ORIGINAL ARTICLE

The Clinico-pathology Loci, Diagnosis and Management of Mediastinal Masses: A Retrospective Study in a Tertiary Care Hospital

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Abstract

Background: The mediastinum is known to be a space within the domain of the thorax housing the important organs, blood vessels, nerves, lymphatics along with the surrounding connective tissue, where the International Thymic Malignancy Interest Group (ITMIG) classification system based on cross sections derived by the CT into prevascular mediastinum, visceral mediastinum and paravertebral mediastinum. The diagnosis of mediastinal neoplasia and it is necessary treatment often becomes challenging owing to the complex anatomy. With the advancement in cross-sectional imaging using CT scan with or without contrasts, diffusion weighted and chemical shift MR imaging, FDG-PET scan, guided biopsies with microscopic examination aided by special stains, the diagnosis of such become unconstrained.

Materials and methods: In our aim to focus on the clinico-pathology locus, diagnosis and treatment of mediastinal neoplasia, we perform a retrospective study in a tertiary care hospital spanning from January 2020 to December 2022, for a period of 3 years in the CTVS Department (IPGMER and SSKM) Hospital, with the number being 42 who had mediastinal masses and they were characterized using the age, gender, clinical stigmata, and were subjected to cross-sectional imaging of the thorax, guided biopsies, histopathological examination, targeted treatment using surgery or the standard therapeutic approach.

Result: Statistical analysis was done using the software SPSS version 20/21, revealing 28 males and 14 females (M:F = 2:1) 28.57% patients for hydatid cyst, 26.19% patients of thymoma, 7% patients for thymic malignancy, 11.90% of patients for lymphoma, 14.28% for pleuropericardial cyst, 9.52% for dermoid, and 2.38% for teratomas. The follow-up period ranged from 1 to 5 years and the mean follow-up was 2.33 ± 1.28 (Mean ± SD). lesions were mostly found in the anterior compartment of the mediastinum (20%) with thymoma being the commonest followed by hydatid, pleuropericardial cysts, dermoid and the lymphoma.

Conclusion: Since they are deemed to be slow growing and gradually would compress the great vessels, heart, spinal cord, vocal cords, stellate ganglion, brachial plexus, superior vena cava, or the diaphragm to explain the symptomology, we have generously discussed and documented the atypical lesions too which must be taken as the differential diagnosis namely atypical lesions namely retrosternal goiters invading the mediastinum, Langerhans cell histiocytosis, mesothelioma, squamous cell carcinoma, adenocarcinomatous lesion, pleomorphic sarcomas, melanomas, primary pleural liposarcoma, malignant epithelioid gastro intestinal stromal tumors, and even solitary fibrous tumors. To sum up, specific radiology with the needle diagnosis and targeted treatment would henceforth be a logical approach to aim a better patient care.

Keywords: Hydratid cyst, Lymphoma, Mediastinum, Mediastinal mass, Myasthenia gravis, Pleuro pericardial cyst, Thorax, Thoracic surgery, Thymoma.

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Introduction

The mediastinum is a space in the thorax that has an assembly of some organs, vessels, nerves, and lymphatics along with the connective tissue matrix which binds them lying in the middle of the thoracic cavity in between the pleura of each lung extending from the sternum to the vertebral column. The more modern International Thymic Malignancy Interest Group (ITMIG) classification system, developed by a multidisciplinary group including radiologists and thoracic surgeons, relies on CT-based anatomic divisions. It divides the mediastinum into three compartments: (1) Prevascular mediastinum—superiorly demarcated by the thoracic inlet, inferiorly by the diaphragm, laterally by the parietal mediastinal pleura and posteriorly by the anterior part of the pericardium. (2) Visceral mediastinum—it is marked superiorly by the thoracic inlet, inferiorly by the diaphragm, anteriorly by the posterior boundaries of the prevascular compartment. (3) Paravertebral mediastinum—this is marked superiorly by the thoracic inlet, inferiorly by the diaphragm, anteriorly by the posterior boundary of the visceral compartment, and posteriorly by a vertical line along the posterior margin of the chest wall at the lateral aspect of the transverse processes (Fig. 1).[1]

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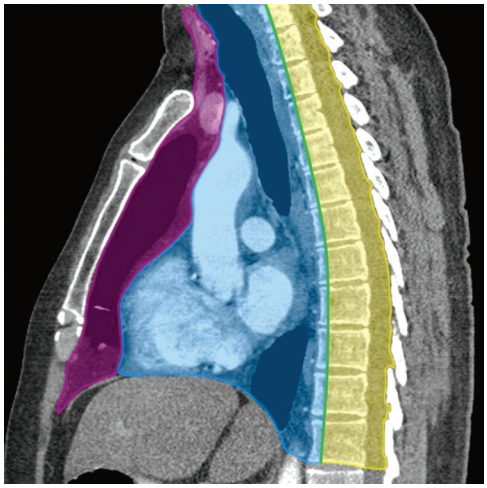

Fig. 1: Mediastinal compartments as defined by the ITMIG classification[1] using multidetector CT image (Sagittal section). (1) Purple-prevascular compartment, (2) Blue-visceral compartment, (3) Yellow-paravertebral compartment, (4) Green line-visceral-paravertebral compartment boundary line

The "mediastinal mass" refers to an entity of neoplasia within the mediastinum. Mediastinal masses are very uncommon lesions that might occasionally present with difficulties to the doctor with respect to the diagnosis and therapeutics. Therefore, the diagnosis of a mediastinal mass may be challenging for clinicians, since lesions arising within the mediastinum include a variety of disease entities, frequently requiring a multidisciplinary approach which includes a careful and detailed history-taking, the clinical examination in integration with the cross-sectional radiological imaging and some specific laboratory findings.

With a regard to the complex anatomical heterogeneity, the precise anatomy of the lesions is of utmost importance where tools of radiology and pathology may be generously used for elucidating, grading and staging of the lesions (if needed) and, therefore, planning a treatment algorithm based on the specific lesion which by virtue would be unique in nature. Although a lateral chest radiogram may be useful, precision is often achieved using multiplanar cross-sections or slices using radiological tools followed by a definitive guided needle aspiration for histopathology and then planning excisions or onco-therapeutics (based on the behavior of the neoplastic tissue). Here, we focus on the modern ITMIG three compartment classification system as written.

Adding a note on radiology, characterization on CT is based on specific enhancement of air, water, fat, and calcium which obtains high resolution images which characterize the tumor based on its relations with the surrounding structures of importance.

Magnetic resonance imaging (MRI) is an ideal tool to evaluate tumors of the mediastinum for elucidation of relationships with the heart, spinal cord, blood vessels, and soft tissues. One such variant of the MRI known as the chemical shift MRI generously differentiates thymic hyperplasia from thymic dysplasia, though it is not regularly used.

Now, diffusion-weighted MRI (DWI), a popular investigation, is another special application that uses the Brownian motion of the water for isotropic diffusion mapping and is thought to march above T1 and T2 flair imaging when it comes to the radiological diagnosis. The role of PET/CT in the evaluation of the mediastinal lesions looks propitious. Histopathological examination includes sequential stages based on morphological analysis. Immunophenotyping deciphers the microscopic description of poorly differentiated neoplasms, the precise characterization of lesions (especially in hematopathology), and the identification of the primary site of origin of neoplastic lesions. Tumor markers of thoracic neoplasms often become an important tool for some early diagnosis. The phenotype of mediastinal lesions is performed on biopsy or surgical specimens in the current pathology practice.[2] The mediastinal pathologies include thymoma, thymic cysts, lymphoma (Hodgkin lymphoma and non Hodgkin lymphoma), germ cell tumor, thyroid mass, bronchogenic cyst, mediastinal lymphadenopathy, pericardial cyst, tracheal tumors, esophageal tumors and conditions like achalasia, diverticulum and hiatal hernia, blood vessel conditions like aortic aneurysms, neurogenic tumors like ganglion cell tumors and paragangliomas, mediastinal lymphadenopathy, extramedullary hematopoiesis (EMH), neuroenteric cyst, conditions affecting your mid-spine (paravertebral conditions), these include infectious, malignant, and traumatic abnormalities that appear in the middle of the spine (thoracic spine).

Due to the neoplastic entities in the thorax, compression of the surrounding mediastinal structures cause symptoms of cough, stridor, hemoptysis, breathlessness, hoarseness, facial and/or upper extremity swelling due to vascular compression (e.g., superior vena cava syndrome), hypotension due to tamponade physiology or cardiac compression, and Horner syndrome due to sympathetic chain involvement, dysphagia due to the pharyngeal compression along with pain.

As per the stage of the tumor, multimodality treatment is conducted, where radiation or neo-adjuvant oncotherapeutics may chemically debulk the tumor to aid in the surgery of the later. A recent survey among members of the European Association for Cardio-Thoracic Surgery revealed neoadjuvant chemotherapy would debulk thymomas for easy resectability. At times, embolization of the tumor would help too.

A number of surgical approaches are possible to address the different mediastinal pathologies. A median sternotomy incision is most commonly used for large tumors and also for bilateral pulmonary tumors for better visualization of the hilar structures, sometimes a thoracotomy incision is required in laterally located tumors and less commonly a classic clamshell or hemi-clamshell incision may be needed. For smaller tumors, robot-assisted and video-assisted thoracic surgery (VATS) has become popular.

However, these techniques are often unsuitable for larger masses. During dissection of large mediastinal masses or masses with extensive adhesion of the tumor, there may be injury to the feeding vessels due to manipulation, leading to serious hemorrhagic complications which are often difficult to control. Appropriate precautions are possible based on the information provided by preoperative imaging. Proximal control of the major blood vessels is often easier through a median incision.

Materials and Methods

Our study was a retrospective observational study, done during the 3-year period between January 2020 and December 2022, in the Department of Cardiothoracic and Vascular Surgery, IPGMER and SSKM Hospital, Kolkata. We included all patients who presented with a mediastinal space occupying lesion (SOL). Our sample size during the period was 42. All patients who were hemodynamically unstable or those who presented in the Emergency Department and children below 18 years were excluded from the study. All the

patients included in our sample population were evaluated by a detailed history and a thorough clinical examination. Several investigations, such as chest x-ray, contrast enhanced CT scan of the thorax, and FNAC were done, as appropriate for making a diagnosis. The patients were also evaluated based on the type of management done, i.e., surgical or conservative, postoperative histopathological examination, follow-up etc. Standard appropriate statistical analysis of the observational data was done using the software SPSS version 20/21. There was no financial transaction in the study.

Results

In our study, out of a total of 42 patients, 28 were male patients and 14 were female patients and the male–female ratio was 2:1. The mean age was 34.97 ± 10.01 (mean ± SD) years, and the range was 19–55 years. The most common symptom in the sample population was chest pain. At Least 32 patients (76%) complained of angina. About 10 patients (23.8%) presented with shortness of breath. A total of 17 patients (40.4%) presented with cough. A total of 12 patients had features of myasthenia gravis, all of whom had raised anti-acetylcholine receptor antibody levels and they were later diagnosed with thymic pathology.

Chest X-ray and contrast enhanced CT scan of chest was done in all the patients as part of our diagnostic protocol and surgical planning. Radiologically guided Fine-needle aspiration cytology (FNAC) or Tru-Cut needle biopsy was done whenever feasible. In our sample population, FNAC or Tru-Cut needle biopsy could be done in 18 patients out of whom five patients had lymphoma, two patients had mesothelial pleural cells, four patients had thymoma, and one patient had dermoid cells. One patient had evidence of malignant cells; five patients had inconclusive reports.

The Echinococcus granulosus IgG antibody test was done in all patients as our pre-surgical work up protocol and was found to be positive in 12 patients (28%) and all were later diagnosed as hydatid cyst.

The management of the patients varied according to the preoperative diagnosis of the patient. In the 13 patients presenting with thymic pathology (thymoma or thymic cancer), the anti-acetylcholine receptor antibody level was raised (>8) in six patients and as per advice from the Neurology Department, prior plasmapheresis was done in five patients while IVIG antibody therapy was given in one patient. All these six patients were later posted for surgery after optimization of the anti-acetylcholine receptor antibody levels. In all the 13 patients, surgery of the tumor was done. Conservative medical management was done in the five patients who were diagnosed with lymphoma. They were referred to the Department of Medical Oncology for further definitive management.

In all other patients, surgical management was done as all the patients presented with mediastinal tumors or cysts, the most common type of incision was median sternotomy. In a few patients, having extensions to either of the two thoracic cavities, thoracotomy incision on the respective side was done for better visualization of the tumor. All the surgical specimens were sent for histopathological examination. The HPE diagnosis has been stated in Figure 2.

In our sample population, about 28.57% patients had hydatid cyst, 26.19% patients were diagnosed with thymoma, and approximately 7% patients had thymic malignancy. Approximately 11.90% of patients had lymphoma and were not operated on. The remaining patients were diagnosed as pleuropericardial cyst (14.28%), dermoid cyst (9.52%), and teratoma (2.38%). All the patients were followed up in our Outpatient Department. The follow-up ranged from 1 to 5 years and the mean follow-up was 2.33 ± 1.28 (mean ± SD).

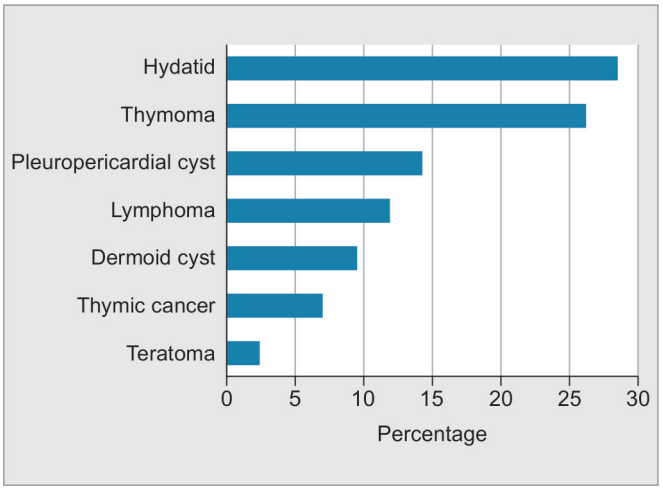

Fig. 2: Incidence of thoracic lesions as seen in our study

Discussion

Mediastinal masses are tumors which have been thought of as sporadic tumors which are challenging to the clinician due to the wide variety of determinants and the possible phenotype. Out of these determinants, three factors have been largely elucidated which includes the precise location of the mass, the age of the patient and the presence or the absence of symptoms. These three determinants often predict the chances of the neoplastic lesions developing into a frank malignancy. The masses in the mediastinum, often, are found to be slow growing and would, at times, compress the adjoining structures namely the great vessels, the heart or the spinal cord. The lesions may further invade and entrap structures like the vocal cords, the brachial plexus, cervical paravertebral sympathetic nervous system, and stellate ganglion leading to the Horner's syndrome, the diaphragm, the superior vena cava, or other important structures, they would produce symptoms which can be broadly classified into some local and systemic symptoms. Shahana et al. had scripted that the maximum number of "thoracic malignancies" would occur in the anterior compartment and they most commonly affect the adults (20% of the study cohort), than children, along with proposing that thymoma would be the most common lesion which is found in the thorax.[3] Facts established by Sridhar et al.[4] substantiated the literature of the clinical symptomology of having breathlessness, followed by cough, chest pain, myasthenia symptoms in the decreasing order of their prevalence, along with designating the symptom of cough to be associated with the masses in the middle mediastinum owing to their proximity with the lung parenchyma and the larger airways. They also produced evidence regarding the use of Endoscopic Bronchial Ultrasound – Fine Needle Aspiration (EBUS – FNA) for elucidating the masses which is thought to be a reliable and more importantly a safer method to diagnose,[5] but the tissue yield remains questionable. Ahuja et al. state that a chest radiogram would arguably be the first imaging modality which is to be used, specifically for a postero-anterior or a lateral view.[6] Now, the American College of Radiology Appropriateness Criteria for Imaging

of Mediastinal Masses suggests the use of advanced tools like the CT scan or the MRI of the thorax to localize the masses or to assess the grading and the neoplasia.[7] The accuracy of such a diagnosis may be accentuated with guided fine needle aspiration of the masses and then to allow microscopic diagnosis using regular and special stains specific to the lesion. It must be observed that fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), has a very limited role in diagnosing/classifying/delineating thoracic masses due to non-specificity of the FDG uptake. But otherwise, for highly aggressive lesions like the germ cell tumors, FDG PET CT may be considered to reveal the extent of the metastasis, predict prognosis or may be a guide for chemotherapeutic regimens. Ackman et al. suggest the use of α-fetoprotein (α-FP), β-human chorionic gonadotropin (βHCG), and lactate dehydrogenase (LDH) as markers for the thoracic neoplasms along with stating that MRI would be a better modality than CT Scans to obtain cross sections to accurately decipher hyperplasia vs frank neoplasms, non-use of contrast agents which would prove beneficial for patients with a kidney compromise and when it would come to cystic vs solid lesions.[7] Nasit et al. further suggested to limit the traditional use of mediastinoscopy, thoracoscopy, mediastinotomy, or frank thoracotomy as initials to diagnose a particular thoracic neoplasm unless indicated and to rely more on radiologically guided core-needle biopsy (CNB) than fine-needle aspiration (97.95 vs 71.42%) as CNB's yield a higher amount of tissue, possibly around half an inch long cylindrical tissue which is obviously a very good diagnostic yield.[5] The specific emphasis provided to the diagnosis in this discussion has been provided as atypical lesions namely retrosternal goiters invading the mediastinum, Langerhans cell histiocytosis, mesothelioma, squamous cell carcinoma, adenocarcinomatous lesion, and pleomorphic sarcomas, melanomas, primary pleural liposarcoma, malignant epithelioid gastro-intestinal stromal tumors and even solitary fibrous tumor of the thorax were located.[8]

Conclusion

In our study comprising of a 3-year period from January 2020 to December 2022, retrospectively, on 42 patients, we, derive the incidence of non-malignant anterior compartment neoplasms to be at a greater incidence of which maximally were subjected to thoracic surgeries and the rest for irradiation and neo adjuvant/adjuvant chemotherapy. Though the lacunae in our study have been dictated earlier and as far as the general literature has been reviewed where pitfalls are a common, we successfully co-ordinate the generalized algorithm of combining the clinical examination, biochemistry, preoperative needle diagnosis, or postoperative pathology along with imparting standard care to the patients. On analyzing, we finally sum up that thymic neoplasms (that is, thymoma and thymic cancers taken together) with or without the symptomatology of myasthenia, would be the most common neoplasm that would occur followed by hydatid, dermoid, pleuropericardial cysts and a small incidence of lymphomas (germ cell variant followed by the diffuse large B cell lymphomas). Thymic carcinoma *per se* was located too. The overall prognosis of the mediastinal lesions was substantially favorable, with a few of the thymic carcinomas being subjected to irradiation and debulking before a thoracic intervention. Variants which have been vividly described in the literature such as germ cell neoplasms, the castle man neoplasm, cholesterol containing neoplasms, and nerve sheath derivatives were not found, which may be attributable to the lacunae in the radiology vs the needle-stain diagnosis according to the clinician's bias as stated earlier. Whereas if the patients with deranged hemodynamics or the pediatric age group, as would be have been considered in our study which too had a fair strength, it would possibly reveal other variants of interest without affecting the general outcome as vividly described. Therefore, on a concluding note, a co-synergy of clinics, general radiology and further affirmation with the needle followed by targeted treatment shall possibly yield the best results, along with unearthing the atypical variants of interest pertaining to thoracic neoplasms.

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