Original Article

Fine-needle aspiration cytology of mediastinal masses: An institutional experience

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Abstract

Introduction: Mediastinal masses are uncommon in clinical practice. Fine-needle aspiration cytology (FNAC) is an important and useful investigation and is considered next to imaging in the diagnosis of mediastinal lesions. **Aim:** To analyze the mediastinal masses diagnosed on FNAC. **Materials and Methods:** We retrospectively retrieved twenty-five cases, which underwent FNAC under ultrasound or computed tomography (CT) guidance for mediastinal masses, over a period of 4 years. Histopathological correlations were done in cases wherever available. **Results:** Among twenty-five cases, which were diagnosed through FNAC, eighteen were males and seven were females with age ranging from 6 to 85 years. Ultrasonography (USG)-guided FNAC was performed in three patients, while CT-guided FNAC was performed in twenty-two patients. Out of twenty-five cases, seventeen cases were malignant, six were benign, and two cases were inadequate. FNAC was useful in the diagnosis of 83.3% of cases. Biopsy and/or cell block correlations were available in fourteen cases. In the malignant category, mediastinal invasion by either squamous cell carcinoma or adenocarcinoma constituted the highest number with eight (47%) out of seventeen cases. Among the nonneoplastic conditions, nonspecific inflammation was the most common cause with two cases (8%) out of total cases followed by one case each of tuberculosis, schwannoma, thymoma, and cystic lesion. **Conclusion:** USG or CT-guided FNAC is a safe, minimally invasive, and cost-effective procedure, which can provide a precise diagnosis in the mediastinal masses, and may obviate the need for an invasive surgical approach.

Keywords: FNAC, mass, mediastinum

Introduction

The mediastinum is the portion of the thoracic cavity present between the pleural cavities, extending anteroposteriorly from the sternum to the spine and sagittally from the thoracic inlet to the diaphragm.[1,2] The mediastinum is arbitrarily divided into superior, anterior, middle, and posterior compartments.[1,2]

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The most frequent lesions encountered in the mediastinum are thymomas, neurogenic tumors, and benign cysts, altogether contributing about 60% of the lesion.[3,4] Age-related differences of tumor biology, host characteristics, or treatment protocol exist in mediastinal lesions.[3] Although age distribution, clinical features, and location of the lesion together with their configuration provide important diagnostic information, many lesions (both benign and malignant) result in similar radiological appearances.[1-4] Therefore, in order to prevent immediate exploration, fine-needle aspiration cytology (FNAC) under ultrasound (USG) or computed tomography (CT) scan guidance has been used increasingly and successfully to resolve the diagnostic foci. Hence, the aim of this study is to analyze

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the cytomorphological features in mediastinal masses through FNAC.

Materials and Methods

This was a hospital-based retrospective study done in the Department of Pathology, consisting of twenty-five patients, who had undergone diagnostic evaluation by imaging modalities between 2013 and 2018. As a part of the work-up, demographic details of the patients, relevant clinical information, physical examination findings, chest radiography, ultrasound, and computed tomography findings were recorded. As it was a retrospective study, informed consent and clearance from the institute ethics committee were not taken. Utmost care was taken not to disclose patients' identity in any form.

The inclusion criteria included all patients, who referred to our hospital with widened mediastinum or with a definite or suspected mediastinal masses on chest radiograph.

Patients with bleeding diathesis (international normalized ratio >2) or severe thrombocytopenia (platelet count <50,000/mm^3), patients with moderate-to-severe pulmonary artery hypertension, or vascular lesions on contrast CT scan were not subjected to FNAC or biopsy.

FNAC was performed using a short beveled sharp 22-gauge, 15-cm long spinal needle attached to a 20-mL sterile disposable syringe under all aseptic precautions after obtaining informed consent. Two percent lignocaine was used as a local anesthetic agent for skin and soft tissue infiltration after sensitivity testing. CT-guided FNAC was performed in twenty patients, while ultrasound-guided FNAC was performed in two patients. Contrast-enhanced CT was performed using a nonionic iodinated contrast. A core needle biopsy (CNB) was attempted in a few cases where the site was appropriate.

Aspirated material was smeared on clean glass slide evenly and as thin as possible, finally air-dried and wet fixed with 90% ethyl alcohol. After fixation, slides were stained by Papanicolaou stain, May-Grunwald Giemsa (MGG) stain and special stains such as Ziehl-Neelsen (ZN) stain, Periodic Acid Schiff (PAS) stain were used whenever necessary. Aspiration smears were studied for the probable diagnosis and finally, the results of FNAC were correlated wherever possible with a tissue biopsy, cell block preparation, and flow cytometry. The tissue biopsy specimens were fixed in 10% neutral buffered formalin solution for further processing in routine fashion and embedded in paraffin. For cell block, the specimens were collected in 10% neutral buffered formalin followed by centrifugation and addition of equal parts of plasma and thrombin with the formation of the clot. The clot was finally removed and processed in the tissue processor. The specimens were collected in EDTA vial in order to process for flow cytometry wherever required.

Results

Among twenty-five cases that were included in the final analysis evaluated through FNAC, the cytological features were adequate to establish the diagnosis in twenty-three cases. There was a wide variation in age ranging from 6 to 85 years with a mean age of 47 years. The most common age group affected with mediastinal mass was between 50 and 59 years. There were eighteen males and seven females with a male to female ratio of 2.6:1.

The mean duration of symptoms was 110 days with duration ranging from 16 days to 810 days. Out of twenty-five cases, twenty-four patients (96%) were symptomatic at the time of presentation. Out of twenty-four patients, the cough was the prominent symptom seen in twenty patients (83.3%) followed by chest pain in eighteen patients (75%), shortness of breath in fifteen patients (62.5%). Among the clinical signs in the twenty-five patients, superior vena cava obstruction was the most common noted in eight patients (32%) followed by cervical lymphadenopathy in seven patients (17.5%), stridor in five patients (12.5%), and pleural effusion in three patients (7.5%). There were twenty cases (80%) confined to the anterior mediastinum, one case (4%) to the middle, and four cases (16%) to the posterior mediastinum.

Ultrasonography (USG)-guided FNAC was performed in three patients, while computed tomography (CT)-guided FNAC was performed in twenty-two patients. Out of twenty-five cases, seventeen cases (68%) were malignant, six cases (24%) were benign or inflammatory lesions, and two cases (8%) were inadequate to establish any diagnosis. FNAC was useful in the diagnosis of 83.3% of cases. The distribution of the cases is enumerated in [Table 1].

Among the males (n = 18), thirteen cases (72.2%) had malignant lesions, four cases (22.2%) had benign lesion, while one (5.6%) was

Table 1: Distribution of mediastinal mass in relation to neoplastic and nonneoplastic category

Sl. no	Cytological diagnosis	Number of cases (n=25)	Percentage
1.	Inflammatory and benign	n=6	24%
Nonspecific inflammation		02	
Tuberculosis		01	
Mediastinal cyst		01	
Thymoma		01	
Benign neurogenic tumor		01	
2.	Malignant	n=17	68%
Metastatic squamous cell		05	
carcinoma		03	
Metastatic adenocarcinoma		04	
Non-Hodgkin's lymphoma		03	
Germ cell tumor		01	
Poorly differentiated carcinoma		01	
Small round cell tumor			
3.	Inadequate	02	8%

inconclusive. Among the females (n = 7), four cases (57.1%) had malignant lesions, one case each (28.6%) was diagnosed as benign and inflammatory. The remaining one case (14.3%) was inconclusive.

Histopathological and/or cell block preparations were available in fourteen cases [Table 2]. Out of the six inflammatory and benign cases, four had biopsy correlation, which confirmed the FNAC diagnoses including one case each of thymoma and schwannoma [Figure 1]. Out of ten malignant cases, CNB was done in five cases including one case each of metastatic squamous cell carcinoma, metastatic adenocarcinoma [Figure 2], germ cell tumor, which was confirmed as mediastinal seminoma [Figure 3], and poorly differentiated carcinoma, which was confirmed as thymic carcinoma. Complete excisional biopsy was done in one case of a small round cell tumor, which was confirmed as Ewing's sarcoma [Figure 4]. Two cases of non-Hodgkin's lymphoma had flow cytometry done on FNAC aspirates along with CNB correlation [Figure 5].

There were two inconclusive cases on FNAC, which did not have any histopathological or cell block correlation.

There was no case of procedure-related mortality. Among the complications, self-limiting chest pain was experienced by ten patients (40%), small pneumothorax with no intervention and being managed conservatively developed in two cases (8%), and scanty hemoptysis was noted in two cases (8%).

Discussion

Diagnosis of mediastinal lesions has been a challenging task for all radiologists and pathologists since it has been considered as a "Pandora's box" within which congenital cysts, benign tumors, primary and metastatic neoplasms develop.[1,2]

The present study consisted of twenty-five cases from different compartments of the mediastinum, where FNAC was done as a primary diagnostic modality. The study revealed that the maximum number of cases was seen in the age group of 50–59 years. Our study revealed that mediastinum is the site for a variety of lesions, both benign and malignant. In the present study, the malignant cases formed the largest category. Out of the total twenty-five cases, 24% of cases were benign, 68% of cases were malignant, and 8% were inadequate. In the studies done by Adler *et al.* and Jareb and Krasovec malignant lesions constituted 75% of the cases.[5,6]

In the malignant category, mediastinal invasion by either squamous cell carcinoma or adenocarcinoma constituted the highest number with eight (47%) out of seventeen cases. Adler *et al.*, Nasit *et al.*, and Assaad *et al.* observed a significant

Table 2: Comparison of cytological and histological diagnosis in neoplastic and nonneoplastic category

Sl. no.	Diagnosis	Confirmation
1.	Inflammatory and benign (n=4)	
	Nonspecific inflammation (2)	Confirmed on CNB
	Thymoma (1)	Confirmed on CNB
	Benign neurogenic tumor-Schwannoma (1)	Confirmed on excisional biopsy
2.	Malignant (n=10)	
	Metastatic squamous cell carcinoma (4)	One case confirmed on CNB Three cases confirmed on cell block
	Metastatic adenocarcinoma (2)	One case confirmed on CNB One case confirmed on cell block
	Non-Hodgkin's lymphoma (2) T-cell lymphoma Acute lymphoblastic leukemia	Both confirmed on CNB and flowcytometry
	Germ cell tumor-mediastinal seminoma (1)	Confirmed on CNB
	Poorly differentiated carcinoma-Thymic carcinoma (1)	Confirmed on CNB
	Small round cell tumor-ES (1)	Confirmed on excisional biopsy

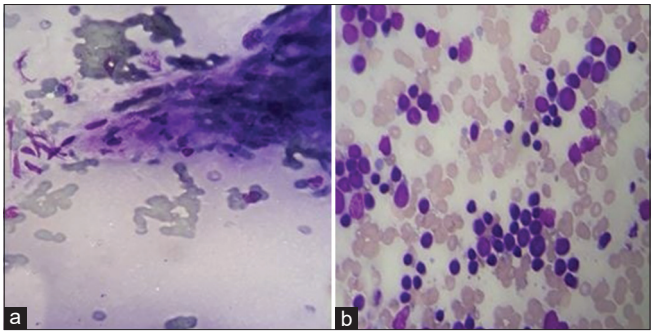

Figure 1: (a) Cytology smear of schwannoma showing spindle cells embedded in a fibrillary background (MGG, ×400). (b) Cytology smear of thymoma showing bland epithelial cells admixed with lymphocytes (MGG, ×400)

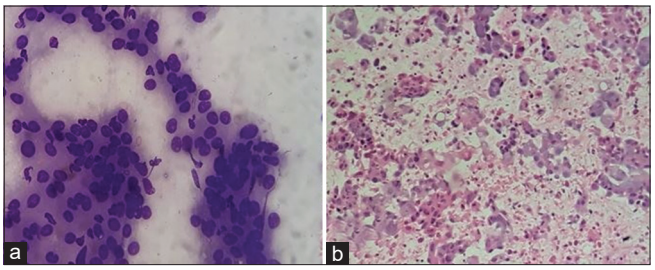

Figure 2: (a) Cytology showing tumor cells arranged in vague glandular pattern (MGG, ×400) and (b) cell block of the same confirming the diagnosis of adenocarcinoma (H & E, ×400)

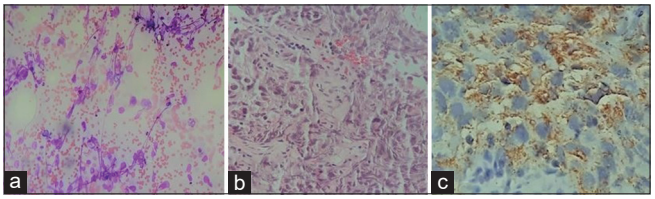

Figure 3: (a) Cytology smear showing fragile tumor cells admixed with lymphocytes (MGG, ×400), (b) biopsy (H & E, ×400), and (c) strong membranous PLAP positivity in seminoma (DAB, ×400)

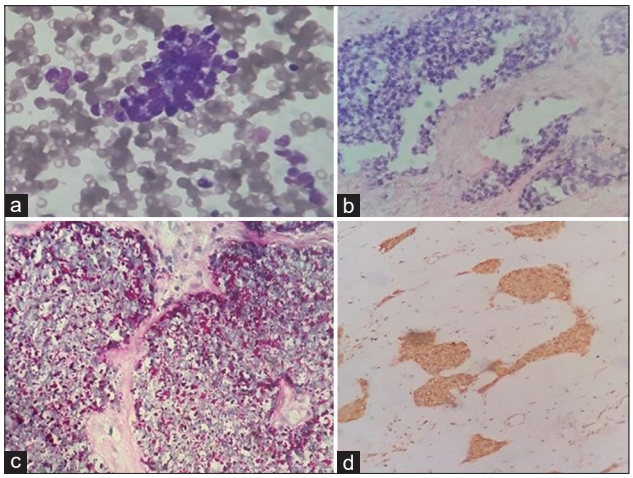

Figure 4: (a) Cytology smear showing small round cells with rosette formation (MGG, ×400). (b) Biopsy showing small round cells (H & E, ×400). (c) The cells are diffuse PAS positive (PAS, ×200). (d) Membranous CD99 positivity in the tumor cells (DAB, ×100)

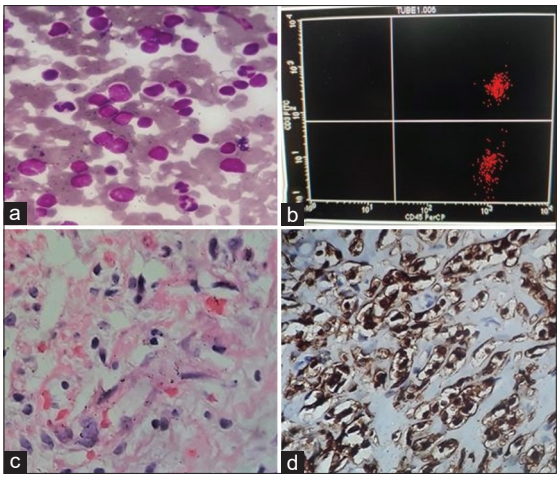

Figure 5: (a) Cytology smear showing blasts with cleaved nuclei (MGG, ×400). (b) Flow cytometry done on aspirate showing surface CD3 positivity. (d) Biopsy showing atypical lymphoid cells (H & E, ×400). (d) Positive for CD3 confirming the diagnosis of T-cell NHL (DAB, ×400)

proportion of metastatic lesions in the mediastinum with 48%, 38%, and 45%, respectively.[5,7,8] Out of eight metastatic cases, six (75%) cases originated from a lung primary similar to Dixit *et al.* who reported the majority of cases with a lung primary.[9]

In the present study, there were two cases of non-Hodgkin's lymphoma, which were confirmed in biopsy and further subtyped through IHC and flow cytometry. There were two cases of thymic neoplasms; one case of thymoma and one case of thymic carcinoma, which was diagnosed as poorly differentiated carcinoma on cytology. Thymic neoplasm requires correlation with clinical and radiological findings.[10] Another case that constituted the malignant category was Ewing's sarcoma, which was initially diagnosed as small round cell tumor on cytology and finally confirmed as Ewing's sarcoma through IHC on biopsy.

Among the nonneoplastic conditions, tuberculosis, schwannoma, thymoma, cystic lesion comprised 4% each out of all the cases. This is in concordance with the study done by Shaheen *et al.*, where nonneoplastic lesions especially tuberculosis comprised 5% of cases.[11] It is also important to note that tubercular mediastinal lymphadenopathy has characteristic CT features of the central area of low attenuation with rim enhancement.[12] A similar feature was seen in the patient with mediastinal lymphadenopathy due to tuberculosis in our study. Apart from tuberculosis, certain fungal infections can also present as a mediastinal mass but such events are rare.[13] There was no case of fungal infections in our study. Neurogenic tumors, most commonly schwannoma, were seen in the posterior mediastinum.[14] The present study also had a case of schwannoma, which was initially diagnosed as a benign neurogenic tumor on FNAC.

We could diagnose twenty-three cases (92%) by FNAC alone and biopsy and/or cell block correlation were available in fourteen cases (56%) to confirm the nature of the lesion. The FNAC material was inconclusive in 8% cases. Similar observations were made by Adler *et al.* (11%) and Nasit *et al.* (8%).[5,7]

The inability to provide a diagnosis by FNAC might be due to several factors like scanty material, poor smear preparation, poor fixation, low cellularity, etc., The procedure-related complications in our study were very less and were comparable with previously published studies.[11,15,16]

FNAC aspirates provide valuable material for ancillary techniques like cell block and flow cytometry. Moreover, cell block provides material for immunohistochemistry. This is of particular importance in sites like mediastinum, which are difficult to access for biopsy.

However, there were few limitations in this study. First, the number of cases in our study was comparatively less. Second, it was not possible to compare FNAC results with CNB in all cases to rule out false negative or false positive results because core biopsy was only performed in those cases, where there was a doubt in FNAC diagnosis. Finally, we could not use newer surgical and diagnostic techniques like endobronchial ultrasound/endoscopic ultrasound EBUS/EUS for evaluation of those cases where FNAC was inconclusive due to financial constraints.

Early detection is the key for prompt management to reduce the overall morbidity associated with the mediastinal masses.[17] Data from our study indicate that image-guided FNAC is a safe, minimally invasive, and cost-effective procedure, which can provide a precise diagnosis in the mediastinal masses like in abdominal masses.[18] Diagnosis based on image-guided FNAC, if followed by primary-care physicians for evaluation of such cases, will lead to an early diagnosis and obviate the need for an invasive surgical approach.

Conclusion

Prompt and correct diagnosis of mediastinal tumors has been the key process in therapeutic decision. Based on the present study,

it is recommended that FNAC can be undertaken as the first invasive procedure under ultrasound or CT scan guidance since it allows adequate sampling of tissue with the lowest possible risk and discomfort to patients. CNB can be performed when cytology diagnosis is uncertain. Our study concluded that with advancing age the incidence of malignant neoplasm increases and there is a wide diversity in the diagnosis of mediastinal mass based on the age, clinical features, radiological findings, and specific anatomical location. Metastatic mediastinal neoplasm remains the most common mediastinal mass followed by primary mediastinal neoplasm like non-Hodgkin lymphoma. Although newer diagnostic modalities have been recently introduced, the conventional transthoracic FNAC under ultrasound or CT scan guidance for mediastinal lesions is still important because of its safety, the easiness with relatively less procedure-related complications, and similar comparable results reducing the need for more extensive diagnostic surgical procedures.

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Conflicts of interest

There are no conflicts of interest.

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