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Original Research Article

Spectrum of malignant mediastinal masses at a tertiary care centre in Central India

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ABSTRACT

Background: Malignant mediastinal masses can develop from structures that are normally located or pass through the mediastinum during development, as well as from metastases of malignancies that arise elsewhere in the body. Since many tumors that occur in the mediastinum are undifferentiated and have overlapping histologic features, one must consider a broad differential diagnosis and perform a thorough evaluation. This is particularly important since appropriate therapy for various mediastinal tumors differs considerably and may significantly impact survival.
Methods: Ours was a retrospective descriptive study of 48 patients who presented or referred to medical oncology department from January 2014 to December 2017 and in whom malignant cause of mediastenal mass was established. All details of the patients pertinent epidemiology, clinical history and pathological including immunohistochemistry details were studied.
Results: Out of 48 patients,14 cases (29.2%) were in adolescent and young adult age group (15-29 years). Majority of the patients were symptomatic (91.6%) with most common being cough (87.5%) followed by chest pain (81.5%) and dyspnoea (79.1%). Four of the patients presented with superior vena-caval syndrome. Most of the tumors (64.6%) are in anterior mediastenum region. Histopathological examination revealed non-hodgkins lymphoma in 31.25%, Hodgkins lymphoma in 18.75%, leukaemia in 6.25%, germ cell tumor in 8.33%, thymic neoplasms in 4.16%, neurogenic tumors in 4.16%, lung carcinoma in 10.4% and metastatic carcinoma in 10.4%.
Conclusions: Malignant mediastinal masses have a broad range of diagnosis, establishing of which is important. While imaging help in narrowing the differential diagnosis, adequate pathological categorization should be done as many patients responds to specific line of therapy.

Keywords: Lymphoma, Malignancy, Mediastinal mass

INTRODUCTION

Mediastinal tumours are rare tumours comprising of only 3% of all tumours occuring in the chest.[1,2] Mediastinal tumours are among the most difficult lesions examined and treated by the oncologist for several reasons. First, many different types of lesions occur in this location. Second, biopsies often consist of small, crushed specimens. Third, few pathologists have significant experience with mediastinal pathology because specimens from this location are relatively uncommon.

The mediastinum is defined as "the space between the lungs." The borders of the mediastinum are the thoracic inlet superiorly, the diaphragm inferiorly, the sternum anteriorly, the spine posteriorly, and the pleural spaces laterally. The mediastinum is divided into anterior, middle and posterior compartments, and this is useful in developing a differential diagnosis when an abnormality

is detected as well as when planning techniques for biopsy or resection. Although clinical history, physical examination, radiological findings, and location of masses in the mediastinum often help in making the diagnosis, tissue diagnosis is the gold standard for the final diagnosis and plan management of mediastinal lesions.

Most common mediastenal tumors (40% to 60%) encountered in children include lymphomas, germ cell tumors, neurogenic tumors, whereas thymic neoplasms, thyroid tumors, lymphomas are the most encountered in adult patients. 30 % to 50% tumors occur in the anterior mediastenum followed by middle and posterior mediastenum.

This study is a single institution study with an aim to assess the epidemiological features, clinicoradiological features, cytological and histopathologocal findings in patients presenting to a tertiary care centre in Central India over a period of 3 years.

METHODS

Study design

Authors retrospectively evaluated the data of patients presenting to Sri Aurobindo Institute of Medical Sciences (SAIMS), Indore with symptoms and signs of suspected mediastenal mass and in whom malignant cause was diagnosed. All medical records of patients between January 2014 to December 2017 were evaluated for demographic and clinical characteristics in respect to age, sex, socioeconomic status, clinical features, cytological and histopathological diagnosis.

All patients underwent workup including hemogram, renal and liver function tests, tumor markers like AFP, beta hCG, LDH, contrast CT scan of neck, chest, abdomen and pelvis, MRI imaging wherever necessary, cytology in presence of pleural effusion and ascites where-ever necessary. CT guided trucut biopsy was obtained in most of the cases. The patients are explained regarding the prognosis of the disease, complications, cost related factors regarding the therapy. Institutional Ethics Committee clearance was obtained.

Paraffin embedded tissue blocks obtained by biopsies from mediastenal masses, were analyzed for histopathology. Diagnosis was confirmed on hematoxylin and eosin (H and E)-stained formalin-fixed paraffin-embedded sections. For cases in which final diagnosis could not be made on routine examination, a detailed immunohistochemical (IHC) panel comprising of cytokeratin (CK), cluster of differentiation 45 (CD 45), CD 20, CD3, CD15, CD 30 and TdT were applied after antigen retrieval by heat extraction of the tris-ethylene-diamine-tetraacetic acid solution. Antibody detection was done with diaminobenzidine following reaction with horseradish peroxidase enzyme. Further, OCT-3/4, alpha feto protein (AFP) and beta-human chorionic gonadotropin (β-HCG) were applied to rule out a mixed component, if any, in a germ cell tumour. Bone marrow and cerebro-spinal fluid (CSF) analysis were performed where-ever necessary.

Statistical analysis

The data was entered in a Microsoft Excel Spreadsheet, after data cleaning and transported and analyzed using SPSS version 20 for windows (SPSS Inc).

Inclusion criteria

All patients with definite or suspected mediastinal masses on imaging and in whom malignant cause of the mediastenal mass was established.

Exclusion criteria

- Patients in whom benign cause of mediastinal mass was established.
- Specific diagnosis of certain lesions on imaging, i.e., achalasia cardia and diaphragmatic hernia where FNAC/biopsy was not needed.
- Contrast CT suggestive of vascular lesions i.e., dilated pulmonary artery, vascular aneurysm, etc.

RESULTS

Age and gender

Of the 48 cases included in this study, 37 (77%) were males and 11 (23%) were females. Age ranged from 2 years to 75 years. Paediatric age group (1 to 14 yrs) constituted 16.6 % and adolescent and young adults (15 to 29 yrs) constituted 29.2%. 27 % patients are in 4th and 5th decade and 27.2 % are in 6th decade and above age group. Among paediatric and adolescent and young adult age groups, males constituted 82% and females 18% (Figure 1).

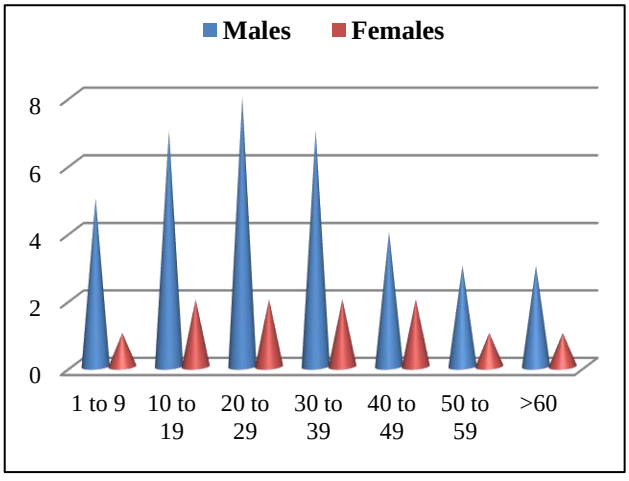

Figure 1: Incidence according to age and gender.

Location

Majority of malignant mediastinal masses occured predominantly in anterior mediastinum which constituted 64.6% (31 cases) of entire mediastinal tumours in this study population. Middle mediastinal tumours accounted for 25% (12 cases) and 10.4% (5 cases) occured in the posterior mediastinum. Of all anterior mediastinal masses, lymphomas (Non-Hodgkins and Hodgkins) accounted for 58% followed by thymic neoplasms 6.4% and 6.4% of germ cell tumours. Majority 46.15% of middle mediastinal tumours are constituted by lymphomas (Non-Hodgkins and Hodgkins) followed by 15.8% each by germ cell tumors, lung carcinoma and metastatic carcinomas. Neurogenic tumours accounted for 4.16% of all mediastinal tumours (Figure 2).

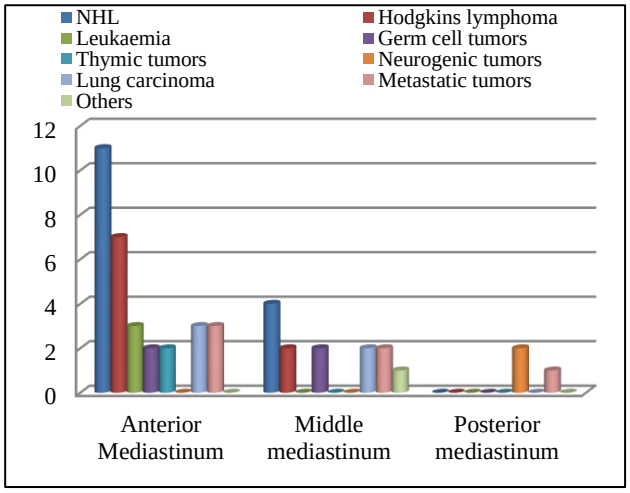

Figure 2: Mediastinal tumours according to location.

Clinical presentation and imaging

The mean duration of symptoms was 120 days (range: 16–420 days). Majority of patients in this study presented with vague chest pain and cough. Of all the 48 patients included in this study, 87.5% had cough at presentation or some point of time as their chief presenting complaint. 81.5% patients had chest pain, dyspnoea in 79.1% patients, weight loss in 41.6%. Fever as the cause of hospital presentation accounted for 18.75% of total patients. Hoarseness of voice was one of the presenting complaint in 16.6% of patients, dysphagia in 8.3%, superior venacaval syndrome accounted for 8.3% of the total clinical presentations. 2% had developed paraneoplastic syndrome (myasthenia gravis). 2 patients had no symptoms and the diagnosis of mediastinal tumour was established as part of screening for other complaint. Although many cases of mediastinal tumours will be obvious on chest radiographs, the main modality of imaging is CT with contrast. After confirmation of mediastinal mass, further characterization can be done by MRI imaging in selected cases. Almost all the mediastinal masses in this study were evident on the CT imaging (Figure 3).

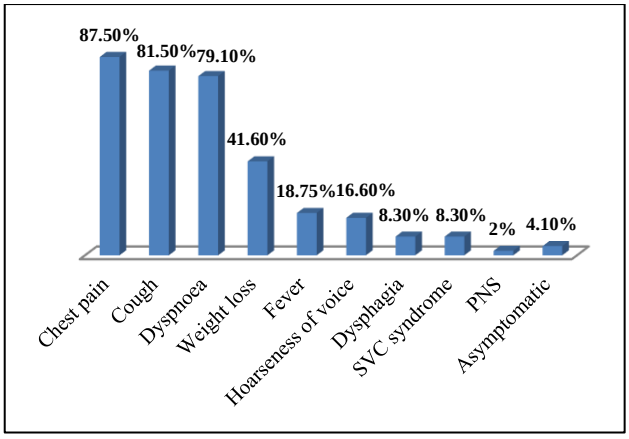

Figure 3: Symptoms at presentation.

Pathological diagnosis

Lymphoma was the major diagnosis among patients with malignant mediastenal tumours. Lymphomas accounted for 50% (24 patients) with age range of 2 to 75 years. Non-Hodgkin lymphoma accounted for majority of lymphomas (31.25%) followed by Hodgkin lymphoma (18.75). 6.25% of patients presented with mediastenal mass were diagnosed as leukaemia later by bone marrow analysis.

Of 24 patients with mediastinal presentation of lymphoma, 18 patients had anterior mediastenal mass and 6 patients had middle mediastinal mass as lymphoma presentation. In paediatric age group, lymphoma accounted for 62.5% whereas in adolescent and young adults, 57% of mediastinal masses are due to lymphoma. Of the 5 patients in pediatric age group, 3 had presented with anterior mediastinal mass and 2 with middle mediastinal mass. Four patients in adolescent and young adult age group presented with anterior mediastinal mass at presentation and rest four with middle mediastinal mass.

Thymic neoplasms accounted for 4.2% of all patients with malignant mediastinal mass. Malignant germ cell tumours presented as mediastinal mass in 8.33 % of total patients in this study. Non-seminomatous germ cell tumors accounted for the majority of germ cell tumors. In this study, all the patients had primary mediastinal germ cell tumours and clinical examination of testes were normal.

Neurogenic tumours accounted for 4.16% of patients presenting with mediastinal mass. Almost all of the neurogenic tumours arise from the posterior mediastinum and most commonly occur in pediatric and adolescent and young adult age group.

Metastatic tumours presenting as mediastinal mass occur in 12.5% of the patient population and lung carcinoma accounts for 10.4% of the cases. Anterior mediastinum is the most common site for metastatic mediastinal tumours.

DISCUSSION

A mediastinal mass can be an incidental finding in patients who undergo plain chest radiography or advanced imaging studies, such as computed tomography or magnetic resonance imaging. The location and composition of a mass is critical to narrowing the spectrum of the differential diagnosis. However, types of mediastinal tumors are usually associated with the patient's age.[2,3] Since many tumors that occur in the mediastinum are undifferentiated and have overlapping histologic features, one must consider a broad differential diagnosis and perform a thorough evaluation of each biopsy specimen. This is particularly important since appropriate therapy for various mediastinal tumors differs considerably and may significantly impact survival. Additionally, it may not be apparent whether the tumor actually arises in the mediastinum or from adjacent lung.

Symptoms, if present, may be due to direct effects of the mediastinal mass or to systemic effects of the illness. In general, malignant lesions are more likely to be symptomatic as in this study.

The initial evaluation of a suspected mediastinal mass consists of a thorough history and physical examination, supplemented by laboratory and imaging studies. The clinical approach includes in-depth history of symptoms, demographic features, and close search for physical signs. The currently available modalities for further evaluation include chest radiographs, ultrasound, CT scan, magnetic resonance imaging (MRI), and nuclear medicine studies.[4] Chest X-ray with posteroanterior and lateral views is indicated in all cases. It provides information on the size, anatomical location, density, and at time composition of the mass. CT scan with intravenous contrast enhancement is an essential tool to evaluate further that provides additional information, i.e., relationship of the mass with adjacent structures, vascularity within the mass, content, and nature (cystic or solid) of the mass. MRI provides useful information in evaluating spinal, vascular, or cardiac invasion. It is more sensitive than CT for evaluating the involvement of the neural foramen or spinal canal invasion in posterior mediastinum and for evaluating thyroid masses. Given its superior tissue contrast resolution and lack of ionizing radiation, MRI has been increasingly utilized for mediastinal mass evaluation nowadays.[5,6] Transesophageal echocardiogram, barium swallow, and testicular ultrasound may be needed in selected cases. Nuclear medicine studies available for mediastinal mass evaluation primarily include positron emission tomography (PET) often co registered with CT (PET/CT) and metaiodobenzylguanidine imaging. Nuclear scans and biochemical studies are useful in diagnosing and evaluating the suspected thyroid lesions, catecholamine-secreting tumor, and malignancy. A combination of these often helps narrow the possibilities when a mediastinal mass is detected on imaging. Laboratory studies or blood tumor markers can also help support a specific diagnosis. In some instances, these are enough for a presumptive diagnosis to guide therapy. As an example, the presence of a large mediastinal mass and elevated tumor markers can very reliably establish the diagnosis of some germ cell tumors. In almost all cases, a tissue biopsy (percutaneous, endobronchial, surgical) may be necessary to confirm a clinical suspicion prior to establishing a therapeutic plan.

In this study of 48 patients, median age was 30 yrs with predominance of males in all age groups. The age range and mean ages are very close to study by Biswajit Dubashi et al and another study by Karki and Chalise.[7,8] In this study, 91.6% of patients are symptomatic at presentation with the most common symptom being cough (87.5%) followed by chest pain (81.5%) and dyspnoea (79.1%). This is in accordance from a study by Davis, et al and Shrivastava et al, in which 85% of the patients with malignant mediastinal tumours were symptomatic.[9,10] Dubashi et al, reported a similar incidence of 97% with other studies reporting a range of 60-88%.[8]

Clinical history, anatomical position and certain details on imaging allows correct diagnosis in many cases when combined with histopathology in presence of similar imaging appearances in many mediastinal tumors.[11]

Ultrasound and CT guided FNA were avoided as these are operator dependent and tissue obtained will not be sufficient all times for further evaluation. In this study, lymphoma accounted for 37.5% of all the mediastinal masses with almost equal distribution in anterior and middle mediastinum. In a study by Sabiston, et al, lymphomas accounted for 16% of all mediastinal tumors.[9] Thymic neoplasms accounted for 27.3% of all patients with malignant mediastinal mass which is comparable to the currently published literature.[5] Malignant germ cell tumors constituted 14.5% of total patients in this study. Comparably, Aroor A et al, reported 13.3% cases of GCTs in a similar study.[12] Neurogenic tumors accounted for 10.4% of all mediastinal tumors and 75% of all posterior mediastenal tumors. These results are like those of a study by Abdel Rahman, et al.[11] Secondary malignant lesions (metastatic) of the mediastinum occurred in 10.4% of cases in this study. This is in comparison to another study reported by Aroor A et al, where the secondary malignant lesions of the mediastinum accounted for 8.75% of the cases.[12]

CONCLUSION

Anterior mediastinal masses are the commonest in this study, so we should pay more attention to any abnormality that is detected incidentally in a routine chest X-ray. Lymphomas are very common cause of mediastinal masses, so we must be least invasive when dealing with any mediastinal mass because the role of surgery is mostly diagnostic in this disease. Mediastinal tumors represent a wide diversity of disease state. The

clinical spectrum of mediastinal masses can range from asymptomatic to those producing compressive symptoms. Although many of these masses have similar imaging appearances, clinical history, anatomical position and certain details seen at CT and MRI imaging allow correct diagnosis in many cases which will be confirmed by histopathological and immunohistochemical studies.

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