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A clinicopathological study of mediastinal masses operated in a tertiary care hospital in Eastern India in 3 years with special reference to thymoma

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Abstract

Introduction: The mediastinum is the central portion of the thoracic cavity, limited by pleural cavities laterally, thoracic inlet superiorly, and the diaphragm inferiorly. Housing numerous organs, it is a veritable Pandora«SQ»s box, within which various lesions may develop. This study was conducted to assess the epidemiologic profile, clinicoradiological features, cytological, and histopathological findings in patients presenting with mediastinal masses in a tertiary care hospital over a period of 3 years. **Materials and Methods:** This is a retrospective study of cases presenting with mediastinal masses attending the Cardiothoracic Surgery Department of Medical College, Kolkata between May 2011 and April 2014. Detailed history, physical, and radiological findings were noted. Fine needle aspiration cytology (FNAC) was performed when feasible. Following surgery, histopathological, and immunohistochemical (IHC) examinations of the specimens were undertaken. **Results:** Of the 22 cases included in our study, ten were anterior, seven middle, and five posterior mediastinal masses. Fifteen cases were male and seven were female. Thymic pathology was detected in seven cases, lymphoma in five, extragonadal germ cell tumor (GCT) in three, schwannoma and pericardial cyst in two cases each and neurofibroma, ganglioneuroma, and retrosternal thyroid in one case each. The age group of the patients for each diagnostic category was found to be of significance. FNAC was done in 15 cases. IHC was required for classification of lymphoma cases (CD45, CD15, CD30, CD20, CD3, Tdt, CD34, and Ki-67). **Conclusion:** This study reflects the incidence of different mediastinal masses in West Bengal with their clinicopathologic correlation.

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Full Text

INTRODUCTION

Mediastinal tumors are rare comprising only 3% of tumors occurring within the chest. [1] The histopathological and radiological features of these tumors are varied. The mediastinum is the central portion of the thoracic cavity, limited by pleural cavities laterally, thoracic inlet superiorly, and the diaphragm inferiorly. It is further divided into anterior, middle, and posterior compartments by many anatomists. [2] Housing numerous organs, it is a veritable Pandora's box, within which variety of both neoplastic and nonneoplastic lesions may develop. [3] The most commonly encountered tumors in children include neurogenic tumors, germ cell neoplasms, and foregut cysts. These account for nearly 80% of the childhood lesions. In adult patients, however, primary thymic neoplasms, thyroid masses, and lymphomas are the most common tumors found. [4] Nearly 50% of all mediastinal masses are anterior mediastinal tumors, which include thymoma, teratoma, thyroid lesions, and lymphoma. [5] In the middle mediastinum, the lesions found are typically congenital cysts whereas neurogenic tumors commonly arise in the posterior mediastinum. [6]

Thymus is an important organ housed in the anterior mediastinum. A thymoma is the most common tumor of the thymus with an incidence of 0.15 per 100,000 person years. [7] Nearly, one-third of all thymomas are associated with myasthenia gravis. Thymectomy in most of these cases is found to provide significant improvement. [8]

This study was conducted to assess the epidemiologic profile, clinicoradiological features, cytological, and histopathological findings in patients presenting with mediastinal masses in a tertiary care hospital over a period of 3 years.

MATERIALS AND METHODS

This is a retrospective study conducted in the Department of Pathology of a tertiary care hospital in Eastern India over a period of 3 years from May 2011 to April 2014. Patients attending the cardiothoracic surgery Out Patients' Department with complaints suspicious of mediastinal masses were selected.

Patients with mediastinal masses who underwent surgical resection of the tumors were included in this study. Patients with esophageal, pulmonary, and metastatic tumors were excluded from this study. A total of 22 cases were included in our study.

Detailed clinical history was recorded, and physical examination was done in each case. Preliminary chest radiographs were obtained which revealed the presence of mediastinal masses. Computed tomography (CT) scan and magnetic resonance imaging (MRI) were further done to attain more detailed information about the mediastinal lesions. Results of routine hemogram and serological tests were also procured. Whenever feasible, CT-guided fine needle aspiration cytology (FNAC) was performed.

Following surgical resection, the specimens obtained were subjected to detailed gross and histopathological examinations. In some cases, immunohistochemical (IHC) analysis was

essential for confirmation of diagnosis. This was done with the paraffin blocks using CD 45, CD15, CD 30, CD 20, CD3, Tdt, CD 34, and Ki-67 after antigen retrieval by heat extraction of the tris-ethylenediaminetetraacetic acid solution. Antibody detection was done with diaminobenzidine following reaction with horseradish peroxidase enzyme. [9]

All relevant data were recorded meticulously and analyzed.

RESULTS AND ANALYSIS

Of the 22 patients included in our study, 15 were males and 7 were females. The male to female ratio was 2:1. Their age ranged from 6 months to 56 years. The mean age of the patients was 18 ° 3 years.

In this study, 10 (45.5%) tumors were found in the anterior mediastinum, 7 (31.8%) in the middle mediastinum, and 5 (22.7%) in the posterior mediastinum. The histopathological diagnoses of mediastinal masses along with their sites have been shown in [Table 1]. The tumors were found to be benign in 63.6% cases and malignant in 36.4% [Table 2].{Table 1} {Table 2}

The age of patients with thymic lesions ranged from 30 to 56 years, whereas lymphoma patients belonged to the first and second decades. Extragonadal germ cell tumor (GCT) patients were between 6 months and 5 years of age. Retrosternal goiter, schwannoma, ganglioneuroma, and pericardial cyst cases belonged to the second decade.

All patients complained of vague chest pain and dyspnea on exertion. The lymphoma patients presented with a cough and weight loss. Dysphagia and hoarseness of voice were noted in cases of retrosternal goiter and a pericardial cyst. Symptoms of myasthenia gravis were detected in all cases with thymic lesions. Superior vena caval obstruction was found in 2 cases of extragonadal GCT and 2 patients with lymphoma [Table 3].{Table 3}

CT-guided FNAC was done in 15 cases. These included 4 cases of thymic lesions, 3 of extragonadal GCT, 5 of lymphoma, 2 of schwannoma, and one case of ganglioneuroma. A provisional diagnosis of benign spindle cell tumor was given in cases of schwannoma and ganglioneuroma. There was no difficulty in diagnosing the cases of GCT cytologically. However, it was not possible to diagnose the thymic lesions on the basis of cytologic smears alone. So, differential diagnoses of lymphoma, thymic hyperplasia, and thymoma were rendered in these cases [Figure 1].{Figure 1}

By histopathological examination, 2 cases of thymic lesions were diagnosed as thymic hyperplasia and the rest as thymoma. Classification of thymoma was done according to the World Health Organization scheme. One case of thymoma was classified as a B1 subtype and the other 4, AB subtype.

Among the 5 cases of lymphoma, 3 were found to be CD 15 and CD 30 positive and they were diagnosed as Hodgkin lymphoma. A diagnosis of T-cell lymphoma was rendered in the other 2 cases as they furnished positive results with CD 3, Tdt, and CD 34 immunostains. The percentage of Ki-67 positive cells was approximately 25% and 40% in the two cases of T-cell lymphoma. The pattern of staining was membranous with CD 3 and CD 34, and nuclear with Tdt and Ki-67 [Figure 2].{Figure 2}

One case of mixed GCT was diagnosed, and it consisted of components of yolk sac tumor and dysgerminoma. Among the other 2 cases of GCT, one was microscopically found to be a case of mature cystic teratoma and the other, dysgerminoma.

DISCUSSION

There is a paucity of data on the incidence of mediastinal tumors, possibly due to the wide variety of these masses. [10] Bekele et al. studied mediastinal lesions in 73 patients over a period of 6 years and found that mean age of the patients was 35.9 ° 10.5 years. The male to female ratio in their study was 2:1. [11] In this study, a similar male to female ratio was found but the mean age of patients was 18 ° 3 years.

In a study conducted by Aroor et al. mediastinal masses were most commonly found in the anterior mediastinum (42.86%) followed by middle mediastinum (11.43%), posterior mediastinum (8.57%), and multiple compartments (37.14%). [1] The incidence of benign mediastinal tumors has been reported to exceed that of malignant tumors by Adegboye et al. [12] However Vaziri et al. reported 60% incidence of malignant mediastinal tumors in their series, which probably could be attributed to the fact that they included metastatic tumors in their study. [13] In this study, the majority of lesions were found in the anterior mediastinum (45.5%). Benign tumors (63.6%) exceeded malignant ones in this series.

The most common symptoms reported in patients with mediastinal tumors are chest pain, dyspnea, cough, and weight loss. [10] Other symptoms include hoarseness of voice, myasthenia gravis, superior vena caval syndrome, fever, and chills. [14] In this study, all patients presented with vague chest pain and dyspnea on exertion.

Even though most mediastinal tumors can be appreciated in routine chest radiographs, the investigation of choice for their detection is CT scan. After confirmation of the presence of a mediastinal mass, further characterization may be done with MRI. [15] CT-guided FNAC has been proven to be a safe and useful method for diagnosis of mediastinal tumors. Pérez Dueñas et al. reported that this procedure is highly sensitive (95.2%) and accurate (93.5%) in diagnosing mediastinal masses. [16]

In this study, the difficulty was encountered in diagnosing thymic lesions cytologically. The same problem has been faced by other authors as well. It has been documented that an erroneous diagnosis of lymphoma may be awarded in case of a lymphocyte-rich thymic tumor. [16] On the other hand, if abundant epithelial component is aspirated from a thymic mass, then it may be mistaken for carcinoma. [17]

Thymic neoplasms are rare lesions with a wide variety of clinical presentations and pathologic features. A thymoma is the most common primary anterior mediastinal tumor with an incidence of 1.5 cases per million. Thymic carcinoma is even rarer. [18] Thymomas may occur in any age group, but they are most commonly found between 35 and 70 years of age. Women of older age group are slightly more affected than males. [8] In this study, age of patients with thymoma ranged from 30 to 56 years.

Patients with thymoma are asymptomatic in 30% cases. [18] Associated paraneoplastic syndromes are found in 50-70% cases. These include myasthenia gravis, rheumatoid arthritis, Cushing syndrome, pure red cell aplasia, limbic encephalitis, and hypogammaglobulinemia. [7] Patients with thymoma present with myasthenia gravis in 30 to 50% cases whereas only a mere 10-15% patients of myasthenia gravis have thymoma. [18] The molecular basis of the association of myasthenia gravis with thymoma still remains largely unknown. [8] The occurrence of myasthenia gravis is considered a favorable prognostic factor influencing the outcome of thymoma since this condition leads to early diagnosis of the tumor. [19] In this study, all 7 cases of thymic lesions were associated with myasthenia gravis.

Thymomas may be detected by chest radiography in 45-80% cases.However, the most sensitive diagnostic and preoperative staging modality of thymoma is CT scan. The usual appearance of thymoma on CT is a round to oval mass situated anterior to the heart and great vessels and inferior to the left innominate vein. In the presence of encasement, pleural dissemination, and vascular invasion, malignancy is suspected. [20]

Thymomas are indolent tumors, but they are malignant with a tendency to spread locally. The most widely used staging system is Masaoka-Koga system which takes into account the local extension of the tumor. [15] The two most important prognostic factors of thymoma include the Masaoka stage and completeness of resection of the tumor. [21]

According to the WHO scheme, thymomas are classified into 5 histologic subtypes. [22] In the present study, 2 cases of thymic hyperplasia and 5 of thymoma have been reported. One case of thymoma was categorized as a B1 subtype and the other 4 as AB subtype.

Surgical resection is the mainstay of treatment of thymoma. [8] Thymectomy and chemoradiation improve symptoms in 50-60% cases of myasthenia gravis. [7]

In this study, 5 (22.7%) cases of lymphoma were diagnosed in the middle mediastinum. By IHC analysis, 3 cases were found to be Hodgkin lymphoma and the other 2, non-Hodgkin lymphoma (T-cell lymphoblastic type). These results are in accordance with those obtained by other authors. It has been reported that 50-70% of primary mediastinal lymphomas are Hodgkin type. [5] Diffuse large B-cell lymphoma and acute lymphoblastic lymphoma are the common non-Hodgkin lymphomas found in the mediastinum. [18]

GCT constituted 13.6% of cases in the present study. Comparably, Aroor et al. reported 13.3% cases of GCTs in a similar study. [6] Neurogenic tumors found in this study included neurilemmomas, neurofibromas, and ganglioneuromas. Similar findings have been outlined by Shrivastava et al. [10] Other mediastinal lesions reported include isolated mediastinal tuberculosis which is a rare entity and usually associated with immunocompromised states. [23]

CONCLUSION

Mediastinal lesions are rare entities and data regarding their clinical and pathological features are limited. Further studies with larger sample size are required to enrich our knowledge regarding the enigmatic mediastinal masses. Thymomas must always be considered as lesions with malignant potential and they require prompt diagnosis and treatment.

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Conflicts of interest

There are no conflicts of interest.

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