



Case report

Thymoma with osseous metaplasia; a case report with a brief literature review

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ABSTRACT

Introduction and importance: The thymus is a primary lymphatic organ within the mediastinum that plays an essential role in developing and maintaining cell-mediated immunity. The current study aims to report a case of intra-tumoral osseous metaplasia of the thymus gland, which is an infrequent phenomenon.

Case presentation: A 43-year-old male presented with weakness and easy fatigability for 2 months. The patient had an elevated anti-acetylcholinesterase antibody (19.5 nmole/L). Magnetic resonance imaging showed a round, capsulated, enhanced mass in the anterior mediastinum measuring 5.5 × 3.5 cm, suspecting thymoma. The patient underwent plasmapheresis three times in one week, under general anesthesia, in a supine position, sternotomy was performed, and the thymoma was totally resected.

Discussion: Thymomas are known to occur in all age groups with the peak of nearly between 35 and 70 years with the median age of 54 years. The sex distribution of thymoma is approximately equal with slight predilection of women in old age groups. However, among all reported cases of thymomas with osseous metaplasia, the majorities are female. The significance of this ossification is still to be clarified.

Conclusion: Although it is rare, secondary changes in thymoma may occur including calcification and ossification.

1. Introduction

The thymus is a primary lymphatic organ within the mediastinum that plays a crucial role in developing and maintaining cell-mediated immunity [1]. It is dedicated for the growth of the immunocompetent T-cells, controlling the expansion and proliferation of naïve T-cells into helper T cells (CD4) and cytotoxic cells (CD8), and mature T-cells migration into the peripheral tissues [2]. Like the other organs, benign and malignant pathologies may derive from the thymus gland. Tumors of thymus gland can be thymomas, thymic carcinoma, thymic neuroendocrine tumor, thymolipomas and thymic cyst. Among all tumors, benign epithelial thymoma is the most common type [2,3]. Thymoma is a subtype of thymic epithelial tumor (TET) which is derived from the epithelial cells of the thymus [4]. It is representing nearly 0.2% to 1.5% of all malignancies [5,6].

The current study aims to report a case of intra-tumoral osseous metaplasia of the thymus gland which is an extremely rare phenomenon with a few cases reported in the literature. This case was reported in line with SCARE guidelines 2020 with a brief literature review [7].

2. Presentation of case

2.1. Patients information

A 43-year-old male presented with weakness and easy fatigability for two months. Past medical, past surgical, drug, and family history were unremarkable.

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2.2. Clinical finding

The patient was conscious. Vital signs were normal. General and chest examinations did not reveal significant finding. He had normal reflexes.

2.3. Diagnostic assessment

Hematological tests were normal. The patient had an elevated anti-acetylcholinesterase antibody (19.5 nmole/L). He was diagnosed as a case of Myasthenia Gravis. Chest X-ray was unremarkable. Magnetic resonance imaging (MRI) showed a round, capsulated, enhanced mass in the anterior mediastinum measuring 5.5 × 3.5 cm suspecting thymoma (Fig. 1).

2.4. Therapeutic intervention

The patient underwent plasmapheresis three times a week (every other day), under general anesthesia, in a supine position, sternotomy was performed and the thymoma was resected including all anterior mediastinal fats from phrenic to phrenic nerves. The histopathological examination revealed thymoma type B2 with intratumoral osseous metaplasia. The size was 4.5 cm in maximum dimension (Fig. 2). There was neither vascular invasion nor lymph node metastasis.

2.5. Follow-up

The postoperative course was uneventful. The patient remained in hospital for three days, and he was discharged on oral analgesic and antibiotics.

3. Discussion

Although the primary neoplasms of the thymus are uncommon, the most common histological form is thymoma [8]. Thymomas are considered to be an exciting pathology because of several reasons, mimicking benign lesion as it has an indolent course which makes them be confused with benign neoplasms. However, all thymomas have the ability to spread and invade other structures which give the characteristic of malignant tumors [9]. WHO histological classification system classified thymomas based on the shape of the neoplastic epithelial cell into the letters (A, B, or AB), and dependent on the increasing emergence of atypia and increasing the proportion of neoplastic epithelial cells to lymphocytes, further classified type B thymomas into (B1, B2, B3) [10]. Type A and AB generally behave like benign tumors, while type B1 is a low-grade malignant tumor, a higher degree of malignancy in type B2, and type B3 is the advanced stage of the diseases [11].

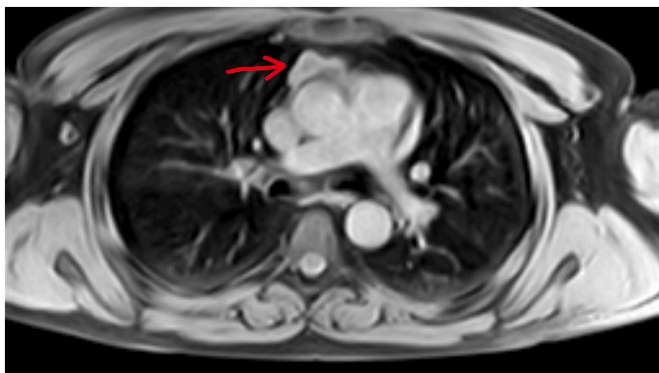


Fig. 1. Magnetic resonance imaging (MRI), axial section showing round homogenous lobulated mass in the anterior mediastinum consistent with thymoma.

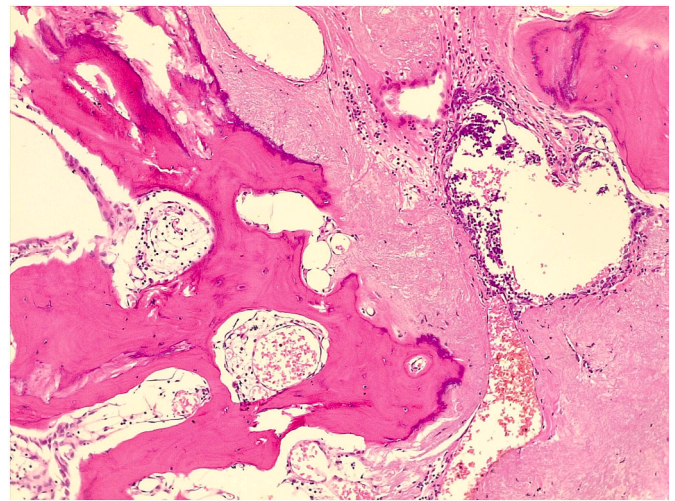


Fig. 2. Thymomas with areas of osseous metaplasia composed of mature bone trabeculae with marrow elements.

Thymomas are known to occur in all age groups with the peak of nearly between 35 and 70 years with the median age of 54 years. The sex distribution of thymoma is approximately equal with slight predilection of women in old age groups [12]. However, among all reported cases of thymomas with osseous metaplasia, the majorities are female [13,14,15]. The significance of this ossification is still to be clarified.

Patients with thymoma have a variable presentation, nearly 30% of all patients are asymptomatic, local symptoms are presented in 40%, and about 30% presents with systemic symptoms [8,16]. They are slow-growing tumors of the thymic epithelial cell with main clinical presentation including cough, chest pain, dysphagia, superior vena cava syndrome, and hoarseness [13]. Thymomas presented with variable size, ranging from a few millimeters up to 34 cm with a mean up to 10 cm at the time of diagnosis [17]. Commonly thymomas are associated with immune and nonimmune-mediated paraneoplastic syndromes including myasthenia graves, pure cell aplasia, systemic lupus erythematosus and Good syndrome [3]. Regarding disease progression, it is known that thymomas are mainly progressing locally into the mediastinum and pleural cavity, the lung is the primary site for distant metastasis, extrathoracic metastasis is extremely rare in which strongly associated with B subtype [18].

Intratumoral calcification and osseous metaplasia are two histological variants of thymomas [14]. The occurrence of calcified thymomas is reported in many studies. There is a various form of calcifications that are known to occur with the most common form in thymoma is the small foci type [19]. However, osseous metaplasia of thymomas is an extremely rare histological variation in thymic tumors, with a few cases being reported in the literature [15]. Although the actual etiology of this ossification is unclear, it is stated that the heterotrophic bone develops when the connective tissue is undergoing metaplasia [20]. However, it is reported that the osseous metaplasia may be induced by mesenchymal cells within the tumor; some others stated that the etiology of osseous metaplasia is thought to be related to the genetic, hormonal, metabolic factor or drug factors [21]. Osseous metaplasia involves the deposition of osteoid with osteoblastic differentiation of mesenchymal stromal cells and formation of bone tissue composed of osteocytes [22].

In asymptomatic patients, thymomas may be incidentally discovered on imaging, or it may be present with compression symptoms due to the mass effect [10]. On imaging, thymomas typically appear as an oval-shaped anterior mediastinal mass with obliterating retrosternal space seen on the lateral view [23]. Chest radiography may show a mass in the anterior mediastinum in 45–80% of the patients. However, if the tumor is small, it may look normal [15]. Calcifications may occur approximately in one-third of thymomas and are often thin and capsular. In

invasive thymoma; pleural thickening or nodularities may be evident [21]. Chest computed tomography (CT) scan is more accurate imaging modality in the diagnosis of thymomas, in which it is highly sensitive for mediastinal masses, thymomas characterized by having a typical appearance on CT [24]. On CT scan, typically, it appears as a well-defined, round, lobulated, and homogenous mass. The tumor may be outlined by fat and may contain punctuate course, or curvilinear calcifications [15]. However, the presence of associated para thymic condition such as myasthenia gravis, it is typically a pathognomonic for the diagnosis of thymoma [16]. The diagnosis can be confirmed through a fine needle aspiration (FNA) or open surgical biopsy, with the success rate of FNA in establishing diagnosis is nearly 60% [12].

Surgery is regarded as the cornerstone for the management of thymomas. In most cases, it is the first-line therapeutic modality for resectable tumors through which the capsule is left intact, and spoiling is avoided [25]. In the literature, at least ten different surgical approaches have been described [26]. Complete resection has been found to be the most significant part in any stage of the disease [27]. Complete surgical resection is possible in 91–94% of all patients with type B1 thymoma, and the recurrence rate is less than 10% [20]. Thymomas are generally radiosensitive and chemosensitive tumors, with a response rate up to 100% [10]. In incompletely resected tumors radiotherapy is recommended and chemotherapy is administered in unresectable stage III and stage IV thymoma [20]. The 10-year survival rate of patients with stages I and II is 80–90%. In higher-stage tumors, the 5-year survival rate ranges from 39 to 72% [10].

In conclusion, secondary changes in thymoma may occur, including calcification and ossification. In addition, there are a few cases reported regarding osseous metaplasia. The etiology of osseous metaplasia is still elusive. However, many systemic factors have been discussed as contributing agents.

Ethical approval

Approval is not necessary for case report in our locality.

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None is found.

CRediT authorship contribution statement

Fahmi H. Kakamad: surgeon managing the case, follow up the patient, writing the manuscript and final approval of the manuscript.

Ari M. Abdullah: pathologist examining the specimen. Final revision and approval of the manuscript.

Berwn A. Abdulla, Marwan N. Hassan: literature review, writing the manuscript, final approval of the manuscript.

Abdulwahid M. Salih, Hiwa O. Baba, Shvan H. Mohammed, Rawezh Q. Salih, Aso S. Muhialdeen: major contribution to the idea, revision and final revision of the manuscript.

Guarantor

Fahmi Hussein Kakamad is the Guarantor of submission.

Registration of research studies

According to the previous recommendation, registration is not required for case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Declaration of competing interest

None to be declared.

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