Retrospective Analysis Of Mediastinal Lesions – A Tertiary care center experience

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Objective: *Mediastinal lesions include a variety of tumors and are of diagnostic challenge to the clinicians. The objective of this study was to review the clinical presentations, diagnostic methods adopted, and treatment offered to the patients with mediastinal lesions.The need for the study is to create awareness of early detection of rare mediastinal tumors because of its varied presentation. Timely diagnosis helps to prevent complications.*

Materials and Methods: *Case records of 20 patients with primary mediastinal lesions during the period 2009 -2013 were retrospectively analyzed from the medical records department of our hospital which is a tertiary referral hospital.Patients data included clinical presentation,diagnostic methods,treatment modalities,outcome and follow –up.*

Results: *20 patients with mediastinal lesions in the age range of 10 to 73 years were analysed. 13 were male and 7 were female.Analysis revealed 8 cases of thymoma,1 undifferentiated thymic carcinoma,2 germ cell tumor,2 neurogenic tumor,2 lymphoid tumor,2 multinodular goiter,1 each of bronchogenic cyst, atypical carcinoid and hydatid cyst.Thymoma was the commonest lesion.Diagnosis involved radiological assessment and tissue diagnosis.*

Conclusion: *The study included only primary mediastinal tumours. Diagnosis required an invasive procedure in most of the patients and thymoma was the commonest lesion.*

I. INTRODUCTION

Mediastinum is a site for neoplastic or non-neoplastic lesions. It could be benign or malignant, primary or metastatic, many of which present as mediastinal masses.[1] Primary mediastinal tumors are uncommon. Approximately 3% of the tumors within the chest are represented by primary mediastinal tumor.[2] Primary mediastinal lesions are most commonly from thymic, neurogenic, lymphatic or mesenchymal tissues. Mediastinal lesions can be classified according to their location as anterior, middle or posterior mediastinal tumour. Mediastinal lesions commonly present with compression symptoms, but they may remain asymptomatic for many years and can be diagnosed incidentally.

II. MATERIALS AND METHODS

We have done a retrospective analysis of twenty patients with mediastinal lesions who presented at our institute from 2009 to 2013. Data included patient's demographic details, clinical presentation, diagnostic methods, treatment modalities, outcome and follow-up. All the pertinent information was obtained from the medical records department of the hospital. Institutional ethical committee clearance was taken for the study.

Patients with the diagnosis of primary mediastinal lesions were included and those with infective etiology, bronchogenic carcinoma and metastatic carcinoma were excluded from the study.In our series 18 cases presented with various symptoms as shown in the Table 1.

Table 1. Symptomatology

Chest pain	8
Breathlessness	6
Cough	5
Dysphagia	3
Loss of appetite	2
Fever	1
Incidental finding	2
Myasthenia symptoms	4
Progressive weakness of limbs and gait difficulty	1

Mediastinal lesion was an incidental finding in routine radiological investigation in 2 cases.

On general physical examination there was no abnormality in any of the cases.Respiratory system examination findings were normal in 18 cases.One patient each had a bronchial breath sound in the right infraclavicular region and decreased air entry in the right infraclavicular region.Abdominal examination

was normal in all cases. 4 cases had myasthenia signs.One patient had right side hemiparesis. Chest x-ray,CECT thorax,routine biochemical,hematological investigations,ECG and Echocardiogram were done in all patients. The type of mediastinal lesions and the treatment offered is shown in Table 2.

Table 2. Clinical profile

Case No	Age	sex	DIAGNOSTIC PROCEDURE	Diagnosis	Treatment offered
1	44	F	CECT Thorax	Multinodular colloid goiter	Excision of goiter
2	38	M	CECT Thorax	Extraspinal neurofibroma	Thoracotomy and excision of tumor
3	33	M	CECT Thorax	Thymoma	Tumor excision
4	52	F	CECT Thorax	Hydatid Cyst	Excision of cyst
5	73	M	CECT Thorax	Bronchogenic cyst	Thoracotomy and excision of cyst
6	42	M	CECT Thorax	Thymoma	Tumor excision and immunosuppressants
7	72	F	Core Biopsy	Thymoma	Tumor excision and Radiotherapy
8	55	F	Core Biopsy	Undifferentiated malignancy of thymus	Tumor excision
9	63	M	FNAC	Atypical carcinoid tumor	Debulking of tumor
10	15	F	Core Biopsy	T cell lymphoblastic lymphoma	Chemotherapy
11	46	M	CECT Thorax	Retrosternal multinodular goitor	Excision of goiter
12	30	M	CECT Thorax	Mature cystic teratoma	Tumor excision
13	63	M	Core Biopsy	Thymoma	Tumor excision
14	10	F	CECT and MRI	Neurofibroma	Laminectomy and excision of tumor
15	35	M	CECT Thorax	Thymoma	Tumor excision
16	65	M	FNAC	Thymoma	Tumor excision,immunosuppressants and adjuant radiotherapy
17	12	F	CECT Thorax	Mature cystic teratoma	Tumor excision
18	45	M	FNAC	Thymoma Myasthenia crisis	Patient died while in crisis
19	40	M	Thoracotomy & biopsy	Hodgkin's Lymphoma	Chemotherapy
20	61	M	Core Biopsy	Thymoma	Refused Surgery

M-male F-female

III. RESULTS

Twenty patients were included in the study. The age range was from 10 years-to-73 years (mean-44.8). Thirteen were male and 7 were female with M: F = 1:0.53**.**

Patients presented with varied complaints like chest pain, breathlessness, cough, fever, dysphagia, loss of appetite, progressive weakness of the limbs and gait difficulty. Myasthenia Gravis and ocular myasthenia was seen in 1 case each. The diagnosis was established by FNAC in 3 cases and CT guided biopsy in 5 cases. Thoracotomy and median sternotomy were done in 6 cases each without attempting FNAC/CT guided biopsy. Thymictumors were the commonest with 8 cases of Thymoma and 1 case of high grade undifferentiated carcinoma.

Table 3 shows the follow up of the patients with thymic tumor.

Table 3. Follow up of Thymic tumors

Case No	Immediate Post-op period	Follow up
Case no 3	No post op complication	3 years –doing well
Case no 6	Myasthenia crisis, Plasma Exchange	5 years -doing well
Case no 7	No post-op complication	6 months follow –up D7 compression #
Case no 8	No post –op complication	No follow-up (Died 4 years post surgery)
Case no 13	Post op uneventful	No follow-up
Case no 15	Post op uneventful	No follow -up
Case no 16	Post op uneventful	Died of respiratory failure 7 months post surgery
Case no 18	No surgery	Died of myasthenia crisis
Case 20	Refused surgery	no follow -up

Complete excision of the lesions was done for germ cell tumor, hydatid cyst, bronchogenic cyst and multinodular goiter. Patient with Hydatid cyst developed fever in the immediate postoperative period, which responded to treatment. Chest x-ray done after 1 year of surgery was normal. Bronchogenic cyst and multinodular goiter cases are doing well 4 years post surgery. CT guided biopsy was conclusive of the diagnosis in one case of lymphoid tumor and another case underwent median sternotomy for the diagnosis. Both the cases have received chemotherapy. There was no follow up of the patient with Hodgkin's lymphoma and the patient with T cell Lymphoblastic lymphoma is still on maintenance chemotherapy. Posterolateral thoracotomy and excision of the neurogenic tumor with laminectomy was done in one case and two stage surgery was done in a case of dumb bell tumor and both the patients are doing well. Case of atypical carcinoid tumor died 2 months post surgery. One case of Mature cystic teratoma patients was followed up for 4 years and another for one month after surgery. Chest x-rays and Serum alpha fetoprotein and beta HCG levels were normal.

IV. DISCUSSION

Mediastinum is defined as the potential space between the two pleural cavities bounded by the sternum anteriorly, vertebral column posteriorly, thoracic inlet superiorly and the diaphragm inferiorly.[3] Mediastinal masses arise from and are associated with each of the organs found within the thorax.[3] Lesions that arise within the mediastinum primarily may extend into the neck or into the retroperitoneum below the diaphragm.

Lesions that arise in the mediastinum are rare.[3] Mediastinal masses include a variety of tumors and are of diagnostic challenge to the clinicians. A mediastinal mass is often an incidental finding when patients undergo chest imaging for an unrelated condition or symptom. The postero-anterior and lateral chest radiographs provide information regarding the location and size of a mediastinal mass. The detection of mediastinal lesions has increased with the use of CT which is the most important imaging modality to know the density of the mass and its effect on adjacent structures.[4]

The most common tumors found in the anterior mediastinal compartment are thymus, lymphatic or of germ cell origin. The masses associated with aberrant parathyroid or thyroid tissue are found rarely.[5] Common symptoms at presentation are cough, chest pain, fever/chills and dyspnea. When compared to other studies, sample size is small in our study due to exclusion of bronchogenic carcinoma,metastatic lesion and infective causes like tuberculosis.Majority of the patients were symptomatic in our analysis which is in comparison with other studies.[6,7] Patients may present with signs and symptoms due to compression or invasion of mediastinal structures.None of the patients in our study had signs of compression of mediastinal structures.

CT or ultrasound-guided percutaneous needle biopsy is now the standard procedure in the initial evaluation of mediastinal masses to get an accurate histologic diagnosis.[8] Some patients may still require an open surgical biopsy.Various diagnostic methods have limitations which explains the need for exploratory thoracotomy for biopsy and proceeding further for excision if found to be operable.[7] In our study, thoracotomy and median sternotomy was done in 6 cases each for the diagnosis.

A. Thymoma

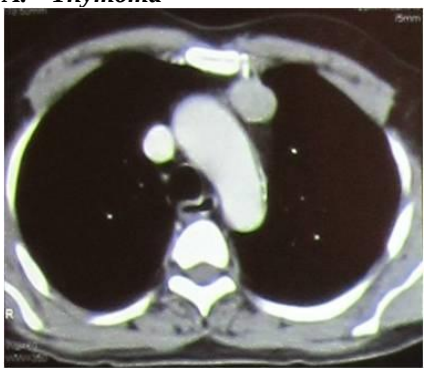

Figure 1 (Case No.16). A well defined homogeneously enhancing soft tissue attenuation lesion is seen in the anterior mediastinum anterior to the aortic arch in a 65 year old male patient.

Ultrasound /CT guided FNAC or trucut biopsy can give the diagnosis. However, diagnosis can be achieved during the time of surgery.[13] Diagnosis was arrived at by FNAC in 2 cases, CT guided biopsy in 5 cases and surgery in 2 cases in our study.

WHO in 2004 has classified thymomas on the basis of the histological findings of the morphology of neoplastic epithelial cells together with the lymphocyte –epithelial cell ratio. The Masaoka –Koga staging system describes thymomas in terms of the local extension of the tumor and is the most commonly used for management decisions.[12]

Thymomas are neoplasms that arise from epithelial cells of the thymus.[9]5-10% of all mediastinal tumors and 20-30% of those found in the anterior mediastinum are primary thymic tumors.[10] Thymomas are discovered incidentally and nearly one half of the patients are asymptomatic.[11]Thymoma is the most common primary neoplasm of the anterior mediastinum. Thymomas are more common in males.

In our study, thymoma was the most commonly diagnosed mediastinal lesion. Other studies also have reported similar findings.[1] There was a male predominance (M-7:F-1) which was noted in other studies as well.[6]

Biswajit et all have done an analysis of 91 cases with primary mediastinal malignancies and thymic neoplasm was the most common tumor.[2]
Thymomas appear as a well defined mass in the anterior mediastinum in the chest radiograph. Thymomas typically present as a spherical or ovoid homogeneously enhancing soft tissue mass in the anterior mediastinumon contrast enhanced thoracic CT scanning (Figure 1). They may present anywhere from the thoracic inlet to the cardiophrenic border. It may be heterogeneous or cystic because of areas of hemorrhage and necrosis.[12]

Surgery remains the mainstay of therapy.[14]Surgery, radiotherapy and chemotherapy either alone or in combination, is the approach to manage thymomas depending upon the tumor type. Thymectomies have been performed traditionally using either a median sternotomy approach or transcervical approach.Minimally invasive video assisted thoracoscopic surgery (VATS) thymectomy technique have been used for eary thymomas. [15]Marulli et allhave used robot assisted thoracoscopic thymectomy in early stage thymoma.[16]They are of the opinion that it is a safe procedure with low complication rate and a short hospitalization. A unique feature of thymomas is its association with Paraneoplastic syndromes, in particular myasthenia gravis.In our study 3 patients had myasthenia gravis and 1 died due to myasthenic crisis

before surgery. One had ocular myasthenia.Thymectomy was performed in 7 patients and all were doing well. 1 patient refused surgery and lost to follow up.

B. Germ cell tumors

Germ cell tumors mainly arise in the gonads. Mediastinum is the most common site for the development of extragonadal germ cell tumors. Both benign and malignant teratomas are classified as germ cell tumors.[3] The most common mediastinal germ cell tumor is benign teratoma.[17] Benign teratomas account for approximately 80 percent of all mediastinal germ cell tumors and 8 percent of all types of mediastinal tumors.[18] These tumors can be seen in any age group, but most common in adults from 20 to 40 years of age.[11] They affect both sexes more or less equally.Teratomas consist of multiple tissue types of totipotent cells containing 3 embryonic layers ectoderm, mesoderm and endoderm.[19]These tumors consist of a disorganized mixture of derivatives of the 3 germ layers-ectoderm, mesoderm and endoderm. They may contain elements of skin and its appendages, cartilage, bone, intestinal and respiratory epithelium and neurovascular tissue. Many patients with benign teratomas are asymptomatic. Symptoms are likely to develop if the cysts become infected and erode into the pericardial space, pleural space or a bronchus. They are often detected on the basis of standard chest radiographs. CT scans of the chest show the extent of tumor, its relationship to surrounding structures and the presence of cystic areas and calcification.Patients with benign teratomas have normal serum tumor markers (Serum alphafetoprotein and β-HCG). Surgical total resection via either thoracotomy or sternotomy is the treatment of choice for benign teratomas.[18] VATS techniques have been used in teratoma resection with promising results.[5]Tumor recurrence is rare following complete surgical excision.[19]

Complete surgical excision of the cystic lesion was done for both the patients in our study and tumor markers were negative (Figures 2, 3A-C).

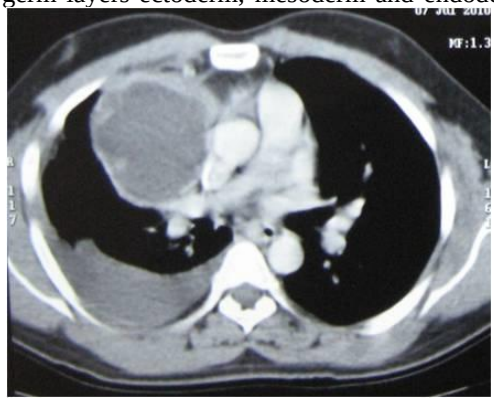

Figure 2 (Case No.12). A well-defined cystic lesion with thickened enhancing wall is seen in the anterior and middle mediastinum on the right side in a 30 year old male patient.

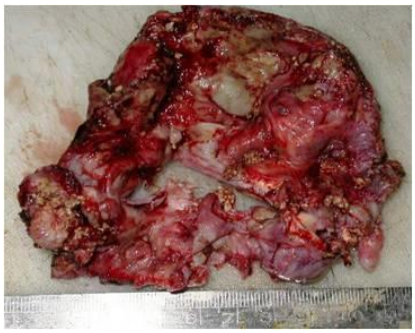

Figure 3A

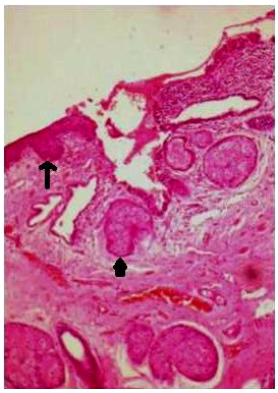

Figure 3B

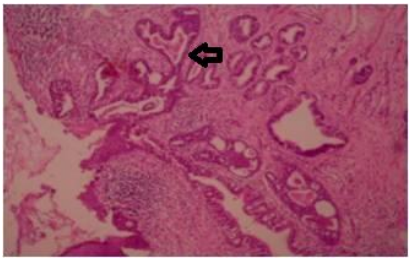

Figure 3C

FIGURE 3A (Case No.12). Benign cystic teratoma, Gross image –Tumor showed solid and cystic areas with gray yellow and calcified areas. FIGURE 3B and C (Case No.12). Histopathology revealed cyst lined by stratified squamous epithelium (epidermis, *thin arrows*) with adnexal structures (*thick arrow)*ectodermal derived and glandular component (*hollow arrow),*endodermal derived – H & E x100.

C. Neurogenic tumors

Neurogenic tumors are the most common neoplasm of the posterior mediastinum. Neurogenic tumors develop from the embryonic neural crest cells around the spinal ganglia and from either sympathetic or parasympathetic components.[3] Nerve

sheath tumors account for 65 percent of all neurogenic tumors of the mediastinum. Benign tumors of nerve sheath origin are classified as either neurilemmoma (schwannoma) or neurofibroma. Malignant tumors are rare.

Most of the patients with neurogenic tumors are asymptomatic. These tumors are detected when chest radiograph is done as a routine medical checkup. Some patients manifest symptoms of spinal cord compression or have cough, dyspnea, chest wall pain and hoarseness of voice.[3] Airway compression is more likely in pediatric patients leading to a predominance of symptoms related to respiratory tract.

Dumb bell tumors are neurogenic tumors that extend into the spinal column through the intervertebral foramen. CT scan shows a well defined lesion abutting the vertebral column. MRI is more useful to assess the involvement of the vertebral column and extension into the spinal cord. Both the patients in our study underwent excision of the tumor and are doing well.

D. Atypical carcinoid tumor

Bronchopulmonary carcinoid tumors are rare and are reported to represent 10% of all carcinoid tumors. Pathologically bronchial carcinoid tumors are divided into typical and atypical forms with variable grade of malignancy.Both typical and atypical carcinoids are the expression of neuroendocrine lung tumors.The spectrum of pulmonary neuroendocrine tumors includes four subtypes such as typical carcinoid,atypical carcinoid,large cell neuroendocrine carcinoma and small cell carcinoma.According to WHO revision in 1999/2004,an atypical carcinoid tumor is defined as a carcinoid tumor with between two and 10 mitoses per 10 high –power fields and /or with foci of necrosis. Atypical carcinoid tumors comprise about 10% of all pulmonary carcinoid tumors.[20] Typical carcinoid tumors of the lung characteristically grow slowly and tend to metastasize infrequently.[20]Atypical carcinoid tumors have a more aggressive clinical and histologic picture.They carry a worse prognosis and metastasize at a higher rate.[20] Carcinoid tumors have a propensity to arise in the right lung.[21]They may secrete hormone like substances causing paraneoplastic syndromes.They can present with cough,hemoptysis,or signs of obstruction and sometimes patients can be asymptomatic.

Radical surgery is the treatment of choice for localized disease.[22]

The medical management of metastatic disease includes biotherapy and chemotherapy.[23]

Our patient succumbed to the disease 2 months post surgery.

Figure 4 shows the histopathology findings of the dissected out specimen in a 63 year old male patient.

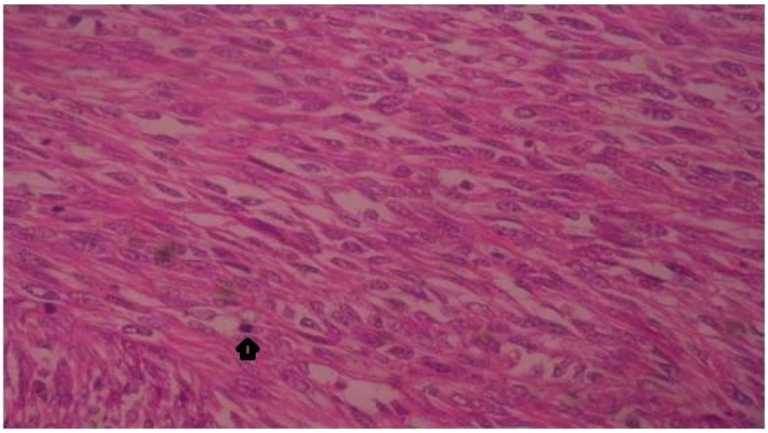

FIGURE 4 (Case No.9). Paraffin sections revealed spindle shaped cells with round to oval nuclei and speckled chromatin and mitosis (*Arrow head*) (>5 per 10HPF) H & E x400.IHC CD45 Negative, Synaptophysin and S100 Positive.

E. Bronchogenic cyst

Bronchogenic cysts are congenital abnormalities that can occur in infants, children and also adults.[24] Bronchogenic cysts make up 60 percent of all mediastinal cysts.[3]They result from abnormal ventral budding or branching of the tracheobronchial tree during embryologic development. Bronchogenic cysts are common in males and usually single, occasionally multiple.[13] They are benign in nature and most often asymptomatic. Compression of the adjacent structures can give rise to symptoms in two-thirds of patients. Plain chest radiographs show the presence of a bronchogenic cyst in upto two-thirds of patients in any age group.[3] It usually appears as a smooth,homogeneous mass that abuts on the mediastinum or hilum or splays the carina. CT thorax

findings consist of the presence of a smooth,rounded mass with uniform attenuation. They are lined by respiratory epithelium and the capsule contains cartilage, smooth muscle and mucous gland tissue.Figure 5 A showing a well defined cystic lesion in the middle mediastinum in a 73 year old male patient. Figure 5 B showing a cut open cyst with a smooth inner surface.

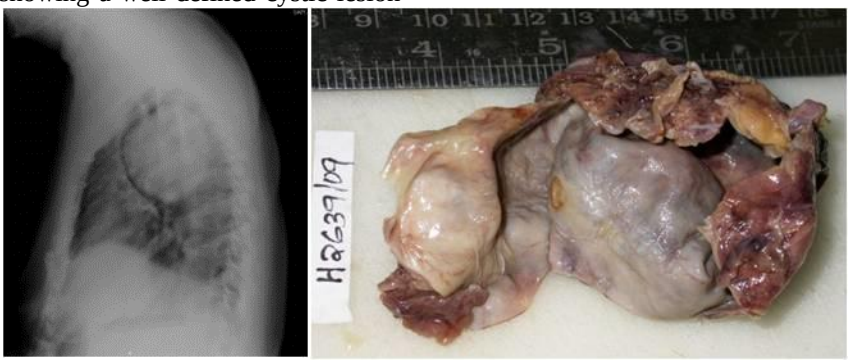

Figure 5A Figure 5B

Figure5A (Case No.5). Showing a well-defined cystic lesion in the middle mediastinum in a 73 year old male patient.
FIGURE 5B (Case No.5). Cut open cyst showing a smooth inner surface.

Surgical excision is diagnostic and therapeutic.[25] VATS may be an acceptable procedure for excision of the mediastinal cysts. However Ribet et all have analyzed the operative records of patients who have undergone VATS procedure. According to them it was hazardous in 11 to 30% of patients because of adhesions and or communication of the cysts with tracheobronchial or oesophageal structures.[26] The subject in our study underwent thoracotomy and complete excision of the cyst and is doing well.

F. Mediastinal Goitre

Mediastinal goitre represents the direct contiguous growth of goitre into the anterior or superior mediastinum.[27] Two patients in our study underwent median sternotomy and excision of the anterior mediastinal mass with the mistaken diagnosis of thymoma. Histopathology was suggestive of multinodular colloid goitre.

G. Lymphoma

The mediastinum is commonly involved in lymphoma. It can present either as part of disseminated disease or solely as a mediastinal mass.[28] Lymphomas are responsible for 15 % of all primary mediastinal masses and 45% of anterior mediastinal masses in children.[29] Patients are often asymptomatic from the mediastinal component.They can have systemic symptoms like fever,weight loss and pruritus. Symptoms of local invasion include retrosternal chest pain, SVC compression with SVC syndrome, dyspnea and cough. Lymphomas can be classified into either Hodgkin's or non-Hodgkin's lymphomas.[3]About 75% of patients with Hodgkin'sdisease present with mediastinal disease, only 5% of patients with non-Hodgkin's lymphoma present with mediastinal involvement.

Chest radiographs reveal large irregular anterior and superior mediastinal masses. Middle mediastinal involvement is also seen. Figure 6 showing chest radiograph of lymphoma patient with mediastinal mass. The patient was treated elsewhere with the diagnosis of pneumonia which lead to the delay in getting proper treatment.

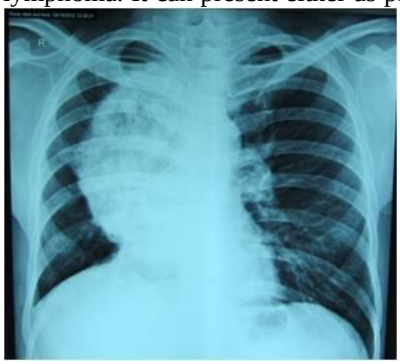

FIGURE 6 (Case 19). Chest X-ray showing a well-defined mediastinal mass extending to right side with convex lateral margin in a 40 year old male patient of Hodgkin's lymphoma.

In isolated mediastinal involvement mediastinotomy or thoracotomy could be required for obtaining tissue for diagnosis. Both patients in our study had only mediastinal involvement.

Treatment depends on the type and stage of lymphoma.Broadly requires chemotherapy and radiotherapy.

V. CONCLUSION

Common symptoms of chest pain, breathlessness and cough found in our study were not specific enough to suspect a diagnosis of mediastinal lesion. Radiological assessment and invasive procedures like thoracotomy and median sternotomy were required for diagnosis and treatment of most cases in our series. Thymus tumor was the commonest lesion.High index of suspicion and routine screening protocol is required for early detection and treatment of mediastinal lesions.Management strategies of mediastinal lesions are based on the histopathological diagnosis and the extent of the disease. Minimally invasive procedures like trans-thoracic FNAC and core needle biopsy should be attempted whenever there is radiological evidence of mediastinal lesion. Early diagnosis and prompt institution of integrated management can reduce the morbidity of patients with mediastinal lesions.

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