RESEARCH ARTICLE

Clinicopathological spectrum of anterior mediastinal lesions with special reference to the role of cytology in diagnosis: A cross-sectional study

Prerana Mondal¹, Dipanwita Nag², Aparajita Samaddar², Srishtidhar Mangal², Nandini Das², Ipsita Saha²

¹Department of Pathology, Rampurhat Government Medical College and Hospital, Rampurhat, West Bengal, India, ²Department of Pathology, Medical College and Hospital, Kolkata, West Bengal, India

Correspondence to: Aparajita Samaddar, E-mail: aparajita.samaddar@gmail.com

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ABSTRACT

Background: Anterior mediastinal tumors comprise only 3% of all chest tumors. They are often of diagnostic challenge to both clinicians and histopathologists owing to their wide variety of clinical presentations and diversity in histomorphological appearance respectively. Hence, there is a need for elaborated studies to make the pathologists and clinicians aware of their diversity. Aim and Objectives: The present study was aimed to evaluate the diverse spectrum of clinical presentations and histomorphological appearances of anterior mediastinal lesions. In addition, cytological and radiological interpretations were correlated with histological diagnosis to assess their comparative role in diagnosis. Materials and Methods: It was a descriptive observational cross-sectional study. Patients diagnosed with anterior mediastinal mass on chest computed tomography (CT) scan were included in this study. Demographic details including clinical presentations and radiological interpretations were recorded. Patients underwent both CT guided Fine needle aspiration cytology (FNAC) and needle core/excisional biopsy. Histological diagnosis was correlated with radiological and cytological interpretations. Results: Of 659 patients presented with chest tumours, 19 were detected as having anterior mediastinal mass on chest CT scan indicating the prevalence of 2.88%. The most common presenting symptom was respiratory distress (73.68%), followed by chest pain (36.84%), superior vena cava syndrome (26.32%) and Myasthenic features (5.26%). About 50% of malignant tumours occurred at the 2nd decade of life. Thymic epithelial neoplasms comprise the major tumour type in this study (52.63%) followed by germ cell tumors (15.79%) and lymphomas (10.53%). Cytology was found to be more effective compared to radiology in diagnosis. Conclusion: Anterior mediastinal tumors are extremely heterogeneous in clinical presentation and histomorphological appearance. CT-guided FNAC can play an important role in their diagnosis along with radiology and histology.

KEY WORDS: Anterior Mediastinum; Mediastinal Mass; Histomorphological Spectrum; Cytology

INTRODUCTION

Mediastinum is a narrow space located between pleural cavities extending sagitally from thoracic inlet above to diaphragm below and anteroposteriorly from sternum to spine. It is further subdivided into four compartments namely superior, anterior, middle, and posterior. Division of the mediastinum into these compartments helps to narrow down the differential diagnosis of newly detected mediastinal masses. Mediastinal tumors are rare and accounting for only 3% of the tumors of the chest. They are often of diagnostic challenge to both clinicians and histopathologists owing to their diversity in clinical presentation and histomorphological appearances respectively. These patients are often asymptomatic at presentation and diagnosed incidentally on radiology. Again in other cases, anterior mediastinal masses
Mondal et al. Clinicopathological spectrum of anterior mediastinal lesions

Mediastinal GCTs are derived from primitive germ cells which fail to migrate completely during the early stages of embryonic development. Primary mediastinal seminoma, although an uncommon tumor, comprises 25–50% of malignant mediastinal GCTs occurring most frequently in men in the age group 20–40 years. Wide diversity of histological types of tumours in the anterior mediastinum makes the diagnosis challenging to histopathologists. Again, previous studies were mostly limited to case reports and discussion on mediastinal masses as a whole without special emphasis on anterior mediastinum which necessitates further study to evaluate anterior mediastinal masses in detail. With the background of this knowledge the present study was conducted to evaluate the clinical presentation and histomorphological spectrum of anterior mediastinal masses in a tertiary care hospital of Eastern India and also to correlate histopathological diagnosis with radiological and cytological interpretation. Hence, the role of cytology in comparison to radiology in the diagnosis of the anterior mediastinal tumor was also assessed.

MATERIALS AND METHODS

The present study was conducted after obtaining Institutional Ethical Clearance (No. MC/Kol/IEC/Non-spon/447/2016 dated 10th February 2016) and informed consents or age-appropriate assents from all the participants or their legal guardians (in case of minors). The identity of the participants was kept confidential. It was a descriptive observational prospective cross-sectional study undertaken at the Department of Cardio-Thoracic and Vascular Surgery (CTVS) and in the Department of Pathology of a tertiary care hospital of West Bengal. The study was done over a period of 2 years from March 2016 to February 2018. Patients attending the CTVS Outpatient Department (OPD) of the hospital with an anterior mediastinal mass on computed tomography (CT) scan within the study period were included in this study irrespective of their age and sex. Patients with masses other than anterior mediastinal location or heart or lung neoplasms or critically ill patients were excluded from this study. Patients without chest CT scan reports were also excluded. Total 659 cases of chest tumour patients attended CTVS OPD during the study period. Out of which 19 cases were detected as having anterior mediastinal masses on CT scan and only those cases were evaluated further. Relevant clinical history with special emphasis on symptoms of mediastinal obstruction or superior vena cava (SVC) syndrome like dysphagia, hoarseness of voice, swelling of the face and dyspnea along with other symptoms like wheezing, chest pain and myasthenic features such as drooping of upper eyelids and muscle weakness was collected. Detailed clinical examination was also performed to rule out the presence of any other primary tumour or lymphadenopathy. Radiological reports were collected from the patients. CT guided fine-needle aspiration cytology (FNAC) from the mediastinal mass was performed and the slides were stained by both Leishman-Giemsa and Papanicolaou stain and were evaluated at the Department of Pathology for the cytological interpretation. Then, the patients underwent either needle core biopsy or excisional biopsy at the CTVS department and the specimens were sent at the department of Pathology for further evaluation. The received specimens were properly fixed in 10% neutral buffered formalin and gross examination was done. After proper processing and microtomy, the haematoxylin and eosin (H and E) stained slides were examined under light microscope and a histopathological diagnosis was made. In case of diagnostic dilemma, immunohistochemical study was performed from the preserved paraffin blocks with relevant markers to arrive at a final diagnosis. Proper positive and negative controls were taken for each marker. Results were tabulated and histopathological diagnosis was correlated with radiological and cytological interpretations to assess their comparative role in the diagnosis of anterior mediastinal masses.

RESULTS

Of total 659 cases of chest tumor patients who attended the CTVS OPD during the study period, only 19 cases were detected as having anterior mediastinal mass on chest CT scan. Thus, the prevalence of anterior mediastinal tumours was only 2.88% in the present study. Age range of the participants...
was between 10 and 60 years. Among the participants 11 were male and eight were female with a ratio of 1.38:1. Thymoma, Non-Hodgkin’s Lymphoma (NHL) and seminoma showed a male preponderance whereas thymic hyperplasia, thymic carcinoma, schwannoma and fibromatosis showed female gender predilection. 66.67% of benign tumors were found in the age group of 31–40 years whereas malignant tumours were more common in younger age group as represented by the occurrence of 50% of the malignant tumors in the 2nd decade of life. All over malignant tumors were found to be more common in anterior mediastinum compared to benign tumours with a ratio of 10:9 [Table 1].

In the present study 17 out of total 19 (89.47%), patients were symptomatic when they attended the CTVS OPD of this hospital for the 1 time during the study period. The most common presenting symptom was respiratory distress (73.68%), followed by chest pain (36.84%), SVC syndrome (26.32%), and Myasthenic features (5.26%) [Table 2]. SVC syndrome was most common in patients with thymic carcinoma. Of five cases of thymic carcinoma evaluated, three patients presented with SVC syndrome. None of the patients had any other primary tumor or lymphadenopathy on clinical examination.

Out of total 19 cases of anterior mediastinal masses evaluated, two cases were diagnosed as thymic hyperplasia, five cases as thymoma and thymic carcinoma each, one case as fibromatosis and schwannoma each, three cases as seminoma and two cases as NHL histologically. According to the World Health Organization (WHO) classification out of five cases of thymoma, two were categorized as Type B2, 1 as Type B1 and two cases as Type B3 [Figure 1].[15] The histological diagnosis was inconclusive in five cases including two cases of thymic carcinoma, one case of fibromatosis, and two cases of NHL. Immunohistochemical study was performed in the above cases either for confirmation of the diagnosis or for proper categorization. Both the cases of thymic carcinoma were positive for CK 5/6, Epithelial membrane antigen, PAX-8, CD-5 and CD-117 with increased Ki-67 labelling index (32% and 51% respectively. They were negative for TdT and CD-34 [Figure 2]. The aforesaid immunohistochemical findings differentiated them from thymoma Type B3 and squamous cell carcinoma of other organs and thus the cases were confirmed as thymic carcinoma.[16,17] The case of fibromatosis was positive for vimentin and desmin and was negative for S-100, CD-34, CD-99 and bcl-2 which helped to differentiate it from other spindle cell tumor of the chest. In the case of two cases of NHL, immunohistochemical study was required for proper categorization. Both the lymphoma cases were positive for CD7, CD99, TdT and were negative for Pan CK (pan cytokeratin) and B cell markers such as CD-20 and PAX 5. One of them was positive for CD10 and the other one was negative for CD-10. Ki-67 labelling index was 60% and 70%. Based on the above pattern of immunohistochemical marker expression, both of them were diagnosed as T-cell lymphoblastic lymphoma (T-ALL).[18]

On gross inspection, the mean diameter of the thymic masses was 6.75 cm in greatest dimension with the largest one being a case of thymic carcinoma (9.5 cm in greatest dimension).

Of total of 19 cases assessed FNAC interpretation was corroborative with the histological diagnosis in 13 cases with a sensitivity of 68.42%, whereas sensitivity of CT scan was found to be 57.89% in this study [Table 3].

<table>
<thead>
<tr>
<th>Age range in years</th>
<th>Benign lesions (%) (n=9)</th>
<th>Malignant tumours (%) (n=10)</th>
<th>Total no. of cases (%) (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st decade (1–10)</td>
<td>0</td>
<td>1 (10)</td>
<td>1 (5.26)</td>
</tr>
<tr>
<td>2nd decade (11–20)</td>
<td>0</td>
<td>5 (50)</td>
<td>5 (26.32)</td>
</tr>
<tr>
<td>3rd decade (21–30)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4th decade (31–40)</td>
<td>6 (66.67)</td>
<td>2 (20)</td>
<td>8 (42.11)</td>
</tr>
<tr>
<td>5th decade (41–50)</td>
<td>2 (22.22)</td>
<td>1 (10)</td>
<td>3 (15.79)</td>
</tr>
<tr>
<td>6th decade (51–60)</td>
<td>1 (11.11)</td>
<td>1 (10)</td>
<td>2 (10.53)</td>
</tr>
</tbody>
</table>

Figure 1: Thymoma: (a) Cytology showing cluster of epithelial cells (LG; ×400), (b) World Health Organization (WHO) Type B1 showing lymphocyte rich morphology, (c) WHO Type B2 showing mixed population of thymic epithelial cells and lymphocytes and (d) WHO Type B3 showing atypical neoplastic epithelial cells (H and E, ×400)
DISCUSSION

In the present study, the prevalence of the anterior mediastinal tumour was found to be only 2.88% of all chest tumours which represented the rarity of them in clinical practice. Out of which thymic epithelial lesions including thymomas and thymic carcinomas comprise the major tumor type followed by GCTs and lymphomas. Benign tumors were more common in the 4th decade of life, whereas most of the malignant tumours occurred at a younger age group of 11–20 years. Among the wide spectrum of clinical presentations, the most common one was respiratory distress in patients with anterior mediastinal mass. In the current study, CT guided FNAC was found to play more important role in diagnosis compared to radiology alone.

The prevalence of anterior mediastinal tumors found in this study was in concordance with the previous study by Macchiarini and Ostertag[7] and Rubush et al.[19] Akshatha et al. also noted similar incidence of mediastinal mass to be 3% in their study.[2] In the present study, most of the cases of mediastinal masses were presented in the age group of 31–40 years (42.11% of all cases) which was a decade later than the finding noted by Davis et al. who found most of the patients with mediastinal mass in their 3rd decade of life.[8] However, 50% of the malignant tumours were found at an younger age group of 11–20 years. So it was concluded that there is more chance of an anterior mediastinal mass to be malignant in younger patients. This finding was in discordance with the study done by Davis et al. who found most of the malignant tumours occurred in the 4th decade of life but they also noted the reported incidence of malignancy in children with mediastinal masses ranges from 27 to 76% in previous studies.[8] Thymic epithelial neoplasms comprise the major tumour types in this study (52.63%) followed by GCTs (15.79%) and lymphomas (10.53%) [Figure 3]. None of the patients had any other primary tumor or lymphadenopathy on clinical examination. Hence, it was concluded that primary tumours are more common in this location compared to secondary ones. Dubashi et al. and Singh et al. also found thymic epithelial neoplasms being the most common tumor type in the anterior mediastinum like this study.[3,9] However Vaziri et al. and Adegoaye et al. Concluded lymphoma as the most common tumor type.[20,21] All over malignant tumours were found to be more common than benign ones with a ratio of 10:9. Other studies also noted 60–70% of anterior mediastinal tumors to be malignant.[2,20] Although this was not supported by Adegoaye et al. and Shrivastava et al. who

![Figure 2: Thymic carcinoma: (a) CT scan showing the mass, (b) Pleomorphic neoplastic cells (H and E; ×400), (c) Neoplastic cells are showing membrane positivity for Epithelial membrane antigen (×400), (d) Neoplastic cells are showing cytoplasmic positivity for CK 5/6(×400)](image)

Table 2: Distribution of presenting symptoms among patients with anterior mediastinal mass (Total no. of patients n=19)

| Presenting symptoms | No. of patients presented with (n=19) | n=19 (%)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory distress</td>
<td>14</td>
<td>73.68</td>
</tr>
<tr>
<td>Chest pain</td>
<td>7</td>
<td>36.84</td>
</tr>
<tr>
<td>SVC syndrome</td>
<td>5</td>
<td>26.32</td>
</tr>
<tr>
<td>Myasthenic features</td>
<td>1</td>
<td>5.26</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>2</td>
<td>10.53</td>
</tr>
</tbody>
</table>

SVC: Superior vena cava

Table 3: Age and sex distribution of anterior mediastinal lesions with correlation of cytological and radiological interpretation with histological diagnosis

<table>
<thead>
<tr>
<th>Histological diagnosis</th>
<th>No.of cases (n=19)</th>
<th>Age range in years</th>
<th>Sex preponderance (M/F)</th>
<th>No of cases correlated with cytological interpretation</th>
<th>No. of cases correlated with radiological interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymic hyperplasia</td>
<td>2</td>
<td>33–35</td>
<td>Female (0/2)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Thymoma</td>
<td>5</td>
<td>38–52</td>
<td>Male (5/0)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Thymic carcinoma</td>
<td>5</td>
<td>20–60</td>
<td>Female (1/4)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Fibromatosis</td>
<td>1</td>
<td>34</td>
<td>Female (0/1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Seminoma</td>
<td>3</td>
<td>15–19</td>
<td>Male (3/0)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>NHL</td>
<td>2</td>
<td>10–12</td>
<td>Male (2/0)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>1</td>
<td>38</td>
<td>Female (0/1)</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

NHL: Non-Hodgkin’s lymphoma
In this study, male preponderance was noted among the patients with male-to-female ratio of 1.38:1 which was comparable with previous studies. In the current study, 89.47% of patients were symptomatic and the most common presenting symptom was respiratory distress (73.68%) followed by chest pain (36.84%), SVC syndrome (26.32%) and myasthenic features (5.26%). Davis et al. found 62.5% of patients with mediastinal mass presented with symptoms which was much lower incidence than our study. In their study, the most common presenting symptom was chest pain (30%) followed by fever and chills (20%), dyspnea (16%), cough (16%) and myasthenic features (7%). Hence, it was concluded from the present and previous studies that in cases of unexplained respiratory distress in a young patient the possibility of anterior mediastinal mass should also be included in differential diagnosis along with other more common causes like diffuse alveolar damage. In the present study, CT guided FNAC was found to be more efficient method for diagnosing anterior mediastinal masses than imaging modalities alone with a sensitivity of 68.42% and 57.89% respectively.

As both the diverse clinical presentations and histomorphological spectrum of anterior mediastinal masses are elaborately discussed in this study, it may help clinicians and histopathologists to diagnose these rare tumours more accurately. However, there are some limitations in this study. This was a cross-sectional study hence the cases could not be followed up. Hence, the survival rate of the patients with anterior mediastinal masses could not be assessed.

**CONCLUSION**

Anterior mediastinal tumours are extremely heterogeneous in clinical presentation and histomorphological types with thymic epithelial lesions being the most common one. CT-guided FNAC can be considered as an effective and rapid method of diagnosis of anterior mediastinal tumors in addition to radiology and histology.

**REFERENCES**

18. Gao XZ, Wei JG, Li SL, Han J, Wang GN, Li WC. Mediastinal...


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