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A clinicopathological study of thymic neoplasms: Nine-year experience at a tertiary care hospital in western Maharashtra, India

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Abstract

Introduction: The thymuses are quite rare neoplastic lesions arising in anterior mediastinum seen in the adults. The histological spectrum varied from the encapsulated thymoma to the thymic carcinomas. Further subtyping into various groups on the basis of morphology with immunohistological findings have gained the popularity as depicted by the latest WHO classification of thymomas. A few studies have been done to ascertain the characteristics of thymic neoplasms in Indian population.

Methodology: 09 years retrospective analysis of the total 17 thymoma cases reported from year 2011 to 2019 were assessed for histomorphological features with clinical findings, age, sex and staging.

Results: The commonest subtypes were of B2 and B1 types with type A, AB and B3 being rare. Mostly the cases were of low grade. Myasthenia Gravis was associated with only 02 thymomas.

Conclusion: The morphological classification and staging of thymomas should be used in surgical pathology reporting.

Keywords: Thymoma, thymic neoplasm, myasthenia gravis

1. Introduction

The thymus is a site for a spectrum of tumours and tumour-like lesions, besides playing a primary role in the differentiation of T lymphocytes. Thymus may be the primary site of thymomas, lymphomas, germ cell tumors and neuroendocrine tumors. Thymomas account for 20-30 percent of tumors in the anterosuperior mediastinum and are the most common tumor in this location in the adults ^[1]. A combination of epithelial cells and lymphocytes results in a varied histomorphology of thymomas. A spectrum of thymic epithelial tumours (TET) exists, comprising encapsulated thymoma, invasive thymoma and thymic carcinoma. They have posed a diagnostic challenge to the pathologists by their array of histological features and has also resulted in varied classification systems in the literature.

The latest 2015 World Health Organization (WHO) classification, subsequent to the International Thymic Malignancy Interest Group (ITMIG) consensus, has revised and refined the histological and immunohistochemical (IHC) diagnostic criteria for a more reproducible subtyping and distinction between different subtypes of thymomas (type A, AB, B1, B2 and B3). The WHO scheme is currently the most widely accepted because it correlates with clinical behavior and outcome ^[2, 3].

A very few studies have been carried out to ascertain the characteristics of thymic neoplasms in the Indian population. Most of the Indian studies available in the literature are based on the clinical and imaging characteristics of thymomas. This study was aimed to evaluate the histopathologic spectrum and clinical profile of thymic neoplasms diagnosed at a tertiary care centre in western Maharashtra, India during a period of eight years (2011-2019).

2. Objective

We aimed to review our experiences with thymic neoplasms and highlight the various aspects of its clinical presentation, histopathology and immunohistochemistry (IHC) in western Maharashtra population.

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3. Methodology

A 09 year retrospective review done on pathology reports and histology slides which were retrieved from the archives of the department of Pathology at a single cardiothoracic centre, Western Maharashtra, India between August 2011 and July 2019. Cases included both thymectomy and tru cut biopsies. The clinical details including age, sex, clinical presentation, status of myasthenia gravis (MG) and capsular microinvasion were obtained from the case files/ reports preserved in the department of pathology.

Immunohistochemistry (IHC) was carried out on respective paraffin embedded tissue blocks and the slides were reviewed by two pathologists to assign the histological typing to these cases as per latest WHO- 2015 classification and staged in accordance with the Modified Masaoka-Koga staging system.

4. Results

Out of total 17 cases, 16 cases of thymic neoplasms^[14] (resections and 02 biopsies) were included in the analysis. One case only showed normal cellular components on histomorphology, hence excluded.

Mean age was 36 years and the age of the patients varied from 01 year to 75 years. There was a male preponderance (men 11 and women 05), with a male-to-female ratio of 2.2: 1. The mean age among women was 49 yrs and among men was 30 yrs. Types A and AB were almost equally distributed between either sex, but thymomas with Type B histology (B1, B2 and B3) were predominant in men (62%). It was also observed that predominantly cases were of stage 1 and no case found in stage III/ IV. However, age of the patient had no effect on the stage of disease. 03 out of 04 children (<10 years) were having type B1 thymomas on histomorphology.

The clinical case details were available in 14 cases, of whom all patients were symptomatic. Most common clinical finding was mediastinal mass in anterior mediastinum. The association of myasthenia gravis (MG) was observed in men (two months to six months duration). Three presented with congenital heart disease. Only 1 patient had local symptoms related to compression including cough, chest pain, dyspnoea and dysphagia. There was no correlation of stage of tumor with myasthenia gravis (MG).

4.1 Gross examination

The weight of the tumour ranged from 2.5 to 100 g. The maximum tumour dimension ranged from 1 to 07 cm, with a mean of 04 cm. few of the tumours were large (more than 6 cm). All had the characteristic lobulated, homogeneous grey-white cut surface. 14 resected specimen were wholly or partly encapsulated, while two were small biopsies. The size of the tumour had no significant association with histology,

stage and the presence of MG in patients.

4.2 Histomorphological findings

The most common histomorphologic type was B2 (06 of 14 cases; 43%) followed by B1 (05 of 16 cases; 31%). Types A, AB and B3 had 1 case in each subtype (6%).

On histomorphology. All the tumours had lymphocyte-rich lobules, separated by thin fibro-vascular septa. The epithelial cells were barely discernible, polygonal in shape with a moderate amount of pink cytoplasm, round to oval vesicular nuclei and small nucleoli.

4.2.1 Type A and AB thymoma: The morphological spectrum of Type A and AB thymomas. The epithelial component of type A thymoma cases showed purely spindle cells in solid sheets and AB thymomas showed an admixture of spindle cells (type A component) with round epithelioid cells (type B-like component). Perivascular cystic change with focal areas of meningothelial whirling noted (Fig.1A - C).

4.2.2 Type B1, B2 and B3 thymoma: Type B1 thymomas showed lymphocyte predominance with few small scattered neoplastic epithelial cells resembling normal thymus (Fig 2A). IHC showed positivity of scattered epithelial cells for Cytokeratin. Type B2 had increased epithelial component as compared to Type B1 composed of large polygonal neoplastic epithelial cells admixed with large number of non-neoplastic immature T cells (Fig 2B). Type B3 looked pink on haematoxylin and eosin (H&E) staining with sheets of epithelial cells that showed nuclear atypia and scattered or absent lymphoid cells (Fig.2C). Three of the 16 cases (18%) showed a mixed pattern in various combinations with a predominant histology of one subtype co-existing with minor components of other subtypes. The two most common such combinations were predominantly Type B2 and type B1. Thymic carcinoma exhibited marked cytological atypia, mature lymphoid cells and lack of organotypic differentiation of thymoma.

4.3 Correlation of Histomorphology with stage

Of the 16 specimens, stage could not be determined in 1 case of lipothymoma and 02 cases of small tru cut biopsies received in multiple fragments. 10 of the 13 resection case (77%) were Stage I disease. Stage IIA disease were seen in the remaining 3 (23%). No case having higher stage was noted (i.e. stage III & IV). It was noted that patients with stage I & IIA tumour were mostly men. Type A and AB thymomas were predominantly (02 of 16) higher stage (II), whereas 10 of 16 cases (62.5%) of lower stage tumours were Type B thymomas (Types B1, B2 and B3).

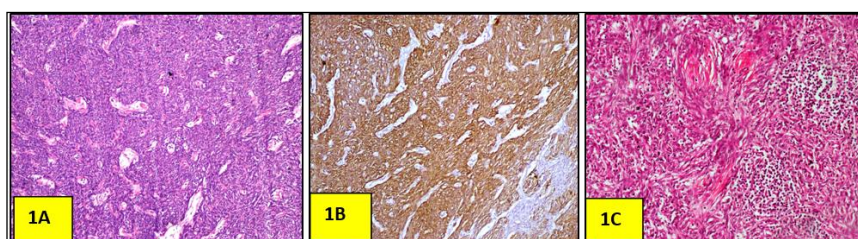


Fig 1A: Type A Thymoma, spindle cell population; 1B: CK Immunohistochemistry highlights spindle cells, 1C: Type AB thymoma, composed of dual population of spindle and round cells.

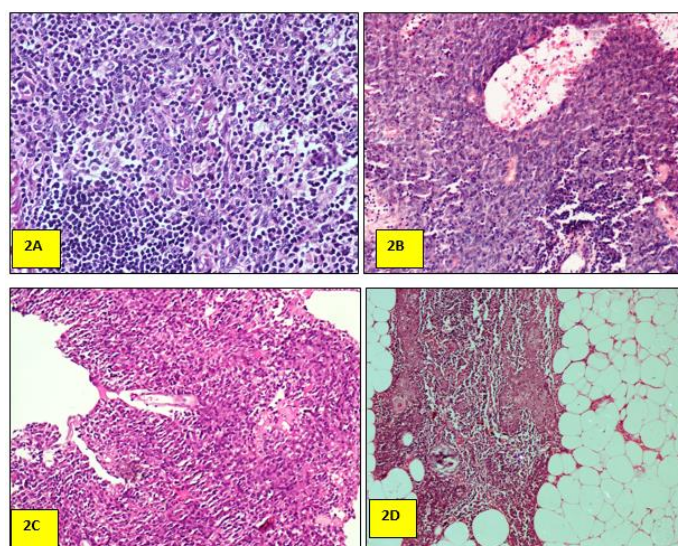


Fig 2A: Type B1 Thymoma, predominantly lymphocytes with occasional neoplastic thymic epithelial cells; **2B:** Type B2 thymoma, predominantly showing large, polygonal epithelial cells; **2C:** Type B3 thymoma, showing large atypical cells; **Fig 2D:** Lipothymoma composed of neoplastic cells with adipocytes.

5. Discussion

Thymomas are relatively uncommon group of benign or low-to- moderate grade thymic epithelial neoplasms. The worldwide incidence of thymomas is about 1.3-2.5 million per year [4]. They usually occurs in older patients of 50 to 60 years old and rare in younger individuals. These may be asymptomatic or present with anterosuperior mediastinal mass, rarely in ectopic locations. They may also present as local obstructive symptoms. Upto half of the tumor are associated with myasthenia gravis (MG), whereas 20-30% patients of MG have thymoma. Rarely associated with other paraneoplastic syndromes like pure red cell aplasia, hypergammaglobulinemia and SLE.

The incidence of thymoma in Indian population has not been precisely defined and in the previous studies including one by Julka *et al.* on 70 cases of thymomas among the Indian patients [5]; histomorphological spectrum was not described. Except for studies by and Sundaram *et al.* [6], Vaideeswar *et al.* [7] and Guleria P *et al.* [17], none of the studies have assessed the histomorphology of thymic neoplasms. These studies have not used recent WHO classification. Sometimes the distinction between thymic carcinoma and type 3 thymoma pose a challenge and its possible that some of these historic reports of thymic carcinomas must have mixtures of type 3 thymoma and carcinoma. Thymic carcinomas may present at an advanced stage and hence may not be amenable to surgical resection. In our resection specimen only one case of carcinoma was noted.

Globally, no sex predilection was noted for thymoma. Indian studies have shown male preponderance same like in our study [5, 8]. Few studies on thymoma have shown female preponderance in indian patients [9].

Thymomas are frequent in the age group of 40-60 yrs, but a wide range has been reported from <10 yrs to >80 yrs [10]. The same has been reflected in our study having 25% cases with age <10 years.

Myasthenia Gravis (MG) was the commonest paraneoplastic syndrome associated with thymoma in our study like previous studies [5]. However, association of MG with lower stage tumors can't be ascertained in our study.

Tumor size of thymic neoplasm is also a prognostic factor

[11]. In our study size varied from 1-7 cm, although showed no substantial association with either the histomorphological type or stage of the disease.

The morphological classification and staging of thymomas have been extensively debated upon since long, with at least 24 histomorphological classifications and 15 staging systems proposed till date [12, 13]. In our study, the latest modifications of WHO 2015 classification of Thymic epithelial tumors was applied. Type B thymomas were predominant with type B2 being the most frequent subtype in our study as also seen in the Indian as well as other Asian studies [14]. Type B1 and type B2 thymoma pose a diagnostic challenge with mixed histomorphology and CK immunostaining was performed in our study along with TDT.

The ITMIG worldwide database1 revealed a higher frequency of Types AB and B3 in Asians and lower incidences of type B2, which was contrary to our findings. In our study, it revealed a higher prevalence of Stage I tumours as seen previously in Indian literature barring a few [15].

The power analysis carried out by the International Thymoma Study Group in Indian population, suggested a study of a larger cohort to establish the characteristics of thymomas in various subpopulations [16].

The limitation of this study was lack of follow up and hence, survival analysis of the various thymoma subtypes and their stages could not be formulated.

6. Conclusion

The thymomas evaluated in our study were most commonly of B2 and B1 histotypes, with Types A, AB and B3 being rare. Most of these were Stage I tumours. MG was associated with only 02 thymomas and hence, no association with lower-stage thymomas was ascertained. The prognostic importance of grading and staging of these rare lesions could not be elucidated in the present study. The difference of the tumour profile in Maharashtrian population (Indian patients) as compared to the Western population suggests the uniqueness of these tumours needing molecular characterization and further evaluation to decode biology of these uncommon thymic neoplasms.

Table 1: List of cases included in the study

Case No.	Age/ Sex	Tumor Size	Clinical diagnosis	Histology (Type)	Capsular infiltration	Modified Masaoka Stage
1	46/M	1.5 cm	-----	B2 thymoma	No	I
2	50/F	2 cm	-----	B1 thymoma	No	I
3	63/M	3 cm	Myasthenia gravis with thymoma	B2 thymoma	Yes	II A
4	44/M	1 cm	? Thymoma	B3 thymoma	no	---, Tru cut biopsy
5	50/F	4 cm	Mediastinal mass	Type A thymoma	yes	II A
6	55/M	2 cm	Ant mediastinal mass	Type AB thymoma	yes	II A
7	2/ M	4 cm	Thymic mass	Type B1 thymoma	no	I
8	24/ F	3.5 cm	Dyspnoea, obstructive symptoms	Type B2 thymoma	No	I
9	47/ F	4 cm	Mediastinal mass	Lipothymoma	no	-
10	34/M	5 cm	Myasthenia gravis	Type B2 thymoma	no	I
11	45/M	6 cm	Thymic mass	Type B1 thymoma	no	I
12	6/ M	7 cm	Congenital heart disease + hypertrophied/vascular thymus	Type B2 thymoma	no	I
13	8/ M	6 cm	Congenital heart disease (VSD)	Type B1 thymoma	no	I
14	29/M	7 cm	Ant mediastinal mass	Type B2 thymoma	no	I
15	75/ F	5 cm	Mediastinal mass	Thymic Carcinoma	yes	USG guided biopsy
16	1/ M	4.5 cm	Tetralogy of Fallot	Type B1 thymoma	no	I
17	55/ M	---	Myasthenia Gravis (Tissue blocks for review)	Normal cellular components	--	---

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8. Conflicts of Interest: None.

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