Case Report

Type A Thymoma with Generalised *Myasthenia Gravis*

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ABSTRACT

Thymoma is a very rare tumour arising from thymus in the anterior mediastinum. A case of a spindle cell thymoma with *Myasthenia gravis* in a 34-year-old female who presented with difficulty in breathing and swallowing with shortness of breath is reported. **[Indian J Chest Dis Allied Sci 2011;53:233-235]**

Key words: Thymus, Mediastinum, Tumour.

INTRODUCTION

Thymoma is the most common neoplasm of anterior mediastinum and originates within the epithelial cells of thymus. It accounts for 20% to 25% of all mediastinal tumours and 50% of anterior mediastinal masses.[1] It has an incidence of 0.15 per 100,000 and 30% to 40% of patients with thymoma experience symptoms suggestive of *Myasthenia gravis*. An additional 5% of patients have other systemic syndromes, including pure red cell aplasia, dermatomyositis, systemic lupus erythymatosus, Cushing's syndrome, and syndrome of inappropriate antidiuretic hormone secretion.[1]

A thymoma is an uncommon tumour, best known for its association with the neuromuscular disorder *Myasthenia gravis*.[2] About 10% to 15% of patients with *M. gravis* have a thymoma and, conversely, 30% to 45% of patients with thymomas have *M. gravis*.[3] Production of autoantibodies against the acetylcholine receptor results from an antigen-driven immune reaction that starts inside the thymus but spreads to extra-thymic sites during the early phase of *M. gravis*. Para-neoplastic *M. gravis* occurs only in type A, AB and B1-3 thymomas.[4] Abnormal micro-environment triggers non-tolerogenic T-cell selection by neoplastic epithelial cells. After transport of substantial number of naïve, potentially autoreactive T-cells to extra-tumorous sites, T-cell activation outside the thymoma initiate the autoimmune process.[4]

CASE REPORT

A 34-year-old female presented with a mass in the anterior mediastinum. She was apparently well two years back when she developed sudden ptosis of the left eyelid with dysphagia and dyspnoea. The muscles of face, eyes and jaws were involved. She had diplopia and difficulty in speech. There was a progressive bulbar and neck muscle weakness. She was diagnosed as a case of *M. gravis* and was treated with intravenours corticosteroids and neostigmine. Computed tomography (CT) of the chest done because of respiratory symptoms showed a well-defined heterogeneously enhancing mass (4.8cm×2.0cm×1.9cm) in the anterior mediastinum (Figure 1) with peripheral calcification. The lungs, bronchi and trachea were normal with a radiological diagnosis of thymoma, the patient was admitted for excision of the mass and after controlling symptoms of *M. gravis*, she underwent thymectomy.

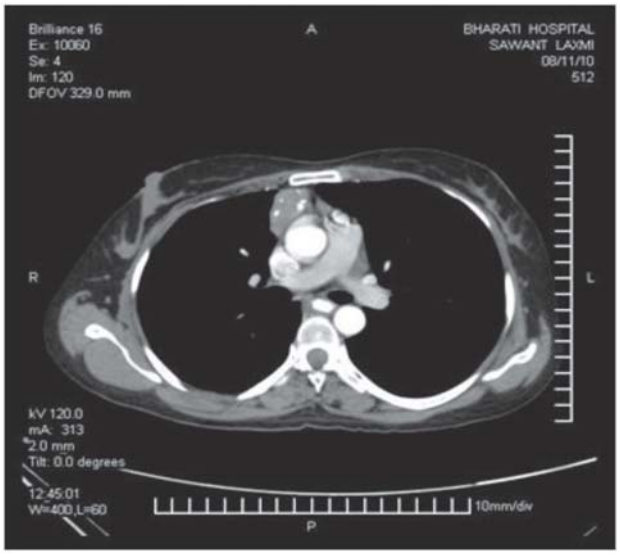

Figure 1. Computed tomography of the chest showing a well-defined mass (arrow) in the anterior mediastinum with peripheral calcification.

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Grossly it was a single nodular, encapsulated firm mass measuring 6.5cmx3cmx1.5cm. The external surface appeared yellowish grey. On cut-section, the tumour appeared lobulated with yellowish and grey areas. Few dark brownish and black areas of haemorrhage/congestion were also noted (Figure 2).

Microscopic examination showed a tumour mass surrounded by a thick fibrous capsule showing dystrophic calcification (Figure 3). The tumour had infiltrated the capsule but was not found traversing across the capsule. The tumour cells were epithelial, present in sheets and short fascicles of spindled tumour cells with elongated nuclei and dense chromatin (Figure 4). Majority of the tumour cells were polygonal with pale cytoplasm and indistinct cytoplasmic borders giving them a syncytial appearance. The nuclei were round to oval, vesicular and had indistinct nucleoli. Mitotic figures were sparse. Activated lymphocytes with convoluted nuclei were distributed throughout the tumour. Perivascular spaces with oedema fluid and lymphoid infiltrate, pseudoglandular formations were few and seen mainly at the periphery of the lobule. A diagnosis of type A thymoma (World Health Organization [WHO] classification) with stage I (modified Masaoka staging system) was made. Immunohistochemistry (IHC) showed tumour cells positive for pancytokeratin proving its epithelial origin (Figure 5).

The tumour was negative for CD5, CD 117 and p53 that ruled out a thymic carcinoma.

Figure 2. Specimen of thymoma showing external and cut-surface

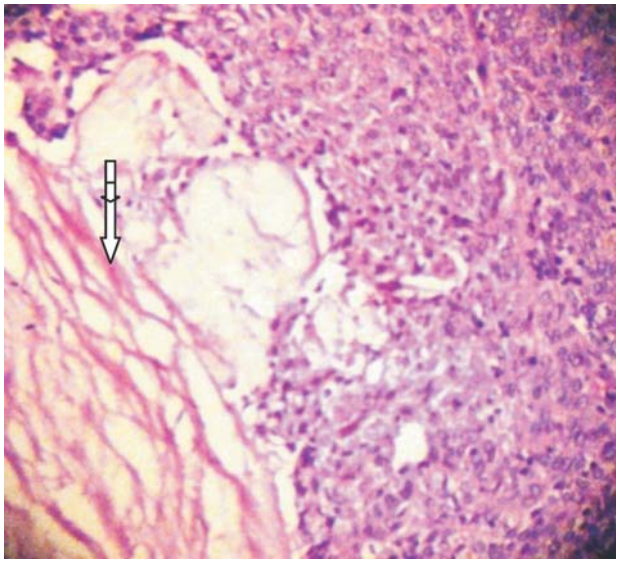

Figure 3. Microscopic photograph of the tumour mass showing thick capsule, pseudoglandular spaces and epithelial component (Haematoxylin-eosin×100).

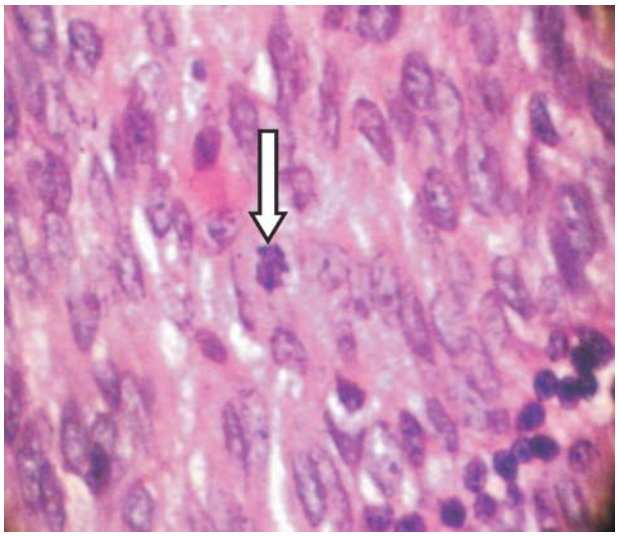

Figure 4. Histopathological picture showing spindle cell component and occasional mitotic figure (Haematoxylin-eosin×100).

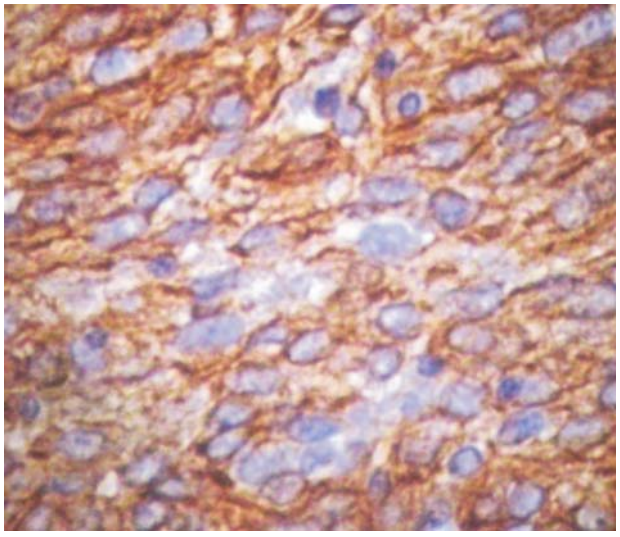

Figure 5. Photomicrograph showing strong pancytokeratin positivity (IHC×400).

DISCUSSION

A thymoma is a thymic epithelial neoplasm exhibiting some organotypic features, accompanied by variable number of reactive lymphoid cells. Organotypic features include lobulation, medullary differentiation, perivascular spaces and the presence of immature T-lymphocytes. The peak incidence is in the 5th and 6th decades of life with a male preponderance.[5] One-third of the patients present with symptoms attributed to mediastinal mass such as dyspnoea and hoarseness. A type A or B thymoma can be associated with *M. gravis* (15% for type A, 40% for type B1 and 50% for type B2 and B3 thymomas). There are no known aetiological factors for a thymoma in humans. The single most important prognostic factor for a thymoma is its tumour stage (modified Masaoka staging system).[5] Apart from that, the completeness of excision and tumour size (>11 cm carrying a bad prognosis) are other important prognostic factors.[5] *Myasthenia gravis* was previously thought to be an adverse prognostic factor but recent studies have not substantiated this.[5]

On electron microscopy, thymoma cells possess multiple inter-digitating elongated cell processes connected by desmosomes. Intra-cytoplasmic tonofilaments are often prominent.[5] Type A thymomas show few genetic alterations with 6p deletion being a recurrent alteration.[5]

The main differential diagnosis in this case was a thymic carcinoma, but was excluded by a negative CD5, CD117 and p53 markers.

On IHC, the epithelial component of a thymoma stains for cytokeratin (CK) and the epithelial membrane antigen (EMA) and variably with CD57.[5] In type A thymoma, interspersed glandular structures show stronger staining for cytokeratin than the spindled tumour cells. Neoplastic epithelial cells of type A thymoma may stain with B cell markers, such as CD20. The lymphoid component is made-up of immature T lymphocytes positive for TdT, CD 1a, CD3 and CD 99a. The differential diagnosis includes neuroendocrine tumours, Hodgkin's lymphoma and non-Hodgkin's lymphoma and thymic carcinoma.

A thymoma is an uncommon tumour with a largely indolent growth pattern. It has malignant potential as a result of its ability to invade locally and metastasise regionally and is often associated with a number of immune- and non-immune-mediated paraneoplastic syndromes. Surgery is the mainstay of treatment, with adjuvant radiotherapy recommended for an invasive thymoma. In incompletely resected and inoperable patients, chemotherapy may be added.[6]

The WHO classification of thymic epithelial tumours reflects their oncological behaviour. Type A, AB and B1 tumours have better prognosis than types B2 and B3 tumours, suggesting the significance of this classification in the clinical practice of thymomas. Type B tumours are more invasive than type A and AB tumours. Type B1 and B2 tumours are frequently associated with *M. gravis* while type A and AB tumours are not. On CT imaging type A and AB tumours tend to be round and have a smooth surface while type B1, B2 and B3 tumours are often flat and have irregular surfaces. Type AB, B1 and B2 tumours possess a significant number of CD4+CD8+ double positive T cells in the tumour.[8]

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