

Clinico-Pathological spectrum of mediastinal lymphomas - A Cross-sectional Observational study from a tertiary care hospital in India

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Abstract

Background : Mediastinal cavity (anterior middle and posterior mediastinum) harbours many vital organs, nerves and vessels of the body and hence can give rise to various mass lesions arising from those organs, both benign and malignant. According to percentage of incidence lymphomas and germ cell tumor top the list. Even though imaging helps to localise the lesion histopathological examinations in the form of image guided trucut biopsy still happens to be the gold standard. However, early diagnosis of these lesions along with further categorisation and grading needs to be done promptly to start treatment and benefit the patients. This study presents an array of such cases with special emphasis to mediastinal lymphoma and their clinico pathologic correlation over a small period of time.

Material And Methods : A cross sectional observational study was done in RGKar medical college over a period of 2 years. CT scan was done along with other imaging techniques to localise the mediastinal mass lesions and then guided tru cut biopsy was done for confirmation, categorisation and grading of the lesions. Immunohistochemistry was done as and when required.

Result: All the available information were meticulously documented in a grand chart along with other variables like age, sex, addictive habits, presenting complaints, anatomical location etc. Spss software was used to calculate statistical significance if any, of these variables with the final etiology or histological diagnosis.

Conclusion : Lymphomas constitute a considerable percentage of mediastinal mass lesions. This study helps in early diagnosis, classification, topographical, demographical and symptomatic correlation help us in initiating early treatment and will be beneficial to the patients in more than one ways.

Key Words: Mediastinal Mass, Lymphoma, Clinico-pathological spectrum

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I. Introduction

Mediastinal masses are always an enigma to surgical pathologist because they are among the most perplexing lesions explored and are relatively inaccessible. There are various lesions occurring here but biopsies are often scanty and crushed. Moreover, very few pathologists have remarkable knowledge about mediastinal pathology since these specimens are rare¹. Thorough evaluation and exact diagnosis of various undifferentiated mediastinal tumors with overlapping histology are needed because their suitable treatment differs considerably and may significantly impact survival.²

The mediastinum is a “forgiving” region of the human anatomy. A benign lesion is usually asymptomatic and a malignant lesion is symptomatic³. Imaging studies help immensely in their initial evaluation⁴. CT scan reveals the exact site and to some extent the nature of the masses. Surgical biopsy (True-cut/ open surgical) remains the gold standard for conclusive opinion. CT-guided needle biopsies are the first diagnostic procedures used in these cases now⁵.

Mediastinal masses are relatively uncommon lesions producing an interesting diagnostic and therapeutic dilemma for the clinician⁶. Shrivastava et al⁶ found thymic pathology in (39%) patients, lymphoma in (29%), germ cell tumors in (13%) patients. In a study by Dubashi et al⁷ superior venacaval obstruction (SVCO) was seen in 28% of the patients and in adults, thymoma (39%), lymphoma (30%) and germ cell tumor (15%) were the common tumors.

Mediastinal lymphoma is uncommon and may be primary or secondary. Mediastinal lymph nodes are usually involved secondarily as a part of the systemic disease.⁸ Only 10% of lymphomas which involve the mediastinum are primary.⁹ Hodgkin's lymphoma (HL), primary mediastinal B-cell lymphoma (PMBCL) and T-lymphoblastic lymphoma (TLL) are the most common primary mediastinal lymphomas.¹⁰ This study aims to detail the histological features of mediastinal lymphomas diagnosed in our Institute,.

Lymphomas comprise of 10 to 14% of mediastinal mass lesions in adults. They represent usually 20% of anterosuperior mediastinal masses and 20% of middle mediastinal masses. Lymphoma may involve the anterior, middle and or posterior mediastinum, frequently as lymphadenopathy or as a discrete mass. It is seen that approximately 75 % of patients with Hodgkin's disease present with mediastinal disease whereas only 5 percent of patients with non-Hodgkin's lymphoma present with mediastinal involvement¹¹.

Although PMLBCL and mediastinal CHL share many clinicopathologic characteristics, their treatment strategies and responses are remarkably different.

This prospective study deals with the evaluation and clinicopathological spectrum of mediastinal lymphomas and was performed to analyze the epidemiologic profile, clinical features, histopathological findings and treatment in patients presenting with a mediastinal lymphoma. The Present study tried to differentiate Hodgkin Lymphoma from Non Hodgkin Lymphoma so that the patients get proper treatment. The main purpose is to delve into the deep sea of mediastinal masses and identify various types of lymphomas. This study also aims to show whether symptoms can provide clues enabling the timely ordering of investigations. It is earnestly hoped that the present study will contribute a small mite in tackling the menacing problem of mediastinal lymphomas. In this study it has been tried to describe distribution of different clinical profiles and radiological presentations of mediastinal lymphomas and take the help of histology to reach the etiological diagnosis for proper treatment.

II. Material and Methods

Study Design: Cross-sectional Observational study

Study Location: R.G.Kar Medical College and Hospital, Kolkata, a tertiary care hospital in West Bengal, India.

Study Duration: From June 2011 to May 2013

Sample Size: 40 Patients.

Inclusion Criteria:

- i. Patients with a mediastinal mass, admitted in R.G.Kar Medical College
- ii. All the patients in the present study were symptomatic

Exclusion Criteria: Patients with critical parameters and moribund patients were excluded.

Procedure Methodology:

The anatomical location of the mediastinal mass was determined by chest radiographs (posteroanterior and lateral views). Computed tomography was performed to assess operability. Neurologic evaluation was carried out in cases of suspected myasthenia gravis. Histopathological study was done as needed by Tru-cut biopsy from mediastinal diseases (Ultrasound guided/CT Scan guided) & open surgical biopsy. Tru-cut biopsy was done in 24 cases & open surgical biopsy was done in 16 cases. The surgical approach was according to the anatomical location of the tumor. Specimens collected from the CTVS department were properly grossed in the Pathology department of R.G.Kar Medical College. Tru-cut biopsies mainly consist of 1.5-2 cm linear tissue pieces. Among the open biopsy specimens solid homogenous lesions were seen only in 12 patients. Solid lesions as large as 24x14x9 cm were and as small as 4x3x3cm were seen..With the help of noninvasive and invasive procedures etiological diagnosis of all the mediastinal cases was performed. Then they were again classified as per topography in the mediastinum.

Statistical Analysis:

All the available information were recorded meticulously and a database was created. The different parameters like age, sex, addictive habits, presenting complaints, clinical features were used to delineate the distribution of mediastinal diseases in the population. Different radiological features of mediastinal diseases were studied. A grand chart was prepared Using MS Excel software and statistical analysis were performed Using SPSS software (Version 16). Chi square test and Fisher exact tests were applied. P value Less than 0.05 were considered significant.

III. Result

Table- 1: Distribution of Age and Sex

AGE GROUP	MALE	FEMALE	TOTAL	PERCENTAGE
0-10	0	0	0	0
11-20	0	1	1	2.5
21-30	8	2	10	25
31-40	10	05	15	37.5
41-50	6	4	10	25
51-60	3	0	3	7.5
61-70	1	0	1	2.5
TOTAL	28	12	40	

Of 40 patients, 28 patients (70%) were male and 15 patients (30%) were female (Table 1). The age range was 9 years to 62years. All the patients in the present study were symptomatic. In majority, multiple symptoms were present in each case. Presentation was mainly dependent on the location of the masses.

Most common (%) age group of mediastinal disease was 31-40 years. Male to female ratio was 1:2 . Mean age of the patients was 35.5 years (Table1).

. Shortness of breath (72.5%), cough (62.28%), Fever(54.18%) were the leading symptoms. Certain clinical features were prevalent in certain topographical position. All the symptoms except chest pain mainly those of superior venacaval syndrome were mostly seen in cases where anterior mediastinum, was involved with or without involvement of the superior mediastinum . Chest pain was most commonly seen in patients of posterior mediastinal involvement. These findings were statistically significant. Diabetes was present in 11.54% patients. 12.26% patients had hypertension. 9.36% patients had hypothyroidism. Three patients had dilated cardiomyopathy. Ischemic heart disease was found in 14.55% cases. Myasthenia gravis was seen in two females.

CTscan revealed the exact location of the tumors. Only one mediastinum was most commonly involved comprising 72.5% of total cases. As single site involvement, anterior mediastinum was the most common site (60%). Overall combined involvement of anterior and superior compartment seen in 20% cases. All cases of superior mediastinal involvement were seen to have anterior mediastinal involvement along with. If anterior and superior compartments are taken together as antero-superior compartment it comprises 80% of total cases.

Among the invasive procedures Trans thoracic CT guided Tru-cut and open surgical biopsy were mainly studied thoroughly in the present study .The surgical approach was decided on the basis of the anatomical location of the tumor. Of the surgical approaches used, thoracotomy was the most commonly used approach amounting to 80.44% of the patients who underwent surgery. Of all the thoracotomy approaches, Left Posterolateral approach was the most common approach.

Table-2: Etiological Diagnosis as Per Topographical Distribution

ETIOLOGICAL DIAGNOSIS	MEDIASTINAL INVOLVEMENT					
	INVOLVEMENT OF SINGLE COMPARTMENT			INVOLVEMENT OF TWO COMPARTMENTS		INVOLVEMENT OF MORE THAN TWO COMPARTMENTS (N6=1)
	ANTERIOR (N1=25)	MIDDLE (N2=05)	POSTERIOR (N3=0)	SUPERIOR +ANTERIOR (N4=16)	MIDDLE +POSTERIOR (N5=03)	
LYMPHOMA (n4=40)	24 (60%)	05 (12.5%)	00	08 (20%)	03 (7.5%)	00

The histopathological diagnosis and sites of the tumors are listed in Table 2. Individually teratomas and lymphomas were the most common etiology comprising 20.69% of total cases. There were 18 cases of non-Hodgkins Lymphoma and 22 cases of Hodgkins Lymphoma. A 42 years female presenting with SVC Syndrome with an anterior mediastinal mass turned to Thymic Lymphoma. Anterior mediastinum was the most common site for lymphoma (60%) followed by antero superior (20%) mediastinum.

Table-3 Distribution of cases by location of mediastinal lymphoma and SVC obstruction, shortness of breath(SOB), chest pain, Anterior D'espine sign and presence of cystic change in CT scan of thorax

Parameter		ANTERIOR & SUPERIOR MEDIASTINAL LYMPHOMA	MIDDLE & POSTERIOR MEDIASTINAL LYMPHOMA	P VALUE
SVC OBSTRUCTION	YES	25(62.5%)	1(2.5%)	0.008*
	NO	7(17.5%)	04(10%)	
SOB	YES	27 (67.5%)	02(5%)	0.024*
	NO	5 (12.5%)	03(7.5%)	
Chest pain	YES	04(10%)	04(10%)	<0.001*
	NO	28 (70%)	1(2.5%)	
Anterior D'espine sign	YES	26 (65%)	1(2.5%)	0.004*
	NO	06(15%)	04(10%)	

*Statistically Significant at confidence interval >95%

IV. Discussion

As there are numerous causes of mediastinal tumors, exact incidence data are deficient. They are infrequent, representing about 3% of the intrathoracic tumors^{12,13}. About 25% to 49% of these lesions are malignant⁹. Our study includes 48.3% malignant cases.

Shrivastava⁶ PC and coworkers analyzed 106 cases of mediastinal diseases and found male to female ratio of 1.9:1 and the peak age group was 3rd and 4th decade of life (56%). It is important to note that like the present study, this study was also done in India. 84% patients presented with chest pain and 59% with shortness of breath. Antero-superior mediastinum was involved in 72%, middle mediastinum in 12%, and posterior mediastinum in 16% cases. In the antero-superior mediastinum thymic neoplasms were the mostly found (54%). Lymphomas were the next. Our study shows most lymphomas are found in antero-superior mediastinum.

A similar study in the black African population¹⁴ constitute 75 males and 30 females, with a mean age of 34 ± 20.4 years. Most patients were symptomatic. Thymic tumor was the most common neoplasm in the antero-superior mediastinum. Most lesions were situated in the antero-superior mediastinum (63.8%), with lymphoma being the most common (21.9%).

A similar study by Dubashi et al⁷ showed male preponderance with mean age of 37.48 ± 17.04 years . 97% of patients were symptomatic . 28% of the patients presented with Superior venacaval obstruction. Most of the lesions were in the anterior mediastinum. In adults, thymoma (39%), lymphoma (30%) and germ cell tumor (15%) were the frequent tumors. The present study shows that most lymphomas are found in antero-superior mediastinum. Vaziri et al showed that the most presenting complaints were dyspnea (41%) and cough (40%). Twelve percent of patients were asymptomatic. The most common complication was Superior Vena Cava (SVC) syndrome. The most common site (65%) was the anterior mediastinum. Malignant lymphoma was the most common malignancy during the first four decades of life.

Davis et al¹⁵ established that 85% of malignant patients were symptomatic, compared to 46% of patients with benign neoplasms . Crausman RS¹⁶ stated that specific clinical features strongly indicate mediastinal pathology. In a study by Singh et al¹⁷ the anterosuperior mediastinum was the most frequent location. Saad R Jr et al¹⁸ showed that Lymphoma was the most common malignancy (13.1%).

Aggarwal et al¹⁹ found 56.25% of Non-Hodgkin Lymphoma and the most common age group was 21-30years. Bone marrow involvement was seen in one case. Our study shows 31-40 years as the most common age group and 45% of Non-Hodgkin Lymphoma. In our study no case showed bone marrow involvement.

A proper evaluation should be done to determine the location and extension of the lesion. Since compression of the vital organs may be a significant risk, early diagnosis and proper surgical removal are mandatory. Also novel approaches in anesthesia, surgical techniques, postoperative care, chemotherapy, immunotherapy and radiotherapy have improved mortality and morbidity, increasing survival and quality of life. In inoperable cases exploratory thoracotomy may be done for diagnosing the mediastinal lesion with the help of histopathology. In operable cases, excision can be done.

V. Conclusion

The Pandora's box, as mediastinum is often referred to, shrouded in mystery since long; truly speaking, it remains an uncharted territory for anatomists, surgical pathologists and cardiovascular surgeons. Not too many workers explored this area of surgical pathology. When delved into the deep sea of this complex compartment for the present study, it came out to be a treasure house of pathological lesions.

As the sample size was very small, the present data might not be the exact reflection of the actual picture of mediastinal SOLs. Also it have not been possible to undertake IHC in all the cases. So a more detailed study on a larger sample size should be performed to bring out the true picture of the enigmatic lesions – the mediastinal masses. More elaborate study is necessary to determine the incidence and prevalence of mediastinal masses.

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