Original Article

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Histopathological Study and Immunohistochemistry of Mediastinal Masses of Anterior Compartment

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Abstract

Background: The mediastinum is the mid portion of the thoracic cavity, further divided into the anterior, middle, and posterior mediastinum. The numerous organs within the mediastinum make it prone to the development of various lesions. About half of all mediastinal masses occur in the anterior compartment. The most common are thymoma, lymphoma and mature teratoma. An accurate histopathological diagnosis is required for the management of mediastinal lesions.

Methods: This is a 2-year prospective study conducted in the Department of Pathology on Biopsies and Resected Specimens of Anterior Mediastinal Masses (AMM) in a tertiary care hospital from September2020-September2022. Sections were studied after staining with hematoxylin and eosin(H&E). Immunohistochemical (IHC) stains were done wherever required.

Result: The present study included 58 cases of AMM. The age of the patients ranged from 2-77 years. Males constituted 68.90 % of cases. The male-to-female ratio was 5:2.2. Cough was the most common presenting symptom. Thymic pathology was detected in 56.8% of cases, of which thymoma is the most common. Thymoma presented with Myasthenia Gravis (M.G.) in 2 cases. Lymphoma constituted 12% of cases. Metastatic carcinoma in 12%, Extragonadal Germ Cell Tumor (EGCT) in 8.6% and lymphangioma in 3.4% cases. Lipoma, sarcoidosis and myofibroblastic tumor each constitute 1.72% cases.

Conclusion: The present study describes the various lesions of the anterior compartment.

Keywords: *Anterior Mediastinal Mass, Myasthenia Gravis.*

Introduction

The mediastinum is the mid portion of the thoracic cavity, compartmentalized into anterior, middle & posterior mediastinum [1]. The anterior mediastinum constitutes numerous organs making it prone to the development of a variety of lesions, be it inflammatory or neoplastic, benign or malignant, primary or metastatic [2]. Mediastinal masses are infrequent lesions and account for approximately 3% of tumors in the chest [3]. More than half of these masses occur in the anterior compartment, the most common being thymoma, lymphoma and teratoma [4]. Most of the lesions are in the anterior mediastinum, with 34.5% benign and 27.6% malignant tumors [5]. Many patients with mediastinal tumors present with chest pain, dyspnoea, cough and weight loss [3]. Among anterior mediastinal masses, thymomas are seen associated with Myasthenia Gravis (M.G.) [6].

An accurate histopathological diagnosis is required for the management of mediastinal

lesions [5]. Core needle biopsies are increasingly used in anterior compartment lesions [2]. The site of the lesion in the mediastinum, correlated with the clinical and radiology findings, aids in narrowing the differential diagnosis [5].

The present study describes the histomorphology of various AMM and correlates with clinical symptoms in a tertiary care teaching hospital in Dakshina Kannada district.

Material and methods

This is a 2-year prospective study conducted in AJIMS & R.C., Mangalore, from September 2020-September 2022 in the Department of pathology on all biopsies and resected specimens of Anterior Mediastinal Masses (AMM). The present study included 58 cases of AMM. The baseline data will be represented in the form of tables and diagnosis. This data will be used to perform a chi-square test to determine the level of significance if any found. The excluded cases were middle and posterior mediastinal masses. The patient's age, sex, site of the lesion and clinical features were obtained from hospital records. Non-surgical (Ultrasonography (USG) or computed tomography (C.T.) guided trucut biopsy) and surgical approaches were

performed to obtain the tissue. The study was conducted after attaining the Institutional Ethical Committee clearance.

Tissue samples received were subjected to histopathological study.

- Paraffin-embedded sections were prepared, serial sections were done and stained with H&E.
- Histomorphology of the lesion was studied.
- Relevant immunohistochemical markers were used wherever needed to confirm the diagnosis.

All the slides of the cases were reviewed, and impressions were recorded.

Result

Of the 58 cases of AMM included in the present study, the age of the patients ranged from 2-77 years. Males were 40 and females were 18. Male to female ratio was 5:2.2. In the present study, biopsies were 75.8%.

The histopathological diagnosis of AMM has been shown in Table 1.

Table 1: Histologic Types of Anterior Mediastinal Masses

Type of AMM	**Number of cases**	**Percentage of cases**
1. Thymic pathology	33	56.80%
2. Lymphoma	7	12%
3. Extragonadal GCT	5	8.60%
4. Metastatic carcinoma	7	12%
5. Spindle cell Sarcoma	1	1.72%
6. Lymphangioma	2	3.40%
7. Inflammatory Myofibroblastic tumor (IMT)	1	1.72%
8. Lipoma	1	1.72%
9. Sarcoidosis	1	1.72%
TOTAL	58	100

Table 2: Clinical Features of AMM

Clinical Presentation	**Number Of Cases**	**Percentage**
Cough	30	51.70%
Dyspnea	15	25.80%
Dysphagia	9	15.50%
Asymptomatic	2	3.44%
Myasthenia Gravis	2	3.44%

Mediastinal lesions show a wide histopathological spectrum. In the present study, thymic epithelial lesions were the most common, constituting 33(56.8%) cases. Among which 31 cases were thymoma. Type B thymoma was the most common histologic subtype and also the subtype associated with Myasthenia gravis. Thymic hyperplasia and thymic carcinoma each constituted one case.

Lymphoma was the second most frequent diagnosis, with 7(12%) cases. Hodgkin Lymphoma (H.L) was seen in 4 patients and Non-Hodgkin's lymphoma (NHL) in 3 cases. All cases of lymphoma were seen in adults and the elderly, except for a single case of NHL in a child of 7 years of age. All 4 cases of H.L are nodular sclerosing subtypes characterized by broad bands of collagen with an entrapped polymorphous population of cells and Reed Sternberg cells (RS) (FIG 1).

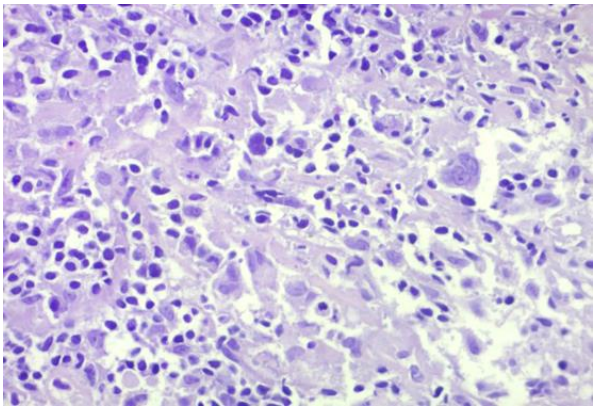

Figure 1: (H&E;40X) Bands of collagen with entrapped polymorphous & R.S. cells.

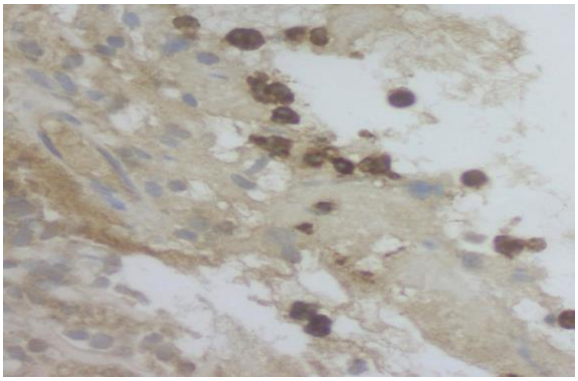

Figure 2: CD15 (40X): Membranous positive staining -R.S. cells.

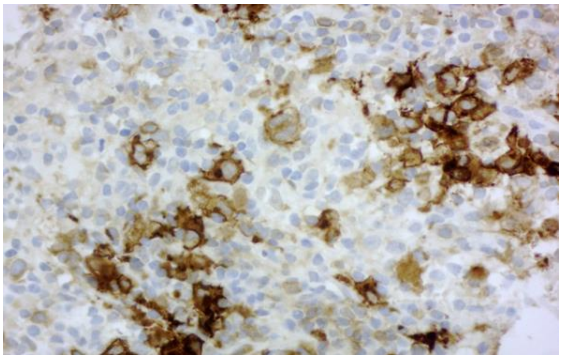

Figure 3: CD30 (40X): Membranous positive staining; R.S. cells

In the present study, metastatic carcinoma constituted 7(12%) cases. Metastatic Squamous Cell Carcinoma (SCC) was seen in 4 cases, while Adenocarcinoma and Neuroendocrine carcinoma (NEC) each constituted one case. One case of metastatic Infiltrating Ductal Carcinoma (IDC) in a 61year old female presented with a complaint of dysphagia and history of breast carcinoma.

In the present study, one of the cases was metastatic NEC which was seen in a 53years male who presented with a complaint of dysphagia. CT-guided biopsy shows pleomorphic tumor cells in rosettes with the streaking artifact. (FIG 4)

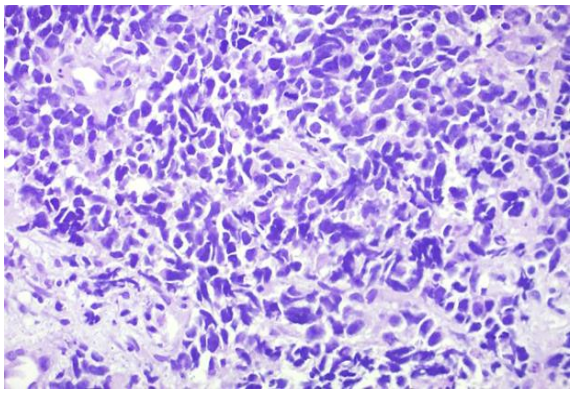

Figure 4: H&E (40X): Tumor cells with streaking artifact

Extragonadal Germ Cell Tumor (EGCT) was the most common tumor (8.6%) after lymphomas and metastatic carcinoma. It comprised 3 cases of mature teratoma and two cases of Germinoma, which showed a preference for the younger age group. One patient with Germinoma was associated with superior vena cava syndrome. Histology showed tumor cells arranged in nests and sheets. Tumor cells are round with intervening stroma showing lymphocytes and apoptotic bodies. (FIG 5A) These cells are positive for vimentin. (FIG 5B). Thus the final diagnosis was Germinoma.

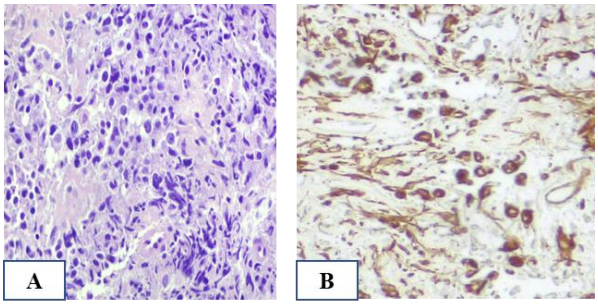

Figure 5: A: H&E (40X): Round tumor cells with lymphocytic stromal infiltrate. B: VIMENTIN (40X): Tumor cells with positive cytoplasmic staining.

Other rare lesions such as lymphangioma in adult and older age groups were seen in 3.4% of patients. Lipoma, sarcoidosis, IMT and spindle cell sarcoma constituted one case each.

One of the uncommon lesions was spindle cell sarcoma in a 60 years male patient who presented with a complaint of breathlessness. In this case, IHC played a pivotal role. Microscopy showed spindle-shaped tumor cells arranged in a storiform pattern and short fascicles with surrounding stroma showing lymphocytes intermingled with epithelial cells (FIG 6A). The negative staining for Pan CK and CD45 excluded type A thymoma. Cells are positive for vimentin (FIG 6B); hence a diagnosis of spindle cell sarcoma was made.

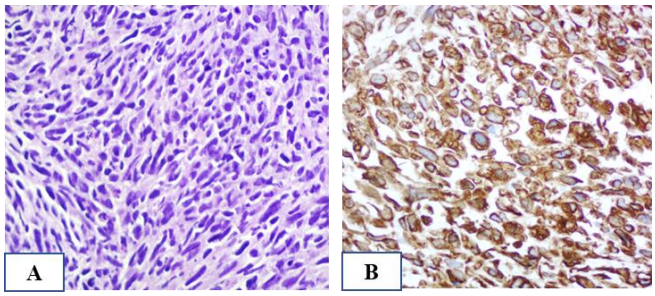

Figure 6: A: H&E (40X): Spindle-shaped tumor cells with intermingled epithelial cells. B: VIMENTIN (40X): Spindle-shaped tumor cells with positive staining.

Discussion

Mediastinal masses pose diagnostic and therapeutic difficulties for the clinician. Recent advances in radiographic techniques like C.T. have improved the ability to identify the extent and nature of the mass and its relation to adjacent organs preoperatively [7]. The utility of monoclonal antibody techniques to immunohistochemistry, along with histomorphologic features and clinical findings, is mandatory for the management of mediastinal masses [8],[5].

In the present study, histomorphology of 58 cases of AMM was studied using H& E stain and IHC was done wherever required.

Thymomas are a group of neoplasms arising from thymic epithelial cells. The combination of epithelial cells and lymphocytes gives rise to multiple variations in the histomorphology of thymomas. Thymomas were located in the anterior mediastinum, but their incidence is rare. [3].

In the present study, thymomas were the most frequent lesions (53.4%), similar to the study done by Sharma P et al. [9].

Thymomas were classified into five histologic subtypes (Type A, B1, B2, B3 & A.B.) according to WHO classification [3]. In the present study, type B thymoma was the most common subtype, similar to the study done by Agrawal M et al. [10].

According to the literature search, thymomas were associated with paraneoplastic syndromes like M.G, Rheumatoid Arthritis (RA), Cushing syndrome and pure red cell aplasia[3]. Myasthenia Gravis was more commonly associated with type B thymomas in the present study and in the study done by Divya S et al. [11].

Approximately 10% of lymphomas encountered in the mediastinum were primary. Correlating clinical features, histopathological examination, including IHC, laboratory tests and radiology findings play a pivotal role in diagnosing and staging lymphomas [12].

Studies by Sundaram S et al [4], Jitendra G et al [13] found that lymphomas were the second most common mediastinal lesions, similar to the present study. Their frequency ranged from 10% to 36%, while in the present study, they constituted 12% of anterior mediastinal lesions. Hodgkin lymphoma was divided into four histologic subtypes-nodular sclerosing, lymphocyte rich, mixed cellularity and lymphocyte depleted [14], with the nodular sclerosing subtype representing the most common in the present study as well as in the study done by Aggarwal et al. [5]

In the present study, all 4 cases of Hodgkin lymphoma subtyped as nodular sclerosing showed membranous positivity of R.S cells with CD15 &30, similar to the study done by Sharma P et al. [9]

Teratoma is a slow-growing benign tumor composed of mature tissues originating from more than one germ layer i.e., ectoderm, endoderm and mesoderm. The most common site of occurrence of teratoma was gonads. Occasionally it was found in extragonadal sites such as the mediastinum, pineal area and sacrococcygeal [15].

In the present study, EGCT (Teratoma & Germinoma) constituted 8.6% of anterior mediastinum masses. A study by Dasgupta S et al. [3] also found EGCT predominantly in the anterior mediastinum.

Malignant GCT are often seen in males and constitutes 10% of mediastinum tumors. These patients present with cough, dyspnoea, chest pain and superior vena cava obstruction [16]. In the present study, one patient with Germinoma was associated with superior vena cava syndrome.

Breast carcinoma is most common in females with the usual site of metastasis being axillary lymph nodes, bone, liver, lungs and brain. The mediastinum was the rare metastatic site for breast carcinoma. Breast carcinoma accounts for approximately 11% of metastatic mediastinal tumors followed by lung and kidney cancers [17]. In the present study, one rare case metastatic Infiltrating ductal carcinoma with history of breast carcinoma was encountered.

Rare anterior mediastinal lesions encountered in the present study were spindle cell sarcoma, lipoma, lymphangioma, IMT and sarcoidosis.

In studies done by M Nishihara et al. [18], Gupta P et al. [19], had found that mediastinal sarcomas were infrequent lesions. Similarly, the present study also showed one rare case: spindle cell sarcoma in the anterior mediastinum, which was diagnosed by correlating the findings of histopathology and IHC. Histologically, spindle cell sarcoma can be either a monophasic or biphasic spindle cell tumor [19].

Lipomas were benign lesions and most of the patients presented with subcutaneous swelling. A study done by Gupta A et al. also found that mediastinal lipoma was rarely found in the list of mediastinal lesions [20], similar to the present study. In the present study, microscopy showed lobules of mature adipocytes traversed by fibrovascular septa.

According to the literature survey, lymphangiomas were infrequent in adults. Their incidence is usually more common in children in the cervical region and originates from the portions of lymphatic sacs [21]. In the present study, two rare cases of lymphangioma were seen, one in adults and one in the elderly who presented with cough. Microscopy showed variably sized vascular spaces lined by flattened endothelial cells embedded in a fibrous stroma.

According to the study done by Sugiyama K [22], IMT can occur in any organ, but its incidence in the mediastinum is rare. In the present study, one rare case of IMT was seen in a 35-year-old male who presented with dyspnea.

Conclusion

In the present study, various lesions of the anterior mediastinum were described. Thymoma was the most common lesion, followed by lymphoma.Other rare lesions encountered were: spindle cell sarcoma, lipoma, lymphangioma, IMT and sarcoidosis.

Abbreviations and symbols:

AMM: Anterior Mediastinal Mass
H&E: Hematoxylin & Eosin
IHC: Immunohistochemistry
MG: Myasthenia Gravis
EGCT: Extra Gonadal Germ Cell Tumor
USG: Ultrasonography
CT: Computed Tomography
IMT: Inflammatory Myofibroblastic Tumor
HL: Hodgkin Lymphoma
NHL: Non-Hodgkin's Lymphoma
RS: Reed Sternberg Cells
SCC: Squamous Cell Carcinoma
IDC: Infiltrating Ductal Carcinoma
NEC: Neuroendocrine Carcinoma
RA: Rheumatoid Arthritis

Declarations

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Competing interest: None

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