

Original Research Article

Pathological Study of Primary Mediastinal Lesions in a Tertiary Care Hospital

Chaitra B¹, Pidakala Premalatha², Inuganti Renuka V³, Vaddatti Tejeswini⁴, Kasula Lakshmi⁵, Potti Ramya⁶^{1,5,6}Assistant Professor, ^{2,4}Professor, ³Professor & Head, Department of Pathology, NRI Medical College, Chinakakani, Guntur, Andhra Pradesh 522503, India.

Corresponding Author:

Chaitra B, Assistant Professor, Department of Pathology, NRI Medical College, Chinakakani, Guntur, Andhra Pradesh 522503, India.

E-mail: dr.chaitra.b@gmail.com

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Abstract

Background: Mediastinum is a small extra pleural anatomic compartment between the lungs where wide variety of lesions occurs. Division of mediastinum is helpful in developing a differential diagnosis. **Aim:** To analyse the pathological features of mediastinal lesions in our hospital. **Materials and Methods:** This is a retrospective hospital based study in tertiary care hospital on all primary mediastinal lesions over a period of six years (January 2012-December 2017). The data were retrieved from the archives of pathology department. **Statistical analysis used:** Microsoft Excel sheet. **Results:** Out of 80 mediastinal lesions, 62 were primary mediastinal lesions. Majority (58.1%) were in anterior compartment with male predominance and male to female ratio of 1.21:1. Age ranged from 11 days to 80 years and adult patients predominate. 44 cases (71%) were of neoplastic nature, among which thymus related tumours predominate followed by lymphoma, germ cell tumours and mesenchymal tumours. Non neoplastic lesions include mediastinal cysts, thymic remnants and thymic hyperplasia, reactive lymphadenitis, tuberculous lymphadenitis and extramedullary haematopoiesis. **Conclusion:** A multidisciplinary workup is needed in arriving at a diagnosis in case of mediastinal lesion for appropriate management of these rare lesions.

Keywords: Mediastinal lesions, thymic neoplasms, thymoma, mediastinal cysts

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Introduction

Although the mediastinum is a relatively small anatomic compartment, the diversity of pathologic processes that may reside in it is impressive.¹ The multitudes of diseases affecting the mediastinum vary considerably² from both non-neoplastic to

neoplastic,³ and they include proliferations of somatic epithelial, lymphoid, mesenchymal, and germ cell types.¹

The mediastinum is the extra pleural space between the lungs.⁴ The borders of the mediastinum are the thoracic inlet superiorly, the diaphragm

inferiorly, the sternum anteriorly, the spine posteriorly, and the pleural spaces laterally.⁵

The mediastinum is divided into anterior, middle and posterior compartment which is useful in developing a differential diagnosis⁶ when an abnormality is detected, as well as when planning techniques for biopsy or resection.⁷ The anterior mediastinal compartment is that which is ventral to the anterior cardiac border and the aortic root; it most commonly harbours thymic epithelial tumours and cysts, germ cell neoplasms, lymphoproliferative lesions, retrosternal thyroid glandular proliferations, parathyroid lesions, aortic pulmonary-type paragangliomas, and nonneurogenic mesenchymal tumours. The "middle" mediastinum is defined on one side by the anterior cardiac silhouette and aortic root and on the other side by the posterior aspect of the tracheal carina; lesions in this region are typically benign cysts, although malignant lymphomas also may be encountered therein. Lastly, the posterior mediastinum is dorsal to the large conducting airways; it principally plays host to neurogenous mesenchymal lesions and enteric cysts.¹

While clinical judgement in combination with radiographic imaging can often narrow the diagnostic possibilities, a definitive pathological diagnosis is required before initiating therapy, especially in cases where surgical resectability is questionable.⁴

Materials and Methods

This is a retrospective hospital based study conducted in tertiary care hospital in southern India, after obtaining institutional ethical clearance, on all mediastinal lesions over a period of six years (January 2012-December 2017). The data were retrieved from the archives of pathology department. A total of 80 cases were retrieved in this period. All cases diagnosed on surgically resected specimens as well as needle biopsies were included in the study.

Relevant clinical information included age and sex of the patients and compartment location of the lesions was recorded for all cases. Haematoxylin and eosin stained slides along with immunohistochemistry (IHC) were reviewed when necessary.

Results

During the study period of six years, data of 80

mediastinal lesions were retrieved and studied. 62 cases were primary mediastinal lesions and 18 cases were secondary deposits in mediastinal lymphnodes from Adenocarcinoma, Squamous cell carcinoma, Small cell carcinoma or Undifferentiated carcinoma with primary mass in other organs, which were excluded from the study.

The age ranged from 11 days to 80 years among the 62 primary mediastinal lesions. There were 34 males and 28 female patients with male to female ratio of 1.21:1. There were 36 cases involving the anterior mediastinum, 14 cases in middle mediastinum, 11 cases in posterior mediastinum and only 1 case involving superior mediastinal compartment.

In this study, 18 (29%) cases were non neoplastic lesions, 44 (71%) cases were neoplastic lesions. (Table 1)

Table 1: Non-neoplastic Primary Mediastinal lesions:

Non-neoplastic	29%
Reactive lymphadenitis	9.7
Thymic remnants	4.8
Thymic hyperplasia	3.22
Thymic cyst	3.22
Bronchogenic cyst	1.6
Epidermoid cyst	1.6
Tracheointestinal Cyst	1.6
Extramedullary haematopoiesis	1.6

The non neoplastic lesions in the mediastinum of thymic origin were thymic cysts (two cases), thymic hyperplasia (two cases) and thymic remnants (three cases).

Other non thymic non neoplastic lesions include reactive lymphadenitis (six cases), tuberculous lymphadenitis (one case), Bronchogenic cyst (one case), Epidermoid cyst (one case), Tracheointestinal cyst (one case) and Extramedullary hematopoiesis (one case) (Table 2).

Table 2: Neoplastic Primary Mediastinal lesions

Neoplastic	71%
Thymus related	
Thymoma	14.5
Thymic carcinoma	6.45
Small cell carcinoma	3.22
Thymolipoma	3.22
Lymphoma	17.7
Schwannoma	12.9
Germ cell tumor	
Benign	4.8
Malignant	4.8
Solitary fibrous tumor	3.22

The neoplastic lesions of mediastinum were thymic neoplasms (27.41%), lymphomas (17.7%), germ cell tumours (9.67%) and mesenchymal tumours (16.12%).

Thymic neoplasms include nine cases (14.5%) were thymoma, four cases (6.45%) of thymic carcinoma, two cases (3.22%) of thymic

neuroendocrine carcinoma and two cases (3.22%) of thymolipoma.

All the 11 cases (17.7%) of Lymphomas were of Non-Hodgkin type, Germ cell tumours include three cases (4.8%) of benign teratoma and three cases (4.8%) of malignant germ cell tumours. Mesenchymal tumours include two cases (3.22%)

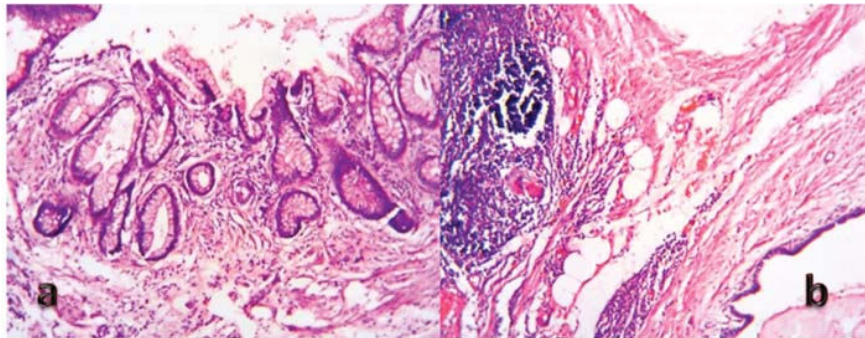


Fig. 1: (a.) Tracheointestinal Cyst showing cyst lined by gastric type of mucosa (H&E, × 100), (b.) Thymic cyst lined by cuboidal epithelium and wall showing thymic remnants (H&E, × 100).

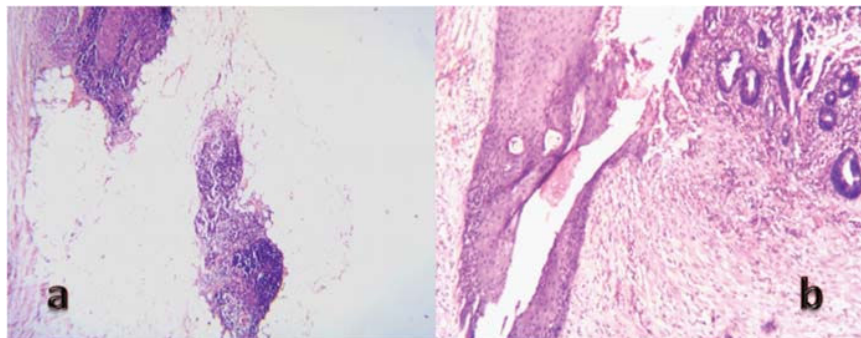


Fig. 2: (a.) Thymolipoma composed of lobules of mature adipocytes admixed with thymic tissue ((H&E, ×100), (b.) Teratoma composed of ectodermal (stratified Squamous epithelium) and endodermal (secretory intestinal type of glands) elements (H&E, ×100).

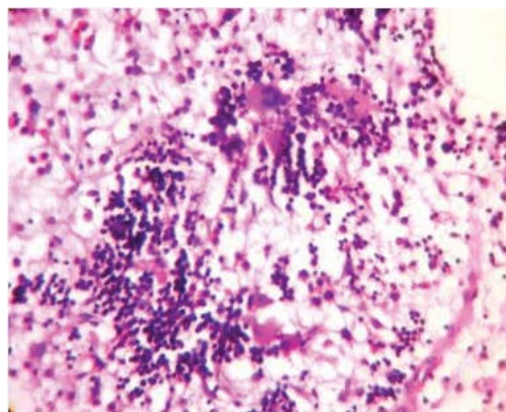


Fig. 3: Extramedullary haematopoiesis comprising megakaryocytes, myeloid and erythroid cells admixed with mature adipocytes (H&E, × 400).

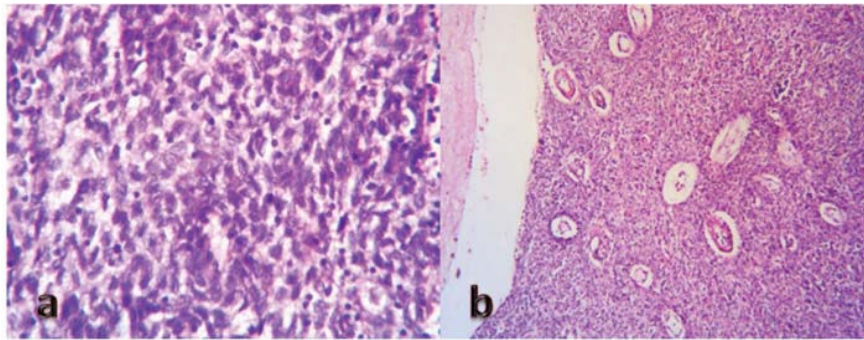


Fig. 4: (a.) Type A Thymoma composed predominantly of spindle type of thymocytes and scant lymphoid cells (H&E, $\times 100$), (b.) Type B2 Thymoma showing plump neoplastic epithelial cells scattered in lymphocyte predominant stroma and many vascular spaces (H&E, $\times 100$).

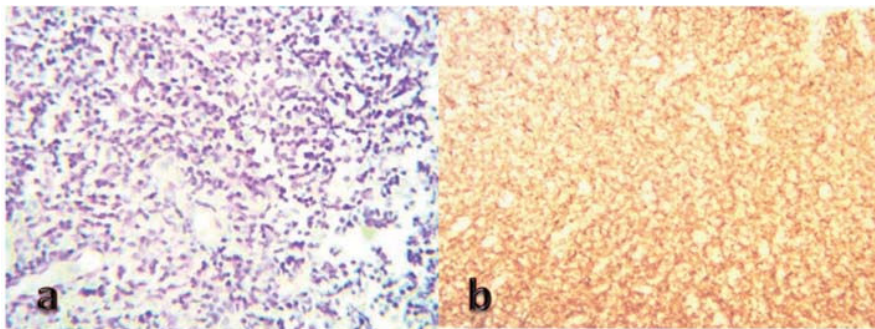


Fig. 5: (a.) Diffuse Non-Hodgkin Lymphoma exhibiting sheets of atypical lymphoid cells (H&E, $\times 100$), (b.) CD20 Positive in the diffuse lymphoid cells (IHC, $\times 400$).

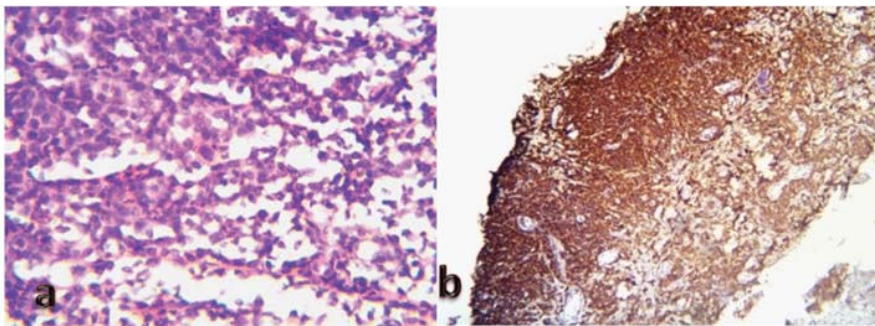


Fig. 6: Diffuse Non-Hodgkin Lymphoma exhibiting sheets of atypical lymphoid cells and few scattered eosinophils (H&E, $\times 100$), (b.) CD3 Positive in the diffuse lymphoid cells (IHC, $\times 100$).

of Solitary fibrous tumour and eight cases (12.9%) of Schwannoma (Figs 1-6).

Discussion

A wide variety of lesions occur in the mediastinum with less frequency, as a result there is lack of

adequate data on the incidence of these lesions.³ These lesions can present with symptoms due to compression of adjacent structures when big or invasion of mediastinal structures.⁸ Smaller lesions might not produce any symptom and incidentally detected during plain chest radiography or advanced imaging studies.⁷

Although most mediastinal lesions can be

appreciated in routine chest radiographs which provides information on size, anatomical location, density and sometimes composition, the investigation of choice for their detection is Computed Tomography (CT) scan with intravenous contrast enhancement provides information about relationship of lesion with adjacent structures, vascularity within lesion, content and nature.^{3,7} Further characterization like evaluation of spinal, vascular or cardiac invasion is better appreciated in magnetic resonance imaging (MRI).⁷

Excision will be done in nonneoplastic and noninvasive tumours which appear completely resectable on imaging, but for lesions with limited resectability on imaging or suspected malignant lesions which respond to chemotherapy, a non-surgical image-guided trucut biopsy is suitable and a definitive pathological diagnosis is required to initiate the therapy in such cases.⁴

In the present study, 62 cases of primary mediastinal lesions were noted with age range of 11 days to 80 years and mean age of 44.85 years similar to Aroor *et al.*⁹ and Aggarwal *et al.*⁴ studies who reported 45.4 and 41.14 years respectively. A much lower mean age was reported by studies done by Dasgupta *et al.*³ (35.9 years), Karki S *et al.*⁵ (35.5 years), Baram A *et al.*¹⁰ (35 years) and M.O. Thomas *et al.*¹¹ (33.7 years).

All the 62 cases were divided into paediatric age group (<15 years) which were 5 cases (8.1%), 40 cases (64.5%) of adult age group and 17 cases (27.4%) of geriatric age group (>60 years). Similarly study done by Aggarwal *et al.*⁴ reported 7.8% of paediatric cases, 71.6% of adult cases and 20.7% of geriatric patients. In contrast, Baram A *et al.*¹⁰ study reported a slight higher frequency among the paediatric cases of 20%.

Among the 62 cases of mediastinal lesions, 34 cases were males (54.8%) and 28 cases (45.2%) were females with a male to female ratio of 1.21:1. Similar male predominance was reported by Baram *et al.*¹⁰ (1.18:1), Aggarwal *et al.*⁴ (1.7:1), Dasgupta *et al.*³ (2:1), Aroor *et al.*⁹ (2.2:1), Shamshuddin *et al.*¹² (2.7:1) and highest by M.O. Thomas *et al.*¹¹ (3.2:1). In contrast a slight female predominance was reported by Karki S *et al.*⁵ (1:1.07).

Knowledge about compartmentalization of mediastinum and the common lesions in these compartments helps us in formulating a differential diagnosis.^{4,5} In this study, out of 62 cases, a majority of 36 cases (58.1%) were noted in anterior mediastinum and middle mediastinum showed 14 cases (22.5%), posterior mediastinum 11 cases

(17.8%) and only one case in superior mediastinum (1.6%). Predominance of anterior mediastinal involvement was also reported by Aroor *et al.*⁹ (42.86%) and Dasgupta *et al.*³ (45.5%) studies. A very high percentage of 70% of lesions involving anterior compartment was reported by Karki S *et al.*⁵ and Aggarwal *et al.*⁴

Similar to this study middle mediastinal involvement was seen next in frequency by Dasgupta *et al.*³ (31.8%) and Aggarwal *et al.*⁴ (19.6%) followed by posterior compartment. In contrast M.O. Thomas *et al.*¹¹ study reported 18.4% cases in posterior compartment followed by 2.6% of cases in middle mediastinum.

Based on histopathological evaluation mediastinal lesions were divided into non-neoplastic (29%) and neoplastic (71%) lesions. A similar predominance of neoplastic lesions were noted in studies done by Aggarwal *et al.*⁴ (62.1%), Dasgupta *et al.*³ (86.4%) and Aroor *et al.*⁹ (85.7%) studies.

Non neoplastic cystic lesions noted in this study were two cases of thymic cysts (anterior mediastinum), one case of bronchogenic cyst (middle mediastinum), one case of epidermoid cyst (superior mediastinum) and one case of tracheo-intestinal cyst (posterior mediastinum). Aggarwal *et al.*⁴ study reported bronchogenic cysts as the predominant type of cyst and involving the posterior mediastinum.

Other lesions were two cases of thymic hyperplasia (3.22%), three cases of thymic remnants (4.8%), six cases of reactive lymphadenitis (9.67%), one case of tuberculous lymphadenitis (1.61%) and one case of extramedullary haematopoiesis (1.61%). Extramedullary haematopoiesis case was a 46 year old male patient who presented with cough with expectoration and shortness of breath since one month, radiological investigations revealed posterior mediastinal mass which on biopsy revealed marrow elements with clusters of megakaryocytes admixed with adipocytes and fibrocollagenous tissue.

Mediastinal tumours are rare and form 3% of all tumours in chest. Among the neoplastic lesions of mediastinum, 15 cases (24.2% of total 62) were tumours of thymic origin. Other studies on mediastinal lesions done by Shamshuddin *et al.*¹² (33.3%), Karki *et al.*⁵ (33.3%) and Dasgupta *et al.*³ (31.8%) have also reported predominance of thymic neoplasms among all neoplastic lesions of mediastinum. In contrast studies by Aroor *et al.*⁹ and Baram A *et al.*¹⁰ reported predominance of

lymphomas (34.28% & 32.94%) among all neoplastic lesions in mediastinum.

Among the nine cases of thymoma, four cases were of AB type, three cases were type A and two cases of type B2 thymoma. Similarly Dasgupta *et al.*³ also reported predominance of Type AB thymoma in their study. Shamshuddin *et al.*¹² reported equal incidence of type AB thymoma and type B2. Aggarwal *et al.* study reported predominance of type B2 thymoma.

Maximum number of thymomas was seen in 40–69 years age group similar to Dasgupta *et al.*³ and Shamshuddin *et al.*¹² studies. Males were more affected than females which was similar to Shamshuddin *et al.*¹² and in contrast to Dasgupta *et al.*³ who reported slight female predominance.

There were four cases of thymic carcinoma and two cases of thymic neuroendocrine carcinoma which were confirmed by CD5 and Cytokeratin, Chromogranin IHC markers. Neuroendocrine carcinomas were diagnosed as primary only after thorough search for primary elsewhere.

There were two cases of thymolipoma which showed lobules of thymic tissue with cortex, medulla and Hassall corpuscles admixed evenly with mature fat and bound by capsule. Thymolipoma was also reported by a study done by Baram A *et al.*¹⁰

All 11 cases of Lymphomas were Non Hodgkin Lymphoma (NHL), B cell and T cell type confirmed on CD20 and CD3 IHC markers. Studies done by Aggarwal *et al.*⁴ and Yadlapalli *et al.*⁷ reported predominance of NHL, in contrast studies done by Aroor *et al.*⁹ Baram A *et al.*¹⁰ and Dasgupta *et al.*³ reported predominance of Hodgkin Lymphomas. Lymphomas involved the middle mediastinum predominantly followed by anterior mediastinum with female predominance.

Six germ cell tumours (9.6%) were noted in this study, of which, three were benign cystic teratoma and three malignant germ cell tumours. 10–15% of all adult mediastinal tumours are primary mediastinal germ cell tumours and 19–25% in children. Studies done by Aggarwal *et al.*⁴ Karki S *et al.*⁵ Baram A *et al.*¹⁰ and Dasgupta *et al.*³ have reported a varied frequency of germ cell tumours of 3.4%, 11.1%, 11.76% and 13.6% respectively. The present study had equal incidence of benign and malignant germ cell tumours. In contrast, malignant germ cell tumours were predominant in Baram A *et al.*¹⁰ study. There was a male predominance among the germ cell tumours cases in this study similar to Baram A *et al.*¹⁰ study.

Two solitary fibrous tumours (SFT) (3.2%) were recorded in this study, one male and one female patient, similarly, Baram A *et al.*¹⁰ also reported an incidence of 2.35%, but both cases were female patients.

Eight benign neural tumours (12.9%), Schwannoma, were noted in the posterior compartment in this study, with age ranging between 22 to 65 years and female predominance. Neurogenic tumours were also reported by Aggarwal *et al.*⁴ (6.9%), Baram A *et al.*¹⁰ (10.59%), Karki S *et al.*⁵ (11.11%) and Dasgupta *et al.*³ (18.2%). All the studies reported neurogenic tumours in the posterior mediastinum. Baram A *et al.*¹⁰ reported a higher incidence (2/3 cases) of malignant neurogenic tumours in pediatric age group in the form of neuroblastoma.

Conclusion

Mediastinal lesions are rare and wide in variety; a complete clinical, radiological and pathological-multidisciplinary workup is the key to proper management of a patient. Histopathological diagnosis of radiologically guided biopsy in nonresectable cases, along with IHC where ever needed, helps in planning further management. Anterior mediastinal lesions are more common, predominantly occurring in males. Neoplastic lesions are more common than non-neoplastic, most common being thymus related, followed by lymphoma, mesenchymal tumours and Germ cell tumours.

Key Messages: Mediastinal lesions are rare and wide in variety; a complete clinical, radiological and pathological - multidisciplinary workup is the key to proper management of a patient. Histopathological diagnosis of radiologically guided biopsy in nonresectable cases, along with IHC where ever needed, helps in planning further management.

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