

A STUDY OF CLINICAL PROFILE AND MANAGEMENT OF PATIENTS WITH MEDIASTINAL TUMOURS

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ABSTRACT

BACKGROUND

A large number of neoplasms and cysts may arise from multiple anatomic sites in the mediastinum and present with myriad clinical signs and symptoms. They affect people of all ages, although apparently more common in young and middle-aged adults.

AIM: The present study was designed to study the location, incidence and various surgical options available for mediastinal tumours.

MATERIALS AND METHODS

This retrospective study includes 24 cases of mediastinal masses admitted in Gandhi Hospital between Jan 2012 and Nov 2012. All details of the patient's pertinent clinical history was obtained from case record file in the department.

RESULTS

Out of 24 cases, 15 (60%) cases are between age group of 10-30 years with equal incidence in gender. Most of the lesions 18 (70%) cases were seen in anterior mediastinum region and 12 (50%) cases were treated with anterolateral thoracotomy surgical approach. Complete resection of tumours was done in 11 (46%) cases. Histopathological examination revealed benign thymomas in 6 (25%) cases as commonest tumour.

CONCLUSION

Anterior mediastinal tumours are more common, which can be treated with anterolateral thoracotomy with very low morbidity and almost nil mortality with good outcomes.

KEYWORDS

Mediastinum, Anterior Mediastinal Tumours, Anterolateral Thoracotomy, Thymoma.

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INTRODUCTION: A large number of neoplasms and cysts may arise from multiple anatomic sites in the mediastinum and present with myriad clinical signs and symptoms. They affect people of all ages, although apparently more common in young and middle-aged adults. Most masses are discovered on routine radiographic examination of the chest in an asymptomatic person. Many of these lesions produce specific or nonspecific symptoms and signs.^{1,2} The natural history varies from those that are asymptomatic to those with benign slow growth causing minimal symptoms to aggressive, invasive neoplasms that are often widely metastatic, rapidly resulting in death. Rapid development in

the technique of thoracic surgery, an increasingly frequent employment of routine chest x-rays and mass radiographic surveys aimed primarily as the control of tuberculosis have revealed a greater evidence of mediastinal tumefactions than heretofore suspected have demanded greater efforts towards more exact diagnosis and have brought about a profound change in attitude toward treatment.³

The precise nature of a lesion in the mediastinum, as elsewhere, cannot be determined without histological examination of the tissue. Nonetheless, a reasonable tentative preoperative diagnosis for each lesion frequently can be made by considering its location in the mediastinum, age of the patient, presence or absence of local or constitutional signs, symptoms and the association of a specific systemic disease state. In addition, the location of the mass explains some of the typical symptoms related to a mediastinal mass because of compression or invasion of adjacent mediastinal structures. Anterosuperior mediastinal masses are most likely to produce the superior vena caval syndrome. Posterior mediastinal masses are most likely to cause spinal cord compression syndromes. Most common mediastinal masses are primary cysts (21%), neurogenic

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tumours (20%), thymomas (19%), lymphomas (13%) and germ cell tumours (10%).

Mediastinal masses are most frequently located in the anterosuperior mediastinum (54%) with the posterior (26%) and middle mediastinum (20%) being less frequently involved.⁴ In the anterosuperior mediastinum, the most frequent neoplasms are thymoma (31%), lymphoma (23%) and germ cell tumours (17%). Posterior mediastinal lesions are usually neurogenic tumours (52%), bronchogenic cysts (22%) and enteric cysts (7%).^{5,6}

Malignant neoplasms represent 25% to 42% of mediastinal masses. Lymphomas, thymomas, germ cell tumours, primary carcinomas and neurogenic tumours are the most common.⁷

The relative frequency of mediastinal mass malignancy varies with the anatomic site in the mediastinum. Anterosuperior masses are most likely malignant (59%) relative to middle mediastinal masses (29%) and posterior mediastinal masses (16%). The relative percentage of lesions that are malignant also varies with the age. Patient in the second through fourth decade of life have a greater proportion of malignant mediastinal masses. The period corresponds with the peak incidence of lymphomas and germ cell tumours. In contrast, in the first decade of life, a mediastinal mass is most likely benign (73%).⁸

The present study was designed to study the location, incidence and various surgical options available for mediastinal tumours.

MATERIALS AND METHODS: This retrospective study includes 25 cases of mediastinal masses admitted in Gandhi Hospital between Jan 2012 to Nov 2015.

Inclusion Criteria: All the patients who were operated for mediastinal tumours are below the age of 40 years.

Exclusion Criteria: Patients with lung malignancies that are directly extends into mediastinum, oesophageal malignancies, cardiac tumours and hernias into mediastinum and features of myasthenia gravis.

Data pertaining to the patient's age, sex, chief complaints, physical examination findings, investigations done, after surgery intraop assessment, histopathology diagnosis and outcome, all the patients admitted to Gandhi Hospital with mediastinal tumours undergo CT scan of the chest (Plain and contrast). All superior mediastinal tumours were approached through median sternotomy. Anterior mediastinal tumours were approached depending upon their encroachment into the hemithorax either by median sternotomy or right or left anterolateral thoracotomy.

An initial assessment of the tumour was done to rule out involvement of the surrounding structures. Whenever possible, complete resection was done. If the tumour was not resectable due to involvement of vital structures, debulking of the tumour mass was tried. Whenever debulking was also not possible, only a wedge biopsy was taken. Posterior mediastinal masses were approached by posterolateral thoracotomy. Patients with β -HCG and α -Fetoprotein levels high were ruled out considering it as malignant germ cell tumours.

RESULTS: Out of 25 patients, 15 (60%) patients belonged to age group 10-30 years, only 4 patients were more than 40 yrs. with equal gender distribution. 18 (72%) patients were symptomatic while only 7 (28%) patients were asymptomatic (Table No. 1). Most common symptom was chest pain (62.5%), cough (32%). (Fig No. 1).

Demographic Data	No. of Patients
Age Distribution In Years	
10-20 Years	7
21-30 Years	8
31-40 Years	6
>40 Years	4
Sex Distribution	
Female	13
Male	12
Symptoms	
Symptomatic	18
Asymptomatic	7

Table 1: Demographic Data of Patients

Sl. No.	Investigations	No. of Patients
1	CHEST R/G	
	Anterior	18
	Posterior	5
	Superior	2
2	Tumour Markers Positive for	
	B-HCG	11
	AFP	12
3	FNAC and Diagnosis	
	Inconclusive	5
	Tuberculosis	1
	Lymphoma	1
	Thymoma	1

Table 2: Results of Investigations Performed

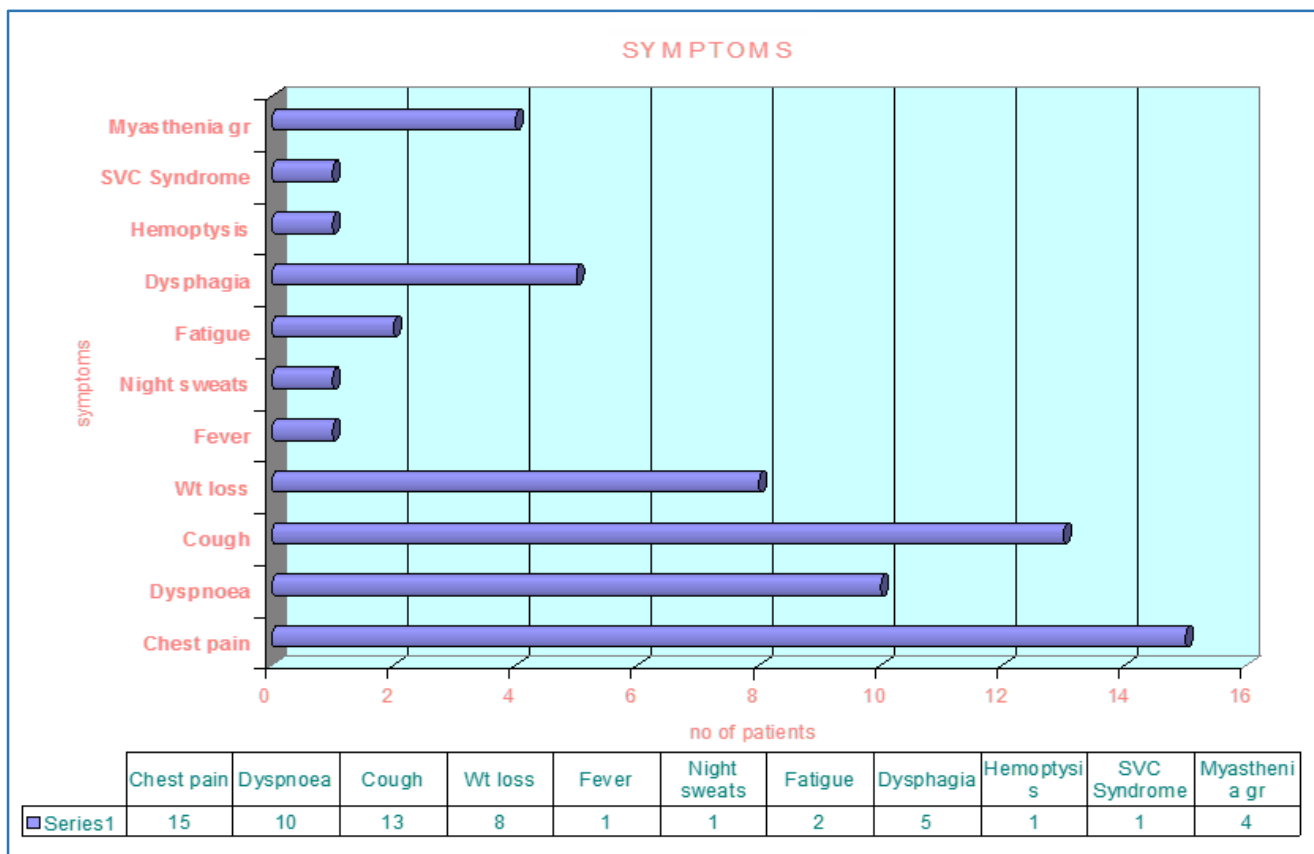


Fig. 1: Common Symptoms of Patients

In investigations, chest radiograph revealed 18 (70%) patients had anterior mediastinal tumour followed by posterior (22%) and superior (8%), respectively. CT scan with plain and contrast was done in all the patients. As a routine, tumour markers (Mainly B-HCG and AFP) were done in all patients who were <40 years with anterior mediastinal tumours. Out of 24 patients, 8 had FNAC diagnosis and 2 had tissue biopsy. 5 FNAC reposts were inconclusive and 1 FNAC gave the suspicion of tuberculosis, which was confirmed by percutaneous CT-guided biopsy whereas 2 cases were diagnosed as tuberculosis and thymoma in biopsy (Table No. 2). Benign Thymoma was the most common tumour present in 6 patients, whereas another 4 patients had thymic carcinoma. Thus, thymoma was the most common tumour present in 40% of the patients. Germ cell tumour was the second commonest tumour. 3 patients had benign germ cell tumour while 2 patients had malignant germ cell tumour. Lymphoma was present in 2 patients. 4 patients were diagnosed to have neurogenic tumours. 2 patients had lymph node tuberculosis. (Fig No. 2).

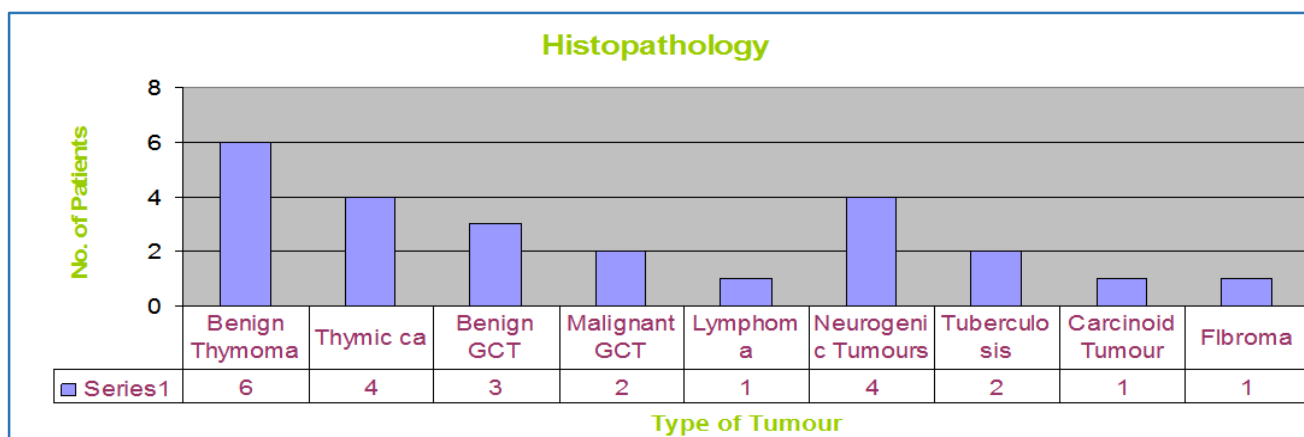


Fig. 2: Histopathological Findings of Mediastinal Tumours

Out of 25 patients, all patients were operated upon except 1. Most of the anterior mediastinal tumours 12 (50%) were operated through anterolateral thoracotomy whereas superior mediastinal tumours 5 (20%) were operated by

median sternotomy. Out of 24 cases, 11 (45%) cases complete resection could be performed. In 3 (12%) cases due to non-resectability of the tumour, only wedge biopsy was performed, whereas in another 3 (12%) cases

debulking of the tumour mass was done. 6 (25%) cases underwent thymectomy where in en bloc excision of the mass with thymus gland was performed.

Surgery Approach	No. of Patients
Median Sternotomy	5
Anterolateral	12
Posterior lateral	7
Intraoperative resectability	
Resectable	18
Non-resectable	6
Procedure	
Thymectomy	6
Complete resection	11
Wedge biopsy	3
Debulking	3
Enucleation	1
Table 3: Surgical Interventions of Mediastinal Tumours	

DISCUSSION: Demographic Data: In the present study, fifteen patients (60%) belonged to the age group of 10 to 30 years. There were only 4 patients with age of more than 40 years. There were 13 male and 12 female patients. The incidence and types of many primary mediastinal tumours and cysts vary with age of the patient group under consideration. The clinical presentation varies from those patients who are asymptomatic (The diagnosis was made during routine chest x-ray), to those with symptoms related to mechanical effects of invasion or compression to those who have systemic symptoms. Of the patients with a mediastinal mass, 56% to 65% are symptomatic at presentation. In the present study, 72% of the patients presented to us with symptoms whereas 7 patients (28%) were diagnosed to have mediastinal tumour incidentally during routine chest x-ray. Out of seven asymptomatic patients presented to us, only 1 patient had malignant tumour, rest of the 6 patients had benign tumour. Lillie WI et al⁹ in their series reported that patient with a benign lesion were more often a symptomatic (54%) that were patients with a malignant neoplasm (15%). The absence of symptoms is therefore usually associated with a benign histological diagnosis. In asymptomatic patients with a mediastinal mass Takeda S et al¹⁰ 76% had a benign lesion. In contrast, 62% of symptomatic patients had a malignant neoplasm during this period. In the present study, chest pain was the commonest presenting complaint and was present in 15 (60%) patient. Cough was the next commonest symptom and was present in 13 (52%) patients. The most common feature in a series of 441 patients were chest pain, cough and fever.¹⁴

Clinical Features: Paralleling the relative percentages of the malignant neoplasm within the different anatomic regions, tumours of the anterosuperior mediastinum are most likely to cause symptoms (75%) relative to the posterior mediastinum (50%) and the middle mediastinum (45%). Myasthenia gravis was present in 4 patients out of 8

who were diagnosed to have thymoma. Although, myasthenia gravis was present in only 16% of patients from the overall series of the patients with thymoma, 50% had myasthenia gravis. Most of the patients (68%) were in the age group of 20 to 40. The sex distribution was approximately equal between men and women. Approximately, 40% of the patients with thymoma had local symptoms like chest pain, dyspnoea and cough. One patient presented to us with superior vena cava obstruction.

Diagnosis: The goal of the diagnostic evaluation in a patient with a mediastinal mass is a precise histological diagnosis, so that optimal therapy can be performed. The preoperative evaluation of a patient with mediastinal mass should achieve the following:

1. Differentiate a primary mediastinal mass from masses of other causes that have a similar radiographic appearance.
2. Recognise associated systemic manifestations that may affect the patient's perioperative course.
3. Evaluate the tracheobronchial tree, pulmonary tree or superior vena cava for possible compression by the mass.
4. Ascertain whether the mass extends into the spinal column.
5. Determine whether the mass is as nonseminomatous germ cell tumour.
6. Assess the likelihood of resectability.
7. Identify significant factors of medical comorbidity and optimise overall medical condition.

The initial diagnostic intervention contained a careful history and physical examination. The posteroanterior and lateral chest films provided important information. Location within the mediastinum, size of the lesion, displacement and alteration of anatomic structures in the mediastinum and adjacent regions, the relative density of the mass with regard to whether the lesion was cystic or solid, whether calcification were present and the pattern of the calcification, information regarding the anatomic location of the mediastinal mass narrowed the differential diagnosis.

CT scan with contrast was obtained in all the patients with the mediastinal mass. Accurate anatomic information about the relationship of the mass to surrounding structures was gained as well as considerable information about the relative invasiveness and the malignant nature of the mediastinal mass. The presence of tumour disruption of fat planes, irregularity of pleural, vascular or pericardial margins by tumour and infiltration into muscle or periosteum could differentiate tumour compression from invasion. Additional information obtained using CT included the presence of chest multiple masses from single large mass.¹¹

MRI was not done in any of the patients in the present study. Literature recommends evaluation of a mass by MRI especially in posterior mediastinal masses to rule out extensions into the spinal column.¹² CT or MRI reliably differentiates mediastinal tumours from mediastinal masses that are of cardiovascular cause and that may appear on

chest film as a mediastinal mass. Several mediastinal masses can be diagnosed preoperatively using their imaging modalities owing to their characteristic location, appearance and attenuation values. Despite accuracy of CT imaging, emphasis must remain on establishing the precise histological diagnosis to avoid mistreating a potentially curable neoplasm. Using CT, the correct preoperative diagnosis is made in approximately 68% of patients. Although, CT scanning is sensitive in the evaluation of mediastinal masses and lymphadenopathy, it is not specific for tumour involvement. Histopathological examination of abnormal mediastinal lymph nodes (>1.5 cm) determined by CT scanning in patients with known malignancies demonstrates that in more than one third of patients, the lymph node was benign.¹³

Serologic evaluation was done in all patients between the age group of 20 to 40 years with an anterior mediastinal mass. Alpha-Fetoprotein (AFP) and beta-human chorionic gonadotropin (B-HCG) were obtained. In the present study, AFP and B-HCG levels were obtained in 14 patients. Two patients had significantly elevated B-HCG and AFP and one patient had elevated levels of B-HCG. Serologic measurements of AFP and B-HCG are useful for differentiating Seminomas from nonseminomas, quantitatively assessing response to therapy in hormonally active tumours. Seminomas rarely produce B-HCG (<7%) and never produce AFP; in contrast, over 90% of nonseminomatous secrete one or both of these hormones. This differentiation is important owing to the marked radiosensitivity of seminomas and relative radio insensitivity to nonseminomas. Increased success has been reported in making a cytological diagnosis preoperatively by using fine-needle biopsy techniques (No. 22 gauge needle) with low morbidity and almost zero mortality. CT scan because of better localisation of the mass and improved placement of needle, has increased the sensitivity of the technique. Although, a precise histological diagnosis is not always possible, a cytological diagnosis of either benign or malignant nature of the tumour can be made in 80 to 90% of patients. Complications related to the procedure include pneumothorax in 20 to 25% of patients with approximately 5% requiring tube thoracostomy, haemoptysis in 5 to 10% with rare occurrences of significant haemorrhagic complications and tumour seeding along the needle tract.

FNAC or percutaneous CT-guided biopsies were performed whenever indicated. FNAC was performed in 8 patients in the present study, 5 were inconclusive where rest 3 could give some histological diagnosis. An increased sensitivity in obtaining a precise histological diagnosis has been reported using cutting needle techniques (No. 16 gauge needle) without an apparent increase in morbidity (23% incidence of pneumothorax).

Needle biopsy was performed in 2 patients in the present series and both gave a histological diagnosis and surgery was avoided. One patient was diagnosed to have lymph node tuberculosis and was discharged on antituberculosis treatment and another patient was

diagnosed to have Hodgkin's lymphoma, lymphocyte predominance and was referred for radiotherapy.

Treatment: Treatment plan was based on the results of the above evaluation. Lesions that appeared resectable on CT scan were resected. For anterosuperior mediastinal tumours, either median sternotomy approach or anterolateral approach was used. Five patients underwent median sternotomy while 12 patients underwent anterolateral thoracotomy. Both the incisions provide optimal exposure for the lesions in the anterior and superior mediastinum. A transcervical approach using sternal elevators has been successful in some centres for resection of tumours in the superior aspect of the anterosuperior mediastinum. Posterior mediastinal masses were excised through a posterolateral thoracotomy. Complete excision was achieved in 13 (44%) patients. Thymectomy was performed in 6 patients. Enucleation was performed in one patient. Six patients had nonresectable tumour. In three patients, debulking of the tumour was done, while in rest of the 3 patients, only a wedge biopsy was taken.

Mediastinoscopy is a useful technique to evaluate and biopsy lesions of the middle mediastinum particularly those located in the anterior aspect of the subcarinal space around the proximal main stem bronchi and around the lower trachea. Often, this technique is used to evaluate associated lymphadenopathy in these particular regions. Lesions in the anterosuperior mediastinum that are thought to be unresectable are best biopsied using a limited anterior second or third interspace parasternal mediastinotomy. Similarly, unresectable lesions in the superior mediastinum, hilar or paratracheal regions can be biopsied through a small lateral thoracotomy in the third or fourth interspace after retracting the apex of the lung inferiorly. A representative section of the tissue obtained should be submitted for immediate frozen section to establish adequacy of the biopsy before closing. A transcervical approach using sternal elevators has been successful in some centres for resection of tumours in the superior aspect of the anterosuperior mediastinum. Thoracoscopy and thoroscopically-assisted procedures have been used to biopsy and resect a variety of mediastinal lesions in carefully selected patients. All the patients underwent procedures safely. There were no major complications. Only 2 patients had bleeding postoperatively, but could be controlled conservatively. Only 1 patient had wound infection and required secondary suturing. This was the patient with teratoma, which ruptured during dissection. There were no mortalities. Patient requiring chemoradiotherapy was referred to a government cancer hospital. Thymic tumour was the most common neoplasms in the present series. Ten patients (40%) had thymic tumours. Six patients had benign thymoma and four patients had thymic carcinoma.

Mixed Lymphocytic are present in 8 patients, 2 patients had lymphocytic variant while one patient had spindle cell variant of thymoma. Thymomas are histologically classified either by the predominance of epithelial or lymphocytic cells or by the morphologic resemblance to cortical or medullary

epithelium. Unfortunately, a wide variance of the cellular composition is often present within the tumour. The differentiation between benign and malignant disease is gross invasion of adjacent structures, metastasis or microscopic evidence of capsular invasion. Fifteen to 65% of thymomas are benign. The relative percentage is partially related to early surgical treatment of myasthenia gravis. If thymectomy is performed early in the course of myasthenia gravis, a greater percentage of thymomas are benign. Germ cell tumour was the second commonest neoplasm in the present study. Five patients had germ cell tumours, 3 patients had benign germ cell tumour and 2 patients had malignant germ cell tumour. Although, these lesions are identical histologically to germ cell tumours originating in the gonads. They are not considered to be metastatic from primary gonadal tumours because mediastinal metastases from primary gonadal tumours are rare and because over 95% of patients with mediastinal germ cell tumours showed no evidence of tumour in the testes. In the present study, all the patients had primary mediastinal germ cell tumour, their testes were normal. In patients with mediastinal germ cell tumours, the current recommendations for evaluating the testes are careful physical examination and ultrasonography. Biopsy is reserved for positive findings. Blind biopsy or orchiectomy is contraindicated.

Teratomas are neoplasms composed of multiple tissue elements derived from the three primitive embryonic layers foreign to the area in which they occur. These tumours are located most commonly in the anterosuperior mediastinum, although 3-8% occur in the posterior mediastinum. Both the teratomas in the present study were present in the anterior mediastinum. The teratodermoid (dermoid) cyst is the simplest form. It is composed predominantly of derivatives of the epidermal layer including dermal and epidermal glands, hair and sebaceous material. The presence of primitive or embryonic tissue distinguishes malignant tumours from benign. Therefore, diagnosis and therapy rely on surgical excision. Malignant germ cell tumours also occur predominantly in the superior mediastinum and represents approximately 4% of the primary tumours and cysts in the series. Unlike the benign teratomas, these tumours have a marked male predominance. Seminomas account for 50% of malignant germ cell tumours and approximately 2 to 4% of all mediastinal masses. These tumours occur predominantly in the anterosuperior mediastinum. In the present study, 2 patients had seminoma. In one patient, complete excision could be achieved while another patient had nonresectable mass. Only wedge biopsy was taken in this patient. Both the patients were referred to cancer hospital for radiotherapy. Although, the mediastinum is frequently involved in patients with lymphoma sometimes during the course of the disease (40 to 70%), it is infrequently the sole site of disease at the time of presentation.

Only 5-10% of patients with Hodgkin's and non-Hodgkin's lymphoma have symptoms solely due to local mass effect. The Hodgkin's lymphomas are subdivided by histological appearance into nodular sclerosing, lymphocyte predominant, mixed cellularity and lymphocyte depleted. Mediastinal involvement is most common with nodular

sclerosing (55 to 75%) and lymphocyte predominant (40%). In the present series, there was 1 patient with mediastinal lymphoma with predominance variety. Treatment of Hodgkin's lymphoma is determined by the stage of disease and is based on radiation and chemotherapy. Surgical excision of all disease is rarely possible and the surgeon's primary role is to provide sufficient tissues for diagnosis and to assist in pathologic staging, a process that frequently requires staging exploratory laparotomy and thoracotomy. Although, extrathoracic lymph nodes are frequently involved and available for biopsy. When the sole site of involvement is the mediastinum, a needle biopsy is often unsuccessful because large tissue samples are needed to make a histological diagnosis particularly with nodular sclerosing lesions.

In the present series, FNAC was tried, but was inconclusive in all, but 2 patients. Patient underwent Tru-Cut biopsy and the report came as Hodgkin's lymphoma. The surgery in this patient was avoided and patient was referred for chemoradiotherapy. Thoracotomy, Mediastinoscopy or Mediastinotomy may sometimes be necessary to obtain sufficient tissue.

Pursel et al,¹⁴ Ginsberg et al¹⁵ and Smythe et al¹⁶ in different eras have performed mediastinoscopic cyst excision with success. It however remains an underperformed procedure for what is a fairly common condition (20% of all mediastinal masses). Because most mediastinal cysts occur in the anterosuperior/middle mediastinum, areas easily accessible to the mediastinoscope, we advocate that mediastinoscopy be attempted for excision of cysts at these locations with more invasive procedures (VATS/thoracotomy) being used for failed mediastinoscopic removal, cysts not accessible to the mediastinoscope or in situations where mediastinoscopy would be contraindicated (Previous mediastinoscopic procedures or suspected malignant cysts with adhesion to surrounding structures).

CONCLUSIONS: Surgical excision is not essential for the treatment of a number of malignant neoplasms. The optimal therapeutic regimen often requires precise histological subclassification. Because, needle biopsy techniques do not usually produce sufficient tissue for this purpose, more invasive procedures are often required, mediastinoscopy, mediastinotomy, thoracotomy and median sternotomy. Lesions that appear resectable should excise. Median sternotomy and anterolateral thoracotomy provide optimal exposure for lesions in the anterosuperior mediastinum. Middle and posterior mediastinal masses are usually best excised through a posterolateral thoracotomy. Surgical treatment of mediastinal tumours can be performed with very low morbidity and almost nil mortality with good outcomes.

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