

Clinicoradiopathological Features among Mediastinal Masses

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Abstract

Background: The mediastinum is a place where various benign and malignant diseases usually manifest as mass and present as interesting diagnostic challenge. The purpose of this study was to describe clinical features, radiological, and pathological information of mediastinal masses to help have an organized approach to diagnosis of mediastinal masses. **Patients and Methods:** This was a prospective, descriptive cross-sectional study conducted over a period of 1 year at our hospital after obtaining ethical committee clearance. Patients with mediastinal masses fulfilling the inclusion criteria were enrolled in the study. Patient's clinical history, radiological features, techniques used to obtain specimens, and cyto-histopathology results from data collected in our total study population were analyzed. **Results:** A total of 73 patients with mediastinal masses were included. Thirty-three of them (45.2%) were malignant and 32 (43.8%) were nonmalignant masses. The masses were commonly located in the middle compartment ($n = 42$ [57.5%]), followed by anterior compartment (20 [27.4%]), posterior compartment (8 [11%]), and multicompartiment (3 [4.1%]). Among middle mediastinal masses, infectious masses were 14 (33.3%), followed by 11 (26.2%) malignant masses. Anterior mediastinal masses were predominantly malignant in nature (90%). Nature of mass was inconclusive in eight (11%) patients. **Conclusion:** Clinical history, anatomical position, and imaging characteristics allow the correct diagnosis in many cases when it is combined with histopathology. The newer endoscopic techniques such as endoscopic ultrasound-guided fine-needle aspiration or biopsy are generally preferred in view of lesser complications and ease compared to more invasive surgical procedures for mediastinal mass evaluation.

Keywords: Endobronchial ultrasound, endoscopic ultrasound, mediastinal lymphadenopathy, mediastinal mass

INTRODUCTION

The mediastinum is the central part of thoracic cavity which is bounded by pleural sacs, sternum, and vertebral bodies.^[1] It contains various structures such as heart, thymus, lymph nodes, major blood vessels, nerves, trachea, and esophagus. Various benign and malignant diseases manifest as mediastinal mass and pose an interesting diagnostic challenge.^[2]

Etiology of mediastinal mass varies with age and gender. These masses can present with multiple symptoms depending on many factors such as age, location, compression of adjacent structures, and nature of the disease. One-third of patients will be asymptomatic.^[3-5]

Mediastinal masses are most often detected by chest X-ray. However, small masses due to mediastinal adenopathy can be detected only by computed tomography (CT). Multidetector CT can show more characteristic features of mediastinal mass and can be helpful in planning further workup of mediastinal mass as well as narrow down the differential diagnosis.

Various classification methods such as Shields, Felson, Heitzman, Frazer, Zylak, and Whitten methods were used for division of mediastinum, and there is no uniqueness in classification across the world.^[6-11] Even though diagnosis can be arrived with the help of clinical and radiological features, tissue diagnosis is often required to guide the management of mediastinal masses.^[12-14]

The objective of this study was to describe the clinical features, radiological features, and cytology or histopathological features of mediastinal masses.

PATIENTS AND METHODS

This descriptive cross-sectional study included all patients with mediastinal mass who underwent biopsy or aspiration

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in our study setting during the study period from November 2017 to December 2018. The study commenced after obtaining institutional ethics committee clearance. After obtained informed consent, 76 patients were enrolled in the study.

Patient's demographic details such as gender, age, body mass index, occupation, and smoking were obtained. Detailed clinical history regarding cardinal respiratory symptoms, constitutional symptoms, and compression symptoms such as hoarseness, dysphagia, dyspnea, and swelling of the face and systemic syndromes such as myasthenia gravis and thyroid dysfunction which are likely to be associated with mediastinal masses were obtained from patients undergoing evaluation.

Radiological features of mediastinal masses recorded included mediastinal widening in the chest X-ray and location of mediastinal mass in CT scan. Various invasive techniques used to obtain cytology or biopsy specimens from mediastinal mass such as image-guided percutaneous biopsy or fine-needle aspiration (FNA), endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), video-assisted thoracoscopic surgery (VATS), and surgical excision by sternotomy or thoracotomy were also noted. Pathology reports of tissue specimens either cytology or biopsy obtained from mediastinal mass were collected. Demographic details, clinical history, radiological features, techniques used to obtain specimens, and cyto-histopathology results from data collected in our total study population were entered in MS Excel (version 2007) and analyzed using SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp).

RESULTS

In this study, 73 patients with mediastinal masses were included in the study. The mean age of the patients was 44.7 years (range 16–75 years) and more prevalent in the age range of 30–50 years. Forty-four patients (60.3%) were male with a male-to-female ratio of 3:2. Only twenty (27.3%) patients were smokers [Table 1]. The presenting symptoms, compressive symptoms, and constitutional symptoms and their frequencies are listed in Table 1. Among the twenty patients with anterior mediastinal mass, seven patients had systemic syndromes of whom, myasthenia gravis was present in five (25%) patients, and they were diagnosed to have thymoma [Table 1]. This association of systemic syndromes with location was also significant ($P < 0.001$).

Anterior mediastinal masses were more common in patients <30 years, whereas middle mediastinal masses were common in patients above 30 years [Figure 1]. Breathlessness and cough were the most common symptoms followed by chest pain. Compressive symptoms were absent in 80% of the patients. The relationship of compressive symptoms to location was found to be very highly significant ($P = 0.000$). Back pain was the only compressive symptom in four of the eight patients who had posterior mediastinal tumors. Five out of the twenty patients with anterior mediastinal mass

Table 1: Clinical characteristics of the mediastinal masses

Clinical parameters	n (%)
Gender	
Male	44 (60.3)
Female	29 (39.7)
Age in years, mean (range)	44.7 (16–75)
Smoking	
Nonsmoker	53 (72.6)
Smoker	20 (27.4)
Symptoms	
Asymptomatic	5 (7)
Cough	31 (42.5)
Sputum	4 (5.5)
Wheeze	4 (5.5)
Hemoptysis	4 (5.5)
Chest pain	15 (20.5)
Breathlessness	36 (49.3)
Compressive symptoms	
None	59 (80.8)
Hoarseness of voice	4 (5.5)
Difficulty in swallowing	2 (2.7)
Back pain	4 (5.5)
Both hoarseness of voice and difficulty in swallowing	3 (4.1)
Facial puffiness	1 (1.4)
Constitutional symptoms	
None	39 (53.4)
Fever	10 (13.7)
Loss of weight	10 (13.7)
Loss of weight, fever, and loss of appetite	6 (8.2)
Fever and loss of weight	6 (8.2)
Loss of weight and loss of appetite	2 (2.7)
Systemic syndromes	
No	64 (87.7)
Myasthenia gravis	5 (6.8)
Hypothyroid	3 (4.1)
Hyperthyroid	1 (1.4)
Imaging: Location of mass	
>1 compartment	3 (4.1)
Anterior	20 (27.4)
Middle	42 (57.5)
Posterior	8 (11)

had compressive symptoms such as hoarseness of voice and difficulty in swallowing and facial puffiness. Only three patients of the 42 patients with middle mediastinal mass had compressive symptoms, either hoarseness of voice or difficulty in swallowing [Figure 2].

Among the mediastinal masses, 33 (45.2%) were malignant and 32 (43.8%) were nonmalignant. Tuberculous mediastinal lymphadenitis was the diagnosis in 15 (20.5%) patients, followed by thymoma and sarcoidosis in 11 (15.1%) patients each and lung carcinoma in 10 (13.7%) patients. Table 2 shows the analysis of the final diagnosis and nature of mediastinal masses.

The chest radiograph showed evidence of mediastinal mass in 78.8% of malignant masses. The chest radiograph showed

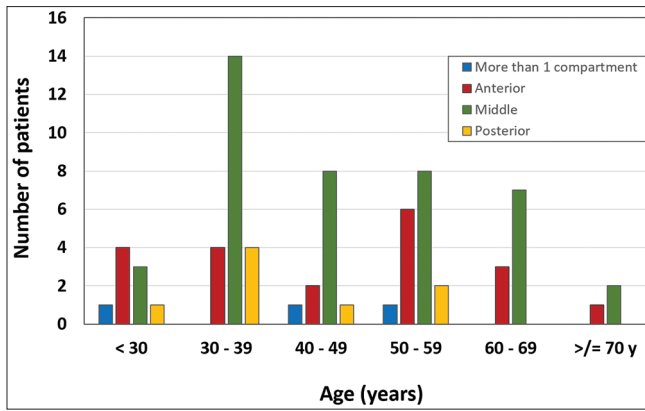


Figure 1: Distribution of location of masses with age

evidence of mediastinal mass in all three (100%) patients with multiple compartment mass, 19 (95%) patients with anterior mediastinal mass, and 8 (19%) patients with a middle mediastinal mass.

Lesion was most common in middle compartment (42 [57.5%]), followed by anterior compartment (20 [27.4%]), posterior compartment (8 [11%]), and multicompartiment (3 [4.1%]). Anterior mediastinal masses were predominantly malignant in nature (90.0%). Infectious masses (33.3%) were more common among the middle mediastinal masses followed by malignancy (26.2%). Two of the three multiple compartment masses were malignant. Half of the posterior mediastinal masses were noninfectious and nonmalignant. Nature of mass was predominantly inconclusive in 16.7%^[7] of middle mediastinal masses. Table 2 shows the distribution of the final diagnosis of mediastinal masses among mediastinal compartment.

EBUS, EUS, and VATS were performed only in middle mediastinal masses in this study population. CT-guided biopsy/FNAC was done in 50%^[10] of anterior mediastinal masses and posterior mediastinal masses. Surgery was done in the rest of the anterior and posterior mediastinal masses. Table 3 shows the analysis of techniques used to obtain specimens among the location of masses. Malignant masses were diagnosed by CT-guided biopsy followed by surgery in 30.3%.^[10] Each EBUS and EUS techniques were used in 31.3% of infectious masses. The final diagnoses were arrived in 65 out of 73 (89%) patients. Among the 73 patients in our study, 33 (45.2%) were malignant, 16 (21.9%) infectious, 16 (21.9%) noninfectious, and inconclusive in 8 (11%) patients.

There was a significant association ($P = 0$) of the technique used to obtain specimens for analysis and the location of the mass [Table 4]. Ten of the total twenty patients with anterior mediastinal mass had a CT-guided biopsy, while the rest underwent surgery. EBUS, EUS, and VATS were performed only in middle mediastinal masses in this study group. CT-guided biopsy/FNAC was done in four (50%) out of eight patients with posterior mediastinal masses, while surgery was done in the rest. The final diagnoses were arrived in 65 out of 73 (89%) patients.

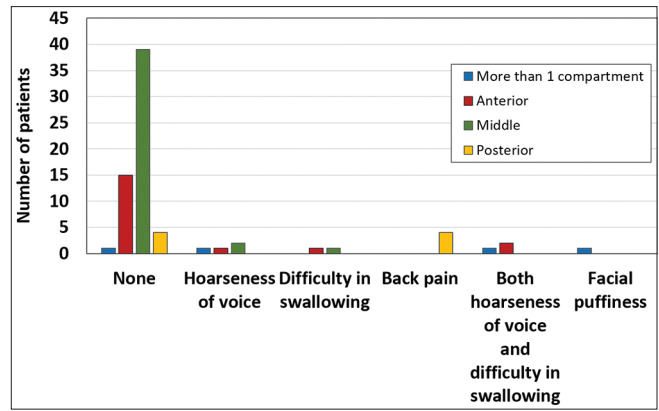


Figure 2: Description of compressive symptoms and the location of masses

Table 2: Analysis of final diagnosis and nature of mediastinal masses

Final diagnosis	n (%)
Malignant	33 (45.21)
Thymoma	11 (15.1)
Lung cancer	10 (13.7)
Neuroendocrine tumor	4 (5.5)
Lymphoma	2 (2.7)
Mature cystic teratoma	1 (1.4)
Retrosternal goiter (papillary cell carcinoma)	1 (1.4)
Solitary fibroid tumor	1 (1.4)
Metastasis	2 (2.7)
Poorly differentiated carcinoma	1 (1.4)
Nonmalignant	32 (43.8)
Noninfectious	16 (21.9)
Castleman's disease	1 (1.4)
Schwannoma	2 (2.7)
Bronchial cyst	1 (1.4)
Thymolipoma	1 (1.4)
Granulomatous lymphadenitis – sarcoidosis	11 (15.1)
Infectious	16 (21.9)
Granulomatous lymphadenitis – tuberculosis	15 (20.5)
Tuberculous paraspinal abscess	1 (1.4)
Inconclusive	8 (11)
Total	73 (100)

DISCUSSION

Mediastinal masses are a diverse group of lesions, and they continue to represent a severe and often fatal problem if diagnosis is delayed. Since many tumors that occur in the mediastinum are undifferentiated and have overlapping histological features, optimal evaluation and diagnosis of mediastinal tumors require an integrated clinical, radiological, and histological approach. The patient demographics in our study showed male-to-female ratio of 3:2 that was similar to others.^[2,13,14]

The mean age in this study was 44.7 years (Range 16–75 years). Variation in the mean age in different studies may be explained by the fact that some studies included infant and pediatric age group patients also in their series.^[15-17] Anterior mediastinal

masses were common in <30 years, common causes being thymoma or lymphoma, while in people > 40 years, mediastinal lymphadenopathy due to metastasis and tuberculosis were common, presenting as middle mediastinal masses.

In this study, 93% (68) of patients were symptomatic. Other studies have shown a varied incidence.^[12,18-22] The common cardinal respiratory symptom with which patients presented was breathlessness (49.3%), followed by cough (42.5%) and chest pain (20.5%). A similar finding was reported in the literature.^[17,19,23] In the present study population, cough was associated significantly with middle mediastinal masses. This

is possibly because 50% of middle mediastinal masses were associated with a parenchymal lesion or are located closer to larger airways with cough receptors.

Systemic syndrome was seen in eight patients among the total of 73 patients. Five (6.8%) of them had myasthenia gravis was the common systemic syndrome and were seen in one-fourth of anterior mediastinal masses (25%). All these patients were diagnosed as thymoma. Baram and Tayeb^[14] reported myasthenia gravis in 27.9% of anterior mediastinal masses. Myasthenia gravis was present in 45.5% of patients with thymoma in our study. Thymomas are related to many systemic syndromes, most common being myasthenia gravis. Nearly 5%–15% of patients with myasthenia gravis will be found to have thymoma and 40%–45% of patients with thymoma will present with myasthenia gravis.

The imaging modalities for evaluation of mediastinal masses include chest radiographs, ultrasound, CT scan, magnetic resonance imaging, and nuclear medicine studies. Chest X-rays showed evidence of mediastinal masses in only 34 (46.6%) cases in our study. CT scan imaging of chest showed that the middle mediastinum (57.5%) was the most common location of mediastinal masses, followed by anterior mediastinal masses (27.4%), posterior mediastinal masses (11.0%), and multiple compartment (4.1%) cases. In other studies, anterior mediastinal mass was more common than middle mediastinal mass. The newer techniques EBUS and EUS are predominant methods used for evaluation of middle mediastinal mass, especially for mediastinal lymphadenopathy. The availability of the newer techniques EBUS-TBNA and EUS-FNA at our hospital enabled us to evaluate more middle mediastinal masses to obtain confirmatory tissue diagnosis. This might explain the higher incidence of middle mediastinal masses in this study. In many studies, EBUS and EUS were not used in mediastinal masses workup. The incidence of masses in the posterior mediastinum was 11.0%, and comparable with studies by Yadlapalli *et al.*^[24] (10.4%) and Aroor *et al.*^[25] (8.57%). The shape of mediastinal mass in CT scan was commonly round in 29 (39.7%) patients followed by irregular in 13 (17.8%) patients. Irregular masses were predominantly malignant in nature, and round-shaped masses were benign in nature.

Table 3: Final diagnosis and location of mediastinal masses

Final diagnosis	n (%)
Anterior mediastinal masses	20 (27.4)
Thymoma	10 (50)
Neuroendocrine tumor	4 (20)
Lymphoma	2 (10)
Mature cystic teratoma	1 (5)
Retrosternal thyroid carcinoma	1 (5)
Thymolipoma	1 (5)
Granulomatous lymphadenitis-Tuberculosis	1 (5)
Middle mediastinal masses	42 (57.5)
Granulomatous lymphadenitis – tuberculosis	14 (33.3)
Granulomatous lymphadenitis – sarcoidosis	10 (23.8)
Lung cancer	9 (21.4)
Metastasis	2 (4.8)
Inconclusive	7 (16.7)
Posterior mediastinal masses	8 (11.0)
Solitary fibroid tumor	1 (12.5)
Poorly differentiated carcinoma	1 (12.5)
Castleman’s disease	1 (12.5)
Schwannoma	1 (12.5)
Bronchial cyst	1 (12.5)
Granulomatous lymphadenitis – sarcoidosis	1 (12.5)
Tuberculous paraspinal abscess	1 (12.5)
Inconclusive	1 (12.5)
Multiple compartment masses	3 (4.1)
Schwannoma	1 (33.3)
Lung cancer (small cell carcinoma)	1 (33.3)
Thymoma	1 (33.3)

Table 4: Techniques used to obtain specimens and the location of masses, n (%)

Technique	Anterior (n=20)	Location		Multiple (n=3)	Total (n=73)
		Middle (n=42)	Posterior (n=8)		
Surgery	10 (50)	0	4 (50)	0	14 (19.2)
EBUS TBNA	0	24 (57.1)	0	0	24 (32.9)
EUS FNA	0	9 (21.4)	0	0	9 (12.3)
EUS biopsy	0	3 (7.1)	0	0	3 (4.1)
CT-guided biopsy	10 (50)	5 (11.9)	3 (37.5)	3 (100)	21 (28.8)
CT-guided FNAC	0	0	1 (12.5)	0	1 (1.4)
VATS biopsy	0	1 (2.4)	0	0	1 (1.4)

EUS FNA: Endoscopic ultrasound-guided fine-needle aspiration, EBUS TBNA: Endobronchial ultrasound-guided transbronchial needle aspiration, VARS: Video-assisted thoracoscopic surgery, FNAC: Fine-needle aspiration cytology, CT: Computed tomography

Heterogeneous character of masses was more common in this study, and it was predominantly malignant in nature.

Management of mediastinal mass is based on clinical, radiological, and pathological features. Each factor contributes to diagnosis and treatment decision. Definitive tissue diagnosis is often required before initiating therapy. Several techniques are available to approach mediastinal mass to get a tissue diagnosis. Advent of newer techniques has made tissue sampling from these sites easier. The choice of technique depends on multiple factors such as location of mass, clinical stability of the patient, availability, expertise on certain techniques, and affordability.

There are several modalities to obtain tissue samples for cytological or histological diagnosis of mediastinal lesions, and each modality has its own advantages and disadvantages. The choice of these techniques in diagnostic evaluation of mediastinal lesions depends on local availability and expertise. In our study population, techniques used to obtain tissue were EBUS-TBNA in 24 (32.9%) patients, followed by CT scan-guided transthoracic needle/biopsy and fine-needle aspiration (FNAC) in 22 (30.2%) patients, surgery (sternotomy or thoracotomy) in 14 (19.2%) patients, EUS-FNA/biopsy in 12 (16.4%) patients, and VATS in 1 (1.4%) patient.

Endoscopic biopsies are generally preferred currently in view of fewer complications and ease compared to surgical interventions. The availability of less invasive techniques such as EBUS and EUS techniques at our hospital enabled us to evaluate mediastinal lymphadenopathy in middle mediastinum, which were difficult to approach using image-guided percutaneous techniques. VATS was done in only one patient. Mediastinoscopy was not done in any patient in our study population. In our study, EBUS, EUS, and VATS were used exclusively to approach middle mediastinal masses, particularly for mediastinal lymphadenopathy.

Mediastinal masses displayed a wide histomorphological spectrum in our study. Thirty-three (45.2%) of malignant and 32 (43.8%) of non-malignant masses were in equal proportions. Dixit *et al.* reported mediastinal masses as benign in 3.6%, malignant in 63.3%, and nonneoplastic in 23%.^[13] Adler *et al.*^[26] and Jereb and Krašovec^[27] reported about 72% prevalence of malignancy, whereas Karki and Chalise^[16] observed only 26% malignant lesions in a small series of 27 cases. This discordance in the frequency of malignant masses and nonmalignant masses among the previously published studies might be due to variability in age group, study sample size, and techniques used for tissue diagnosis. Among nonmalignant masses, tuberculosis was the common cause, which included tuberculous mediastinal lymphadenopathies in 15 (20.5%) patients and paraspinal abscess in 1 (1.4%) patient, followed by sarcoidosis each in 11 (15.1%). Thymoma was the common malignant mass in 11 (15.1%) patients, followed by lung carcinoma in 10 (13.7%), neuroendocrine tumors in 5.5%,^[4] and lymphoma in 2 (2.7%) in our study group.

Tuberculosis was the common cause of mediastinal lymphadenopathy in 20.5%,^[15] followed by sarcoidosis in 15.1%^[11] and metastasis in 2.7%.^[2] Similar studies were done by Dixit *et al.*^[13] who reported tuberculosis in 20.1% of cases and Kaur *et al.*^[25] in 15% of cases and Shaheen *et al.*^[15] in 5% cases, whereas Adler *et al.*^[26] reported tuberculosis in none of the patients. This gross difference in the occurrence of tuberculosis is probably due to low prevalence of tuberculosis in Western countries compared to developing countries. Mediastinal lymphadenopathy is expected to be the common mediastinal masses because this is caused by high prevalent disease such as tuberculosis, lung cancer metastasis, lymphoma, and sarcoidosis, especially in very high tuberculosis-prevalent country like India. However, mediastinal lymphadenopathies are difficult to biopsy as they are close to major vessels and airways and located commonly in the middle compartment. Hence, mediastinal lymphadenopathy is underrepresented in many studies owing to the difficulty in obtaining a tissue diagnosis. The newer techniques such as EBUS and EUS make approaching such masses with ease and less complications.

Thymoma was reported in 15.1%^[11] of mediastinal masses in our study which was close to 8.3%^[10] in the study by Kaur *et al.*^[23] and Davis *et al.*^[19] showed that thymic masses represented 17% of all mediastinal lesions, in which thymoma was 14.7%. Similar to other studies, thymoma was predominately located in anterior mediastinum in our study. Lymphoma accounted for 2.7% of the mediastinal masses in our study and was very less compared to other studies. Davis *et al.*^[19] reported 16% and Dixit *et al.*^[13] reported 19.4%. Lymphomas are predominately seen in children rather than adults and peripheral lymphadenopathy usually associated with mediastinal mass in many lymphomas which are easily assessable for biopsy to confirm diagnosis. In our study, we had not included children and those who had a biopsy site other than mediastinal mass. These might be the reasons for lymphoma being reported less in our study group.

Schwannoma occurred in 2.7 (2%) of patients with mediastinal masses in this study and is similar to the study by Aggarwal *et al.*^[28] (3.4%). Schwannoma is the most common mediastinal neurogenic tumor, being responsible for 50% of mediastinal neurogenic tumors in adults. Bronchogenic cyst, thymolipoma, tuberculous paraspinal abscess, mature cystic teratoma, retrosternal goiter (papillary cell carcinoma), solitary fibrous tumor, and Castleman's disease each was reported in 1.4% of patients in our study. Heterogeneous group of mediastinal masses reported in our study signifies the requirement of accurate diagnosis in mediastinal mass for further management.

CONCLUSION

We conclude that the mediastinum is a complex anatomical region of thorax which is affected by various mediastinal lesions. CT scan is usually the investigation of choice for mediastinal mass for localization and to plan appropriate approaches to reach the mediastinal mass to obtain tissue for

pathological examination. The newer endoscopic techniques such as EBUS and EUS-guided fine-needle aspiration or biopsy are generally preferred in view of fewer complications and greater ease compared to surgical procedures for mediastinal mass evaluation. Clinical history, anatomical position, and imaging characteristics allow correct diagnosis in many cases when it is combined with histopathology when imaging appearances are similar in many mediastinal tumors. Specific diagnosis is required in mediastinal lesions since numerous malignant and nonmalignant processes occur at this site with a different management plan to facilitate timely treatment.

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Conflicts of interest

There are no conflicts of interest.

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