Original Article

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Clinico-Pathological Analysis of Thymic Epithelial Tumours: An Institutional Study

Divya S, Sreeja Raju*, Joy Augustine and Ajay Kumar

Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala. India

ABSTRACT

Background: Thymic epithelial tumours are anterior mediastinal neoplasms and they exhibit a spectrum of histomorphological features.

Methods: In this study we analysed the clinico-pathological spectrum of thymic epithelial tumors at our institution. It is a retrospective and descriptive study done at our Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala over a period of ten years from August 2008 to August 2018. Histological sections of each case were meticulously analysed. Immunohistochemistry was done if needed.

Result: In this study 17 cases of thymic epithelial tumors were analysed. A male preponderance of 58.8% was observed. Age ranged from 24 to 73 years with a mean age range of 54.4 years. Most common histological subtype of thymoma was Type B and Type AB. 4 cases were associated with myasthenia gravis. Masaoka Stage I was commonly observed.

Conclusion: Thymic epithelial tumors are a unique group of anterior mediastinal neoplasms which also pose a diagnostic challenge. This study highlights the significance of clinico-pathological correlation and staging of thymic neoplasms.

Keywords: *Anterior mediastinum, Thymic epithelial tumours, Myasthenia gravis, Masaoka staging*

Introduction

Thymomas are a group of neoplasms which arise from or exhibit differentiation towards thymic epithelial cells[1]. Thymic epithelial tumors (TET) include thymomas and thymic carcinomas (TCs). Even though thymomas are the commonest of anterior mediastinal neoplasms accounting for about 20% of mediastinal neoplasms, their overall incidence is rare[2]. Usually thymomas are slow growing tumours, but around 40% of them may show rapid increase in growth. Complete surgical resection is the primary treatment of choice. The most common paraneoplastic disease associated with thymoma is myasthenia gravis (MG). Around 30-40% of patients with thymoma have associated myasthenia gravis[3]. Morphologically there are two major types of thymoma: type A and type B. In type A, the neoplastic epithelial cells have a spindle or oval shaped nucleus with a uniform bland cytology. In type B, the tumor cells have a predominantly round or polygonal appearance. Type B thymomas are further subdivided into B1, B2, and B3 depending on the degree of atypia and lymphocytic component. Thymomas combining type A with type B features are designated type AB. Non-invasive thymoma in general is associated with a good prognosis. Staging rather than histologic classification provides the most important prognostic information. The prognosis of patients with thymoma largely depends on the Masaoka stage of disease. Patients with stage III or IV tumour have poorer prognosis compared to patients with stage I and II tumors[4]. In our study we evaluated TETs resected at our centre over a period of 10 years. A correlation of clinical and histopathological features was done.

Materials and Methods

We conducted a retrospective study over a period of 10 years. In each case the clinical and radiological data were retrieved from the hospital records and all the histopathological slides were reviewed independently by two pathologists. Each patient was evaluated under the following parameters - age, sex, presenting complaints, association with myasthenia gravis, radiological imaging, histological type in CT guided biopsy if any and in the excision biopsy specimen, presence or absence of capsular invasion and Masaoka stage. The specimens consisted of both excision and CT guided tru-cut biopsies. Tissue was fixed in 10% buffered formalin and processed. The blocks were serially cut, each of 3-5µ thickness and the sections stained with Hematoxylin and Eosin. The histopathological findings were studied and relevant immunohistochemistry was done in required cases. Histological typing was done using the WHO system of classification for thymomas. Masaoka staging was followed for all cases.

Result

In this retrospective study conducted at our centre over a period of 10 years we analysed 17 cases of thymoma which we received at our department. In this study age range of patients were from 24 to 73 years with a mean age of 54.4

years. Majority of cases were seen in the 61 to 70 age group. Only 2 cases were noted below 40 years of age.

In our study a slight male preponderance was noted with 10 males (58%) and 7 females (41%). In majority of cases the presenting complaint was cough, closely followed by shortness of breath. Other symptoms included chest pain and generalized weakness. In one case it was an incidental finding of a mass on chest radiograph. 4 cases showed association with myasthenia gravis. All 4 cases were seen in male patients who presented with symptoms related to muscle weakness. In all cases chest X -ray along with CT scan was done. In one case alone MRI was done. All cases confirmed the presence of mediastinal mass with invasion detected only in 3 cases radiologically .

CT guided biopsy was done in 9 cases and in which a definite diagnosis of thymoma was reported in 6 cases. 2 cases were inconclusive and 1 case was reported as carcinoid.

All 17 patients underwent excision biopsy. Mean tumor size was 8.9cm. The smallest tumour size noted was 2.5cm in maximum dimension.

We observed 2 cases of Type A thymoma, 7 cases of Type B and Type AB thymoma and one case of Thymic carcinoma. Of the Type B thymomas we observed 3 cases each of B2 and B3 thymomas and one case of Type B1 thymoma. MG association was detected in 2 cases of type B2 thymoma and one case of type B1 and type AB respectively.

Immunohistochemistry was done in B1 thymoma in which we had a differential diagnosis of lymphoma. Cytokeratin positivity confirmed Thymoma. A total of 9 cases showed evidence of capsular invasion on microscopy.

Table 1: Masaoka staging and correlation.

Stage	Description	No of cases
I	Macroscopically encapsulated and no microscopic capsular invasion	8
IIa	microscopic transcapsular invasion	2
IIb	Macroscopic invasion into thymic or suuronding fatty tissue or grossly adherent to (but not breaking through) mediastinal pleura or pericardium.	3
III	Macroscopic invasion into adjacent organ(s)	1
IVa	Pleural or pericardial dissemination	1
IVb	Lymphogenous or hematogenous metastasis	2

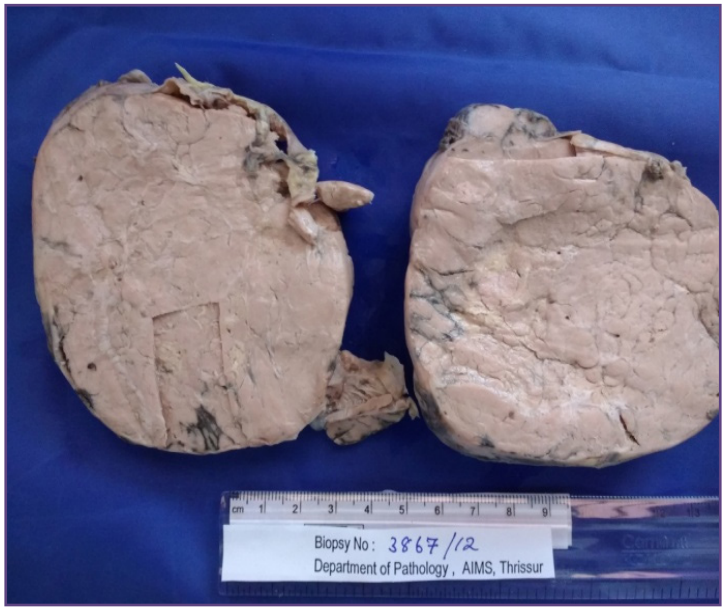

Fig. 1. Gross showing lobulated appearance of thymoma.

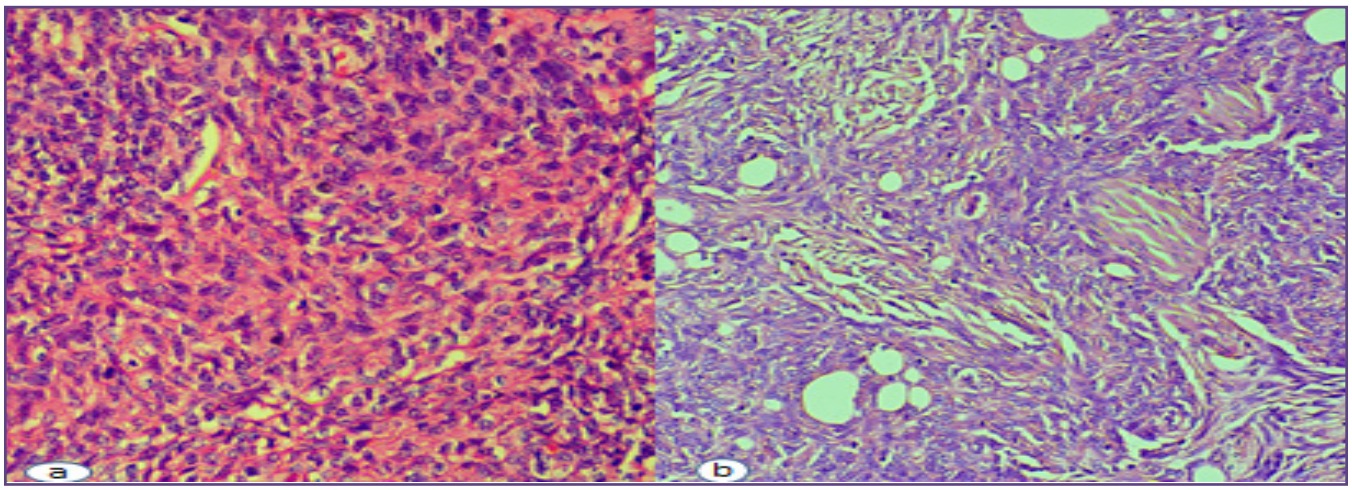

Fig. 2(a) Type A thymoma showing spindle shaped cells arranged in fascicles (H&E ;400X).(b)Type AB Thymoma with lobules of plump cells and lymphocytes(H&E;400X).

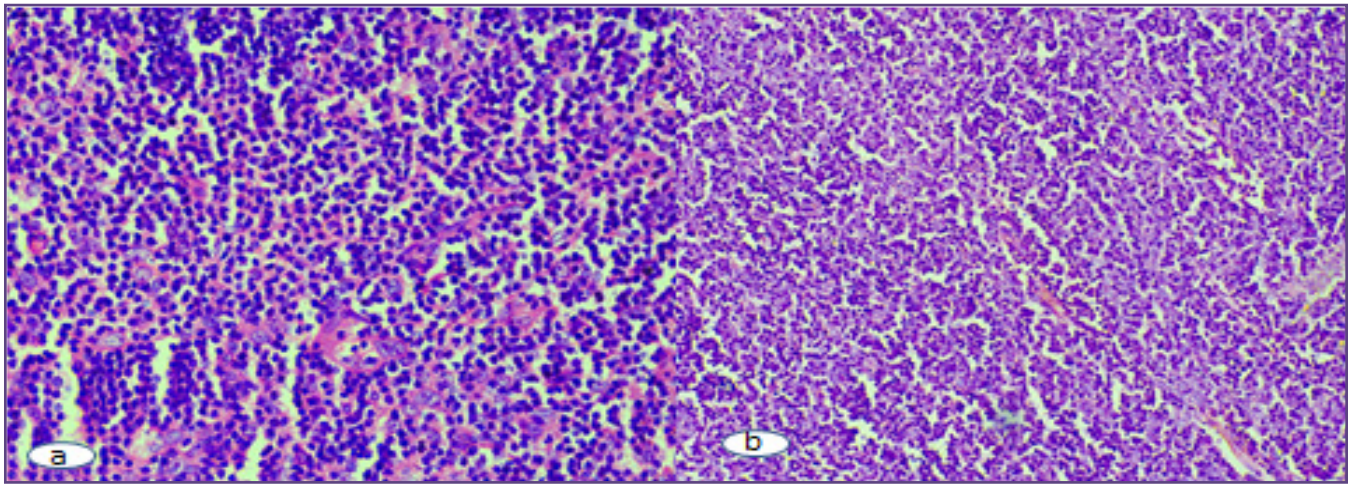

Fig. 3a)Type B1 thymoma showing predominant population of lymphocytes(H&E;400X) b)Type B2 thymoma showing polygonal cells with vesicular nuclei admixed with lymphocytes(H&E;200X).

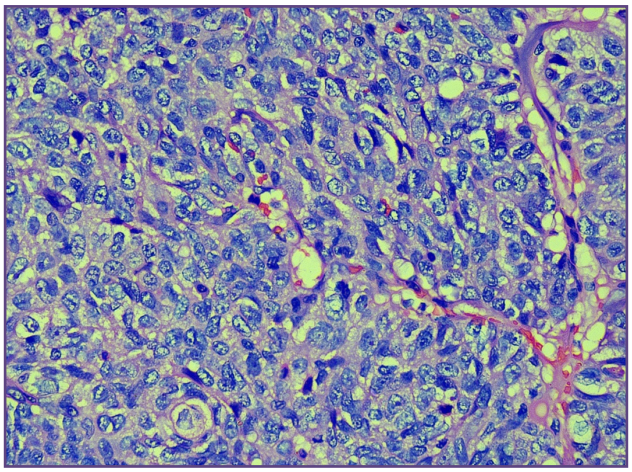

Fig. 4 :Type B3 thymoma with polygonal cells and squamous eddie(H&E;400X).

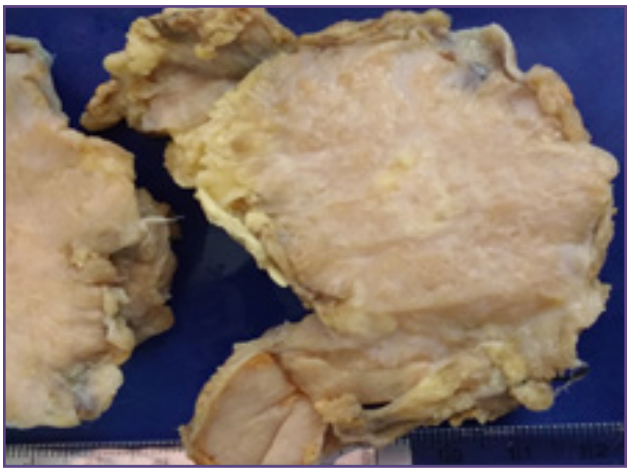

Fig. 5: Gross showing invasion into adjacent fatty tissue.

Discussion

Thymomas are the most common neoplasms of the anterior mediastinum with an incidence of 1.5 cases per million[5]. Several systems of classification of thymomas have emerged over the years. All our cases were analysed according to the WHO classification. In our study mean age was 54.4 years. This is in agreement with the study by Sperling et al [6].Our study showed slight male preponderance which was in concordance to the findings by Shamshuddin F et al[7] .

With exception to one case where it was an incidental finding, all other cases in our study were symptomatic. This is similar to the study done by Brita Sperling et al[8].

There is considerable variation in the size of thymomas. Thymomas are usually encapsulated, lobulated grey-white to yellowish lesions. Foci of infiltration can also be appreciated grossly.Hemorrhage , cystic degeneration and necrosis can also be noted. It is advisable to take multiple sections to rule out foci of microinvasion. In our study mean tumor size was 8.9cm which is in concordance with the analysis of Sperling et al[6] .

In our study we found 7 each of epithelial and lymphoepithelial types of thymomas (AB and B) which is in agreement with studies on histologic type of thymomas done by Lewis & coworkers[9],Masaoka & co-workers[10], Chen & co-workers[11] , Nakagawa & co-workers[12] and Weis C A & co-workers[13]. Of the type B thymomas in our study we observed 3 cases each of type B2 and B3 thymoma.

Various autoimmune diseases have been noted to be associated with thymomas of which MG is most common. In our study we observed 4 cases of MG. All cases were seen in male patients. Most common symptom associated with MG was muscle weakness and ptosis. Presence of MG was confirmed by neostigmine test. Symptoms attributed to MG were found in only 23.5% of patients. Our incidence is comparatively low when compared to other studies where an incidence of 30% to 60% was observed[6].MG was most frequently observed in type B2 thymoma along with each of Type B1 and Type AB thymoma. This is in agreement with the first Indian study done by Rathod et al[14].

Thymoma is curable disease with good clinical outcome and needs multidisciplinary approach. Surgery remains the primary treatment in thymoma therapy and median sternotomy with complete thymectomy is the operative approach. Complete resection is the aim to avoid recurrence. In this study excision was done in all cases[15]. Post operative adjuvant therapy in the form of radiation is recommended for invasive thymoma regardless of the resection status. In patients with stage II and above, adjuvant radiation therapy may be beneficial to reduce local recurrence without effect on survival. In our study 8 cases with invasion received adjuvant radiotherapy. In localized, surgically resectable thymoma, chemotherapy is being adopted in selected patients with inoperable or gross residual disease; eventhough it has not been recommended as the treatment of choice. Staging is the single most important prognostic factor predicting outcome. In our study maximum number of cases belonged to Masaoka stage I.

In our study treatment outcome could not be analysed as few patients were lost to follow up.

Conclusion

Thymic epithelial tumours are a unique group of anterior mediatinal neoplasms. This study highlights the significance of clinico-pathological correlation of thymic neoplasms over a period of 10 years .

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***Corresponding author:**
Dr. Sreeja Raju, Assistant Professor, Department of Pathology, Amala Institute of Medical Sciences, Thrissur, Kerala, India Pincode-680555
Phone: +91 9656110119
Email: sreejaraju_06@yahoo.co.in

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