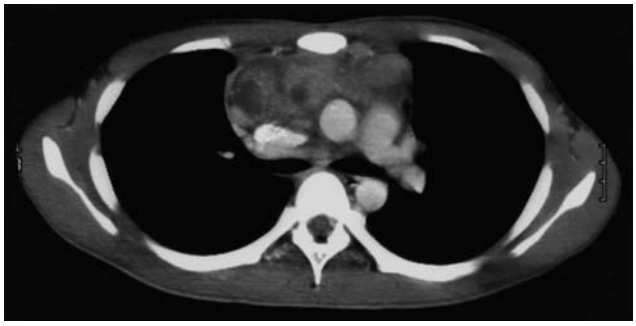

Fig. 1. A chest CT scan revealing a nonhomogeneous mass 10 × 5 cm in the anterior mediastinum, displacing the superior vena cava and ascending aorta.

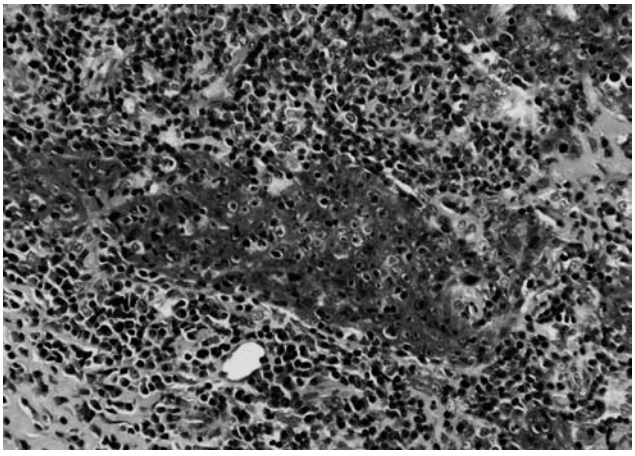

Fig. 2. Multicrest cells with a large orbicular nucleus solidly aligned with mainly lymphocytic inflammatory cells in the background. (H&E stain: ×40)

2000, a chest CT scan revealed a nodule measuring about 1 cm in diameter in segment 9 of the right lung, which continued to grow. Surgical intervention was carried out in June, whereupon the tumor was found to have invaded part of the right upper lung lobe, the pericardium, and the left brachiocephalic vein. These lesions were resected concurrently, and the nodule in segment 9 of the right lung was also excised.

No obvious residual tumor tissue was seen in the intrathymic neoplastic lesion because it had been irradiated prior to the operation. A histopathological examination of the lesion in the right lung revealed a cobblestone-like proliferation of atypical cells containing a discrete nucleolus. These cells were aligned in an epithelial fashion mainly against lymphocytic inflammatory cells in the background, and undifferentiated tumor cells with epithelioid characteristics were also noted (Fig. 3). Immunohistochemical staining showed only a few cells to be positive for cytokeratin. The tissue specimen was negative for placental alkaline phosphatase. Therefore the lesion was diagnosed to be neoplastic tissue with epithelioid characteristics that developed in the thymus, with few of the distinct epithelioid characteristics seen in most invasive thymomas, and it was also extremely poorly differentiated. The tumor was considered at this time to be either a type B3 TET or a type C TET, but atypia of the tumor cells was prominent, and it was also difficult to distinguish between the two types solely based on these results. So the tumor cells were stained for T cell markers, CD5 and CD99, as well as for the c-kit proto-oncogene, KIT. The cells tested were negative for CD5 (Fig. 4A); the lymphocytes infiltrating the tumor tissue stained positive for CD99 (Fig. 4B) and negative for KIT (Fig. 4C). Therefore a diagnosis of type B3 TET was made.

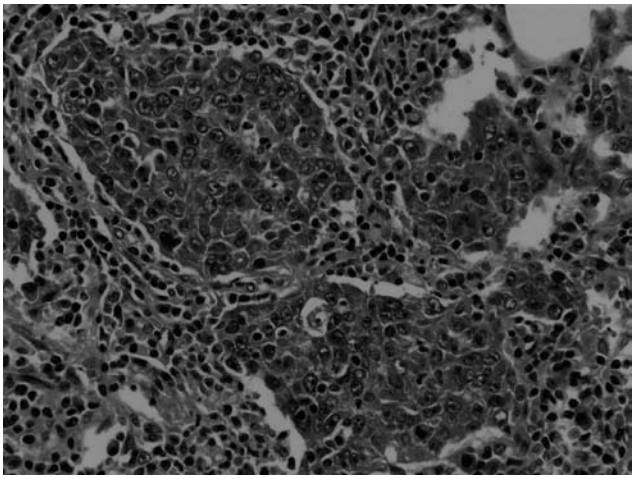

Fig. 3. Section showing a cobblestone-like proliferation of atypical cells containing a discrete nucleolus, aligned in an epithelial fashion against mainly lymphocytic inflammatory cells in the background and undifferentiated tumor cells with epithelioid characteristics. (H&E stain: ×40)

Further treatment was planned. The patient was reluctant to continue treatment at this hospital, however, and he was discharged on the 11th postoperative day.

Discussion

Thymic lesions account for approximately 2%–3% of all pediatric mediastinal tumors and include thymic cysts, hyperplasia, carcinoma, and thymomas. Thymomas, which represent less than 1% of all mediastinal tumors, are rare mediastinal tumors in the pediatric population. Fewer than 30 cases of thymoma in children have been

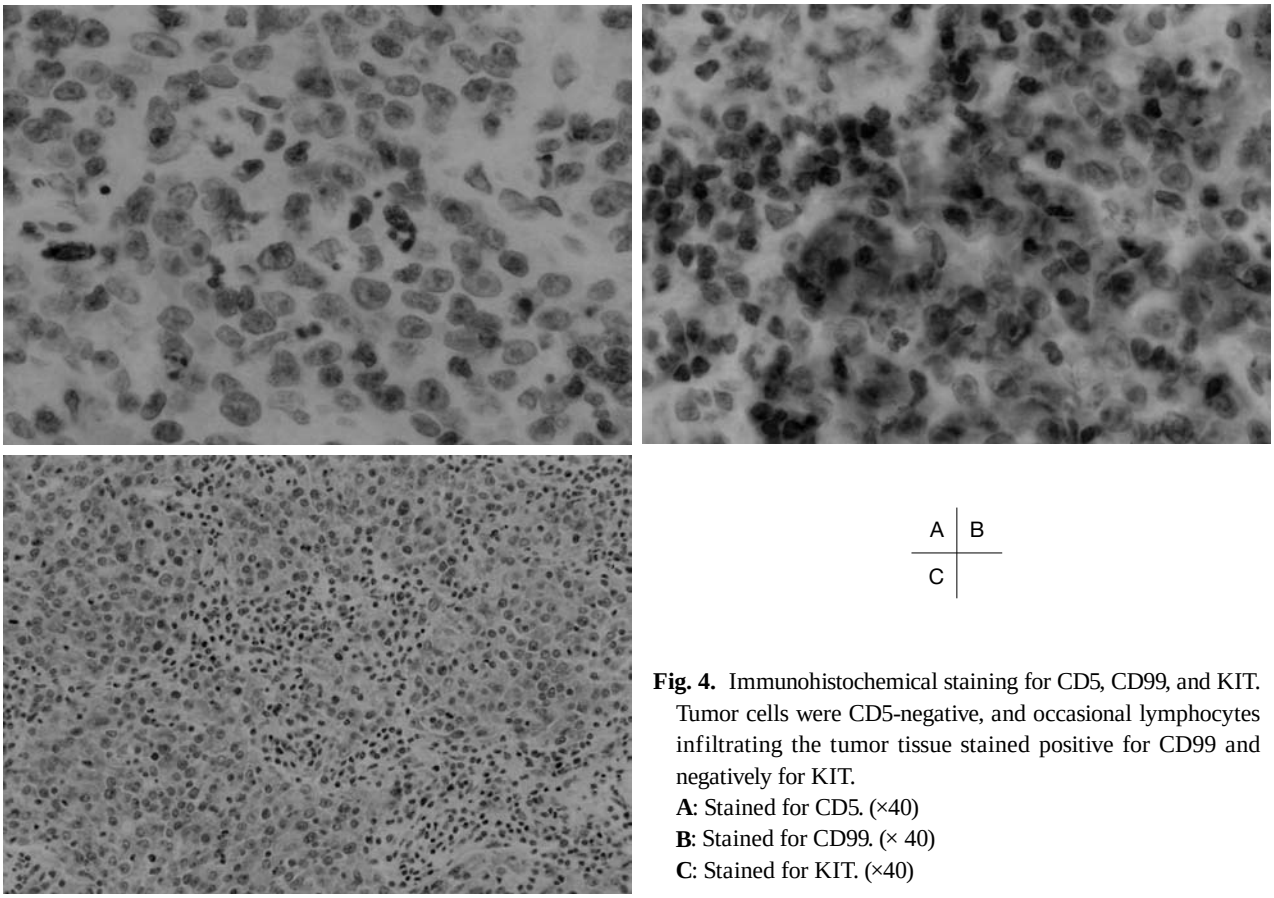

Fig. 4. Immunohistochemical staining for CD5, CD99, and KIT. Tumor cells were CD5-negative, and occasional lymphocytes infiltrating the tumor tissue stained positive for CD99 and negatively for KIT.
A: Stained for CD5. (×40)
B: Stained for CD99. (× 40)
C: Stained for KIT. (×40)

described in the literature.[1] These tumors are typically aggressive and are associated with poor outcomes.[1] Surgery is mainly indicated for the treatment of thymoma, and radiation and chemotherapy have also been widely used as an adjuvant and palliative therapy.[2]

Thymic epithelial tumors, usually defined as thymoma or thymic carcinoma, have a variable morphological appearance as well as heterogeneity regarding their oncological and biological behavior.[5,6] Moreover, the histological classification of TETs has been confusing and controversial.[4] To provide a universal system for clinicians and researchers to compare the results of studies performed using several different classification systems in 1999, the WHO International Committee has made an attempt to establish a consensus on the classification of TETs.[4]

According to these criteria, thymomas can be stratified into six histological subtypes (types A, AB, B1, B2, B3, and C) based on the morphology of the epithelial cells and the lymphocyte-to-epithelial cell ratio. A few studies have investigated the applicability and clinical significance of the WHO histological classification of thymoma since its publication in 1999.[2–4] This classification was reliable and reproducible when it was evaluated by experienced pathologists.[5]

Although controversy remains regarding the terminology and subclassification of TETs, many investigators recognize borderline lesions that represent an intermediate form between thymoma and thymic carcinoma.[8] The WHO criteria defines that a B3 thymoma represents a particular tumor group that remains controversial in the literature. According to the Müller-Hermelink classification, this group was classified as a well-differentiated thymic carcinoma, thus representing a more aggressive variant of TET than the other subtypes.[3] This particular group is an intermediate stage between subtypes B1–B2 and type C, rather than being graded as the other type B TETs.[3]

Immunohistochemical staining was performed with monoclonal antibodies against CD5, CD99, and KIT to differentiate between a type B3 TET and a type C TET. CD5 is a useful diagnostic marker of primary thymic carcinomas. Taken together, CD5 and CD99 (or other immature T-cell markers such as TdT and CD1a) may be

especially useful for evaluating mediastinal and other biopsy samples of possible thymic epithelial neoplasms and also for the subtyping of these tumors.[7] CD5 reactivity (assessed on epithelial cells) can also be used in conjunction with CD99 reactivity (assessed on accompanying lymphocytes) to help categorize TETs as follows: $CD5^-$/$CD99^+$ in benign and invasive thymomas (including well-differentiated thymic carcinoma), and $CD5^+$/$CD99^-$ in true thymic carcinomas.[7]

KIT, a protein product of the c-kit proto-oncogene, is a transmembrane tyrosine kinase receptor for stem cell factor. Its expression has been documented in a wide variety of human neoplasms, including acute myeloid leukemia, mast cell tumor, germ cell tumor, ovarian carcinoma, malignant melanoma, GI stromal tumor, small cell lung carcinoma, neuroblastoma, and breast carcinoma.[9] Nakagawa et al. demonstrated that most thymic carcinomas (80%) were positive for KIT and that most thymomas (96%) were negative for KIT.[9]

In the present case, tumor cells were proven to be CD5-negative and CD99-positive with findings in support of the histological features characteristic of a benign, invasive thymoma; a final diagnosis of type B3 TET was made based on a negative KIT result. A TET itself rarely occurs in juveniles or adolescents, and this tumor has rarely been reported since the introduction of the WHO histological classification. A strict diagnosis based on the new classification is essential for the prognostic assessment of similar cases as well as for an accurate delineation of its frequency. Immunohistochemical staining for CD5 and CD99 is useful for the diagnostic typing of TETs. The future accumulation of case reports based on accurate diagnoses will hopefully corroborate the validity of this new classification.

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