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Case Report

Ossifying thymoma accompanied by osteochondroma in a male adolescent: a case report

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Abstract: Osseous metaplasia of thymomas is exceedingly rare. This study reported the case of a 15-year-old male adolescent who was histologically diagnosed with ossifying thymoma and left tibial osteochondroma. Chest computed tomography (CT) identified a large, distinct, dense soft tissue mass with almost complete calcification in the patient's left anterior mediastinum. Contrast-enhanced CT imaging revealed that the tumor parenchyma had lightly homogeneous contrast enhancement. Ossification increases the difficulty of preoperative diagnosis and treatment. Therefore, we proposed that ossifying thymoma should be considered preoperatively in the differential diagnosis of a calcified mass that arises in the anterior mediastinum, especially when accompanied by osteochondroma. However, differentiation based on imaging criteria alone can be difficult.

Keywords: Thymoma, ossifying, osteochondroma

Introduction

Osseous metaplasia of thymomas is extremely rare. To the best of our knowledge, only seven cases of ossifying thymomas have been described in current English-language literature [1-7]. These cases exclusively involved females. Herein, we report the case of ossifying thymoma with tibial osteochondroma in a 15-year-old male adolescent.

Case report

A healthy 15-year-old boy presented to our hospital (the Affiliated Yantai Yuhuangding Hospital of Qingdao University, Yantai, China) in June 2016 with a 1-year history of left knee pain. A magnetic resonance scan of the left knee revealed a cartilage-capped bony projection on the external surface of tibial metaphysism. The projection contained a marrow cavity that was continuous with that of the underlying bone (**Figure 1**). Prior to surgery, a chest radiograph showed a large, partially visible mass with extensive calcification in the anterior mediastinum. Plain chest computed tomography (CT) scanning revealed a large, well-defined, 10.4 cm × 6.8 cm × 16.3 cm, dense mass in the soft tissue of the left anterior mediastinum. The mass was almost completely calcified. Upon contrast-enhanced CT imaging, the tumor parenchyma showed lightly homogeneous contrast enhancement. Moreover, no tumor vessels were visualized and no remarkable fat component was discernable (**Figure 2**). The tumor had no mass effect on adjacent structures. The CT findings suggested a benign tumor of the anterior mediastinum. The boy did not have a history of myasthenia gravis. Routine laboratory studies were within normal limits, and no tumor markers were identified.

A benign osteochondroma was resected from the patient's left tibia. The patient subsequently underwent a median sternotomy and extended thymectomy with complete resection of the mass. Gross examination revealed that the mass was solid, well-encapsulated, and measured 10 cm × 7 cm × 16 cm. The mass was mostly composed of ossified tissue. Lots of nodular substance, which exhibited staggered growth with bone tissue, adhered on the tumor surface. The outer surface of the tumor was tightly adhered to the anterior parietal pleura

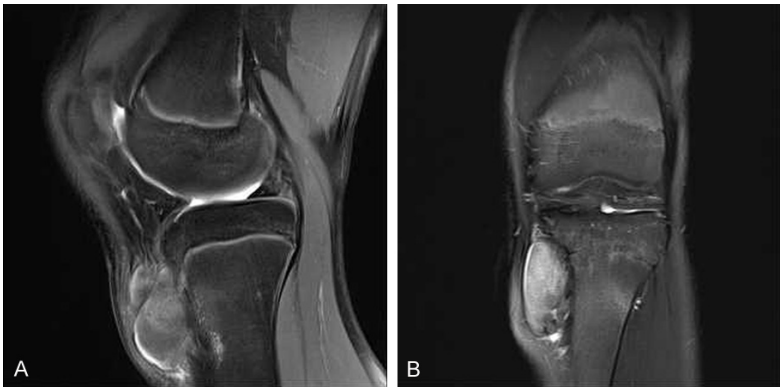

Figure 1. Tibial osteochondroma. MRI SAG-T2WIFS (A) and COR-T2WIFS (B) images reveal a cartilage-capped bony projection that arises from the external surface of tibial metaphysism. The projection contains a marrow cavity that is continuous with that of the underlying bone.

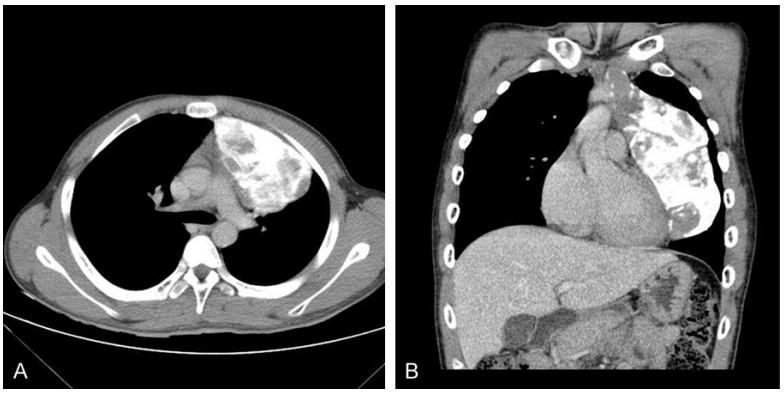

Figure 2. Ossifying thymoma. Chest CT. Axial (A) and coronal (B) contrast-enhanced images reveal a solid, well-defined mass with almost complete calcification in the anterior mediastinum.

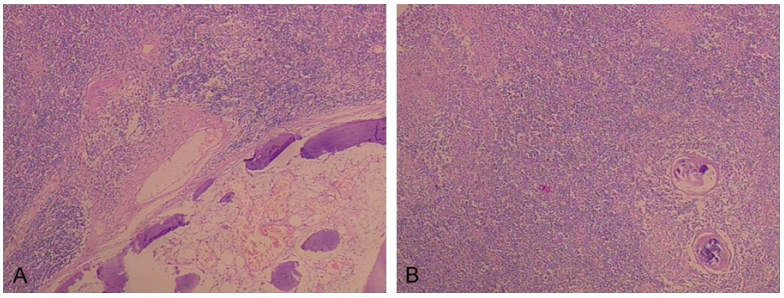

Figure 3. Pathological features of ossifying thymoma. Ossifying areas contain extensive areas of mature lamellar bone formation (A). Thymus corpuscles and hyperplasia of lymphoid cells (B). Focal calcification scattered under the background (hematoxylin and eosin stain, × 40).

and the left upper lobe of the lung. Microscopy revealed ossifying areas with extensive areas of mature lamellar bone formation, thymus corpuscles, and hyperplasia of lymphoid cells with focal calcification scattered in the background (**Figure 3**). Immunohistochemical staining revealed that the tumor cells strongly stained positive for CK19, CD7, CD99, and CD3; partially stained positive for CD5; and partially and weakly stained positive for TdT. The tumor cells stained negative for CD20, CD34, and PAX5. The results of histology and immunohistochemical staining were consistent with a rare type of thymoma with osseous metaplasia.

The tumor was classified as Masaoka stage I in view of the fact that it was encapsulated grossly and confined to organ microscopically. No chemotherapy or radiotherapy was required. The patient demonstrated no evidence of disease at a follow-up 6 months after diagnosis. No other osteochondromas have been found in the patient. His immediate family had no history of thymoma and osteochondroma.

The present study was approved by the ethics committee of the Affiliated Yantai Yuhuangding Hospital of Qingdao University (Yantai, China). Written informed consent was obtained from the patient.

Discussion

Thymomas are slow-growing, thymic epithelial tumors and account for 20% of mediastinal tumors. Thymoma incidence peaks at the age of 40 to 50 without significant difference between males and females. Thymomas only comprise 1%-2% of mediastinal neoplasms in children [8]. Thymomas can occur in any part of the neck to the diaphragm, but

are usually located in the anterior mediastinum. Some patients may be asymptomatic and 40% of adult patients will present with complaints that are related to a paraneoplastic syndrome similar to myasthenia gravis (up to 50%). In addition, other patients may have symptoms that are associated with mass effects from the tumor such as the compression or invasion of adjacent structures.

CT is commonly used to examine thymomas. Plain CT shows clear-edged, uniformly dense, solid, round, oval, or lobulated masses. Enhanced CT shows homogeneous enhancement. Cystic or necrotic regions can be present in up to 30% of tumors and are more common in large tumors. Low density on CT indicates hemorrhage, necrosis, and cystic change. Calcification occurs in up to 10% of thymomas [9]. Moreover, arc calcification is common in the cyst wall and intratumoral calcification mainly exhibits a stippled and nodular pattern. The invasiveness of thymomas manifests as the invasion of the surrounding structures, including vessels, the heart, pleura, diaphragm, or chest wall.

When calcification is radiologically detected in mediastinal tumors, teratoma and thymic tumors should be differentially diagnosed. A close correlation between teratoma and the radiologic detection of calcification or ossification in tumors is well documented. Although ossification is frequently observed in teratomas [10], it is exceedingly rare in thymomas. To the best of our knowledge, only eight ossifying thymomas have been reported thus far [1-7], including the present case. Our study is the only case that involved a male adolescent. All other cases involved women, including three elderly women, one middle-aged woman, two children, and one adolescent. There are a variety of clinical manifestations of ossifying thymoma that are similar to thymoma: a case without clinical symptoms; a case with peripheral T cell lymphocytosis; two cases with myasthenia gravis; three cases with limb pain; and one with dyspnea on exertion, intermittent fever, and generalized weakness. Moreover, CT revealed that ossification has various manifestations in the reported cases, such as nodular calcification in one case, central calcified rim in two cases, complete calcification in one case, extensive calcification in two cases, and almost complete calcification in two cases.

Ossification in thymomas should be differentiated from more common calcifications. However, radiologic identification is difficult. Pathologic calcification, including dystrophic and metabolic calcification, is common and is defined as aberrant deposition of calcium salts. Heterotrophic ossification is defined as mature lamellar bone that developed within soft tissues. In heterotrophic ossification, mesenchymal stromal cells differentiate into osteoblasts and deposit osteoids. Then, woven bone is remodeled into compact lamellar bone that contains osteocytes. Heterotrophic ossification is rare with a tumor incidence of only 0.067% [11]. Heterotrophic ossification is regulated by systemic and local factors. Systemic factors include drugs, as well as endocrine, metabolic, and genetic factors. Several growth factors have been postulated as local factors, such as platelet-derived growth factor, transforming growth factor β1, insulin-like growth factor 1, and bone morphogenetic protein.

The case we reported was accompanied by tibial osteochondroma. The patient's immediate family had no history of thymoma and osteochondroma. Given that special studies were not performed, the cause of osseous metaplasia in our case remained elusive. Bikhchandani *et al*. [3] reported a giant ossifying malignant thymoma in a child. The thymoma was accompanied with multiple sclerotic foci in vertebral bone, sacroiliac joints, ischium, sacral ala, and femurs. Farmakis *et al*. [7] reported one thymoma in an adolescent. The case also presented osseous metaplasia, osteochondromas, osseous metaplastic pseudotumor, and multiple sclerotic foci. The patient's half-sister had a pelvic osteosarcoma. Moreover, the patient's half-sister and her mother also had multiple benign bony exostoses. Although very rare, 3/8 (37.5%) of ossifying thymomas were accompanied by bone disease, which may be caused by genetic factors and may be associated with EXT-1, EXT-2, or EXT-3 gene mutations that are commonly seen in multiple hereditary exostoses. Collecting additional cases of ossifying thymoma will be necessary to elucidate the pathogenesis of osseous metaplasia.

The prognosis of thymomas depends on tumor stage. The WHO and Masaoka classification systems are the most common tumor staging systems [12, 13]. Surgical resection is currently the most effective thymoma treatment and can

be achieved in almost all patients with stage I and stage II thymomas. The ability to completely resect the thymus gland is an important prognostic factor in a locally advanced thymoma [14]. Radiotherapy is recommended in the case of incomplete resection. Chemotherapy is proposed for unresectable stage III and stage IV thymomas [15, 16]. Platinum-based combination chemotherapy drugs are standard for thymic tumor treatment [17]. However, Bikhchandani *et al*. [3] reported one giant ossifying malignant thymoma in a child who did not respond to chemotherapeutic drugs. The presence of mature bone in the tumor was considered to be a dominant factor in failing treatment.

In conclusion, we presented a case of ossifying thymoma with tibial osteochondroma in a male adolescent.The presence of ossification increases the difficulty of preoperative diagnosis and treatment. Despite its rarity, ossifying thymoma should be considered in the differential diagnosis of calcified masses that arise in the anterior mediastinum, particularly when accompanied by osteochondroma.

Disclosure of conflict of interest

None.

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