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Case Report

Sclerosing thymoma with extensive ossification and myasthenia gravis: an extremely rare case in the anterior mediastinum

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Abstract: Sclerosing thymoma is a rare variant of thymomas, recently recognized in pathology. Since its first description in 1994, only 15 cases have been reported. Furthermore, osseous metaplasia in sclerosing thymoma is an even unusual characteristic. To date, only 7 such cases have been described, while half of them show the symptom of myasthenia gravis. Herein we present a 57-year-old female with ossifying sclerosing thymoma and myasthenia gravis, which is the first case in literature of type B3 sclerosing thymoma with extensive ossification and myasthenia gravis. In consideration of its rarity, awareness of the possible occurrence of extensive ossification and sclerosis in thymomas helps to avoid a diagnostic pitfall, especially in mediastinoscopic biopsy specimens.

Keywords: Sclerosing thymoma, osseous metaplasia, myasthenia gravis

Introduction

Thymoma is the most common neoplasm exhibiting differentiation towards the thymic epithelial cells in thoracic cavity. Sclerosing thymoma (ST) is recognized as an exceedingly rare variant in pathology. In 1994, Kuo reported 2 cases of an unusual histologic form of thymomas, and firstly proposed a new term of ST [1]. So far only 15 cases have been published since the first description [2-4]. Histologically, ST is characterized by abundant hyalinized fibrous collagen scattered with small cellular aggregates exhibiting the features of a conventional thymoma and multiple calcifications. However, osseous metaplasia is an extremely unusual feature, and only 7 cases of ossifying thymoma have been reported so far [5-8]. Herein we present a 57-year-old female with ossifying ST and myasthenia gravis, which is the first case in literature of type B3 ST with extensive ossification and myasthenia gravis.

Patient and methods

A 57-year-old female patient with a 3-year history of myasthenia gravis was treated medically and showed significant improvement, but muscle weakness and difficulty in swallowing persisted. Chest computer tomography scan indicated a 3.0 cm×3.0 cm×2.5 cm nodule in the anterior meidiastinum containing a high-density areas that was assumed to represent calcification (**Figure 1A**). Contrast-enhanced CT scan demonstrated heterogeneous enhancement (**Figure 1B**). Physical examination and the laboratory results, including serum tumor markers, were found within normal limit. Considering thymoma, thymectomy was performed and the symptom of myasthenia gravis relieved after surgery. The patient had an uneventful postoperative course and no adjuvant treatment was performed. The patient is alive with no evidence of recurrence for 36 months until this report submission.

Results

The resected tumor was a 3.0×3.0×2.0 cm mass, the cut surface was cystic and hard with multiple ossifications or calcifications (**Figure 2A**). Histological examination revealed a largely encapsulated collagenous neoplasm scattered with small cellular islets composed of a dual

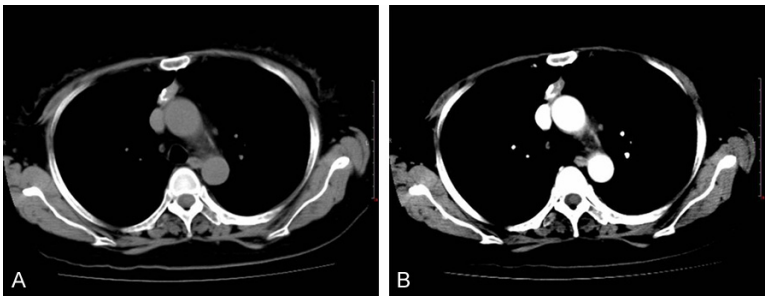

Figure 1. Imaging features of sclerosing thymoma. A. Unenhanced Computer tomography (CT) scan revealed an anterior mediastinal mass with oval shape, relative smooth margins and focal high density. B. Contrast-enhanced CT scan demonstrated heterogeneous enhancement.

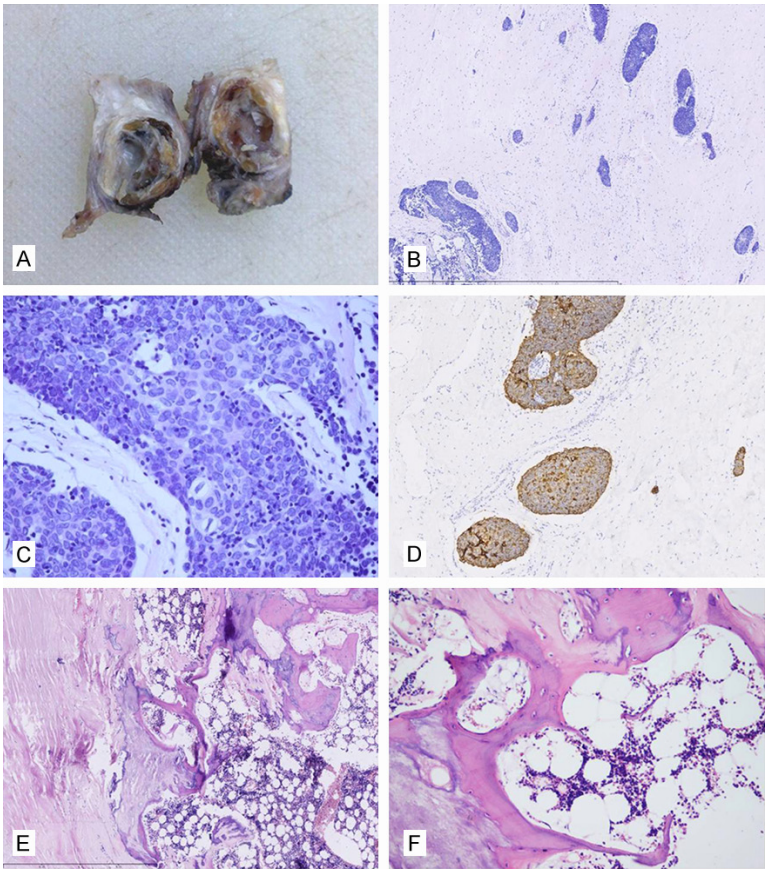

Figure 2. Pathological findings of sclerosing thymoma. A. Bisected gross specimen showed cystic change and a hard area with multiple calcifications and ossifications. B. Small cellular islets were embedded in the extensive hyalinized fibrous tissues (low power). C. The cellular islets were composed of epithelial cells and a few lymphocytes. D. The epithelial cells showed strong immunoreactivity for CK19. E. Hypocellular hyalinized stroma with multiple calcifications and ossifications. F. Higher magnification of osseous metaplasia including areas of mature lamellar bone tissues with hyperplastic bone marrow.

cell population of epithelial cells and lymphocytes (**Figure 2B**). As paucity of intraepithelial lymphocytes, the epithelial cells with large nuclei and conspicuous nucleoli formed tumor cell sheets exhibiting the characteristics of conventional type B3 thymoma (**Figure 2C**). Multiple dystrophic calcifications and osseous metaplasia were noted within the extensive sclerosing stroma, including areas of mature lamellar bone tissues with osteocytes and hyperplastic bone marrow (**Figure 2E**, **2F**). Foci of hemorrhage, cystic degeneration and cholesterol clefts were also present. Immunohistochemically, the epithelial cells were immunoreactive for CK, CK19, CK5/6, P63, and negative for CD5, CD117 (**Figure 2D**). Ki67 highlighted a moderate proliferative rate (about 15%+). Based on these histopathological findings, it was diagnosed as type B3 ST with osseous metaplasia according to WHO diagnostic criteria.

Discussion

Thymomas are common thymic neoplasms composed of epithelial cells and varying amounts of non-neoplastic lymphocytes. As a special variant, ST is an extremely rare entity with only 15 cases been reported since its first description. Some authors considered that changes of extensive hyalinization and sclerosis of ST might be an ancient change rather than a regression phenomenon [2]. Focal areas of calcifications have been described in ST, but ossification appears to be extraordinarily rare. In English literature, there are only 8 reported cases of thymoma with osseous metaplasia, including our case. Ossifying thymoma manifests in 5 adults (35~73 years)

and 3 children (8~13 years), while half of them show the symptom of myasthenia gravis. Interestingly, only females are affected. The microscopic WHO type of these ossifying thymomas include type A, B1 and B3. The present case is the first case in literature of type B3 sclerosing thymoma with extensive ossification and myasthenia gravis.

Bone formation is a complex process of pluripotent stromal cells that undergo differentiation to form osteoblasts with deposition of osteoid and remodeling of woven bone into compact lamellar bone containing osteocytes [5]. The precise etiology of ossification in thymoma is still unclear, although several hypotheses have been proposed [7, 8]. Both systemic and local factors are thought to be involved into the progression. Systemic factors concludes endocrine, metabolic, genetic factors and drugs while multiple cell mediators such as transforming growth factor β1 and bone morphogenetic protein have been recognized as local factors. The tumoral microenvironment might have induced the osseous metaplasia as a result of these cell mediators. All the patients of reported ossifying thymomas are females, it might be related to endocrine or metabolic factors. And 2 of the 3 children patients are associated with multiple distant bone lesions and the tumors are giant with extensive ossification which implied that genetic factors may also play a role.

ST with ossification needs differentiating from other intrathoracic tumors which may also ossify or scleroses, including teratoma, lung cancer, solitary fibrous tumor and mesothelial lesions, etc. Predominant mesenchymal hyalinization and sclerosis scattered with small cellular aggregates in our case almost misled us to diagnose as invasive carcinoma. Whether sclerosis is the result of ancient change or gradual coalescence of thick fibrous septa that are commonly seen in thymomas, it remains unclear. Collection of further cases is necessary to identify the pathogenesis of the ossification and sclerosis.

Although the malignant potential of type B3 thymoma is higher than type A, B1 and B2, accompanied by extensive sclerosing stroma and osseous metaplasia might imply a better prognosis. No recurrence or metastasis of STs and thyomas with ossification have been reported after complete surgical excision in varying follow-up periods.

In conclusion, it is the first case of type B3 sclerosing thymoma with extensive ossification and myasthenia gravis as far as we know. In consideration of its rarity, awareness of the possible occurrence of extensive ossification and sclerosis in different types of thymomas helps to avoid a diagnostic pitfall, especially in mediastinoscopic biopsy specimens.

Disclosure of conflict of interest

None.

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