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Sensitivity and specificity of fine needle aspiration for the diagnosis of mediastinal lesions

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A B S T R A C T

Fine needle aspiration cytology (FNAC) of mediastinal masses allows for rapid on-site evaluation and the triaging of material for ancillary studies. However, surgical pathology is often considered to be the gold standard for diagnosis. This study examines the sensitivity and specificity of FNAC compared to a concurrent or subsequent surgical pathology specimen in 77 mediastinal lesions. The overall sensitivity for mediastinal mass FNAC was 78% and the overall specificity was 98%. For individual categories the sensitivity and specificity of FNAC was respectively as follows: inflammatory/infectious (33%, 99%), metastatic carcinoma (93%, 100%), lymphoma (84%, 97%), cysts (25%, 100%), soft tissue tumors (100%, 100%), paraganglioma (50%, 100%), germ cell tumor (100%, 99%), thymoma (87%, 94%), thymic carcinoma (60%, 100%), benign thymus (0%, 100%), and indeterminate (100%, 90%). For different locations within the mediastinum the sensitivity and specificity of FNAC was respectively as follows: anterosuperior mediastinum (80%, 98%), posterior mediastinum (33%, 95%), middle mediastinum (100%, 100%), and mediastinum, NOS (79%, 99%). Thus, mediastinal FNAC is fairly sensitive, very specific, and is a valuable technique in the diagnosis of mediastinal masses.

1. Introduction

A wide array of tumors occur within the mediastinum and treatment is dependent on the specific diagnosis. It can range from clinical follow up to surgery, chemotherapy, and/or radiation [1]. While a triple approach incorporating clinical context, radiology, and pathology is utilized to diagnose tumors prior to therapy, surgical pathology is often considered to be the gold standard for diagnosis.

Fine needle aspiration cytology (FNAC) is a relatively non-invasive technique that can be used alone or in conjunction with core needle biopsy prior to therapy, allows for rapid on-site evaluation, and is helpful in triaging material for ancillary studies such as flow cytometry, immunohistochemistry, and molecular studies.

The aim of our study was to determine the sensitivity and specificity of FNAC in the diagnosis of mediastinal lesions compared to a concurrent or subsequent surgical pathology specimen (core biopsy or resection).

2. Materials and methods

Mediastinal FNACs from 107 patients were retrieved from the files of the New York Presbyterian Hospital/Weill Cornell Medicine Pathology Department between 2006 and 2015. Seventy-seven of the 107 patients had concurrent or subsequent surgical pathology specimens (core biopsy or resection). Appropriate IRB approvals were obtained from Weill Cornell Medicine.

The cytology and surgical pathology specimens were processed in the usual manner. The direct smears were either air-dried, methanol fixed, and then stained with the Diff-Quik stain or immediately fixed in 95% ethanol and then stained with the Papanicolaou stain. The surgical pathology specimens were fixed in 10% buffered formalin, processed, and embedded in paraffin. Standard 5-μm sections were prepared and stained with hematoxylin and eosin.

Appropriate ancillary tests, including immunohistochemistry, flow cytometry, and molecular studies, were used to make specific diagnoses (Figs. 1–3). The final diagnosis was considered to be the surgical pathology diagnosis if available and the cytology diagnosis if no surgical pathology diagnosis was available.

The sensitivity and specificity of FNAC was determined by using the concurrent or subsequent surgical pathology (core biopsy or resection) as the gold standard.

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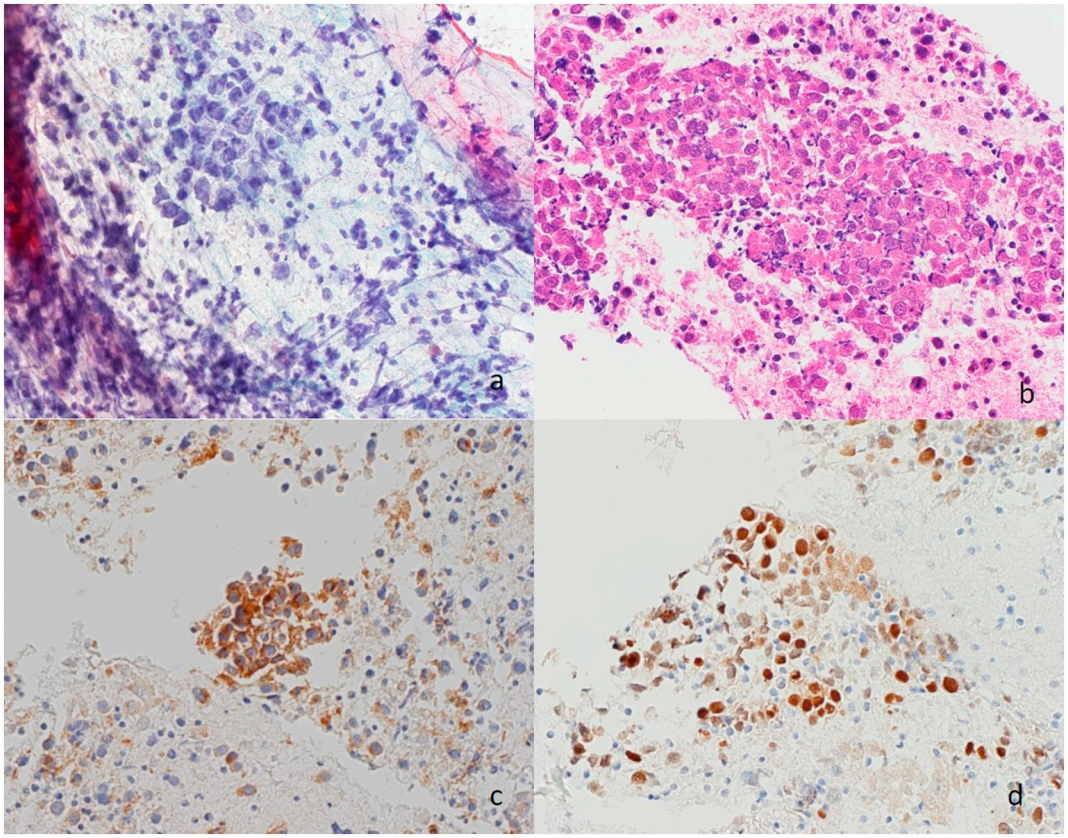

Fig. 1. These images are of a seminoma. Fig. 1a is a seminoma stained with Papanicolaou stain (40×). Fig. 1b shows the cell block of the seminoma stained with hematoxylin and eosin (40×). Fig. 1c shows that the seminoma is positive for the immunohistochemical stain PLAP (40×). Fig. 1d shows that the seminoma is positive for the immunohistochemical stain OCT4 (40×).

3. Results

The age range of the 107 patients with mediastinal FNAC was 7 to 88 years old of which 38.3% were males and 61.7% were females. They were all biopsied using some form of guidance: Transthoracic Computed Tomography (CT) (92), Endobronchial Ultrasound (14), and Endoscopic Ultrasound (1). Of the 107 patients, 77 patients had either a concurrent or subsequent surgical pathology specimen (core biopsy or resection). The 107 FNAC specimens and the 77 surgical pathology specimens were located respectively in the anterosuperior mediastinum (65, 49), posterior mediastinum (6, 3), middle mediastinum (2, 1), and mediastinum, not otherwise specified (NOS) (34, 24).

The final diagnoses of the 107 FNAC specimens and the 77 surgical pathology specimens were respectively as follows: infectious/inflammatory (7,6), metastatic carcinoma (24, 15), lymphoma (20, 19), cysts (6, 4), soft tissue tumors (5, 3), paragangliomas (2, 2), germ cell tumors (2, 2), thymoma (20, 15), thymic carcinoma (6, 5), benign thymus (2, 1), indeterminate (12, 5), and benign thyroid (1, 0) (Table 1).

The overall sensitivity for mediastinal mass FNAC was 78% and the overall specificity was 98%. The sensitivity and specificity of FNAC in the individual categories were respectively as follows: inflammatory/infectious (33%, 99%), metastatic carcinoma (93%, 100%), lymphoma (84%, 97%), cyst (25%, 100%), soft tissue tumor (100%, 100%), paraganglioma (50%, 100%), germ cell tumor (100%, 99%), thymoma (87%, 94%), thymic carcinoma (60%, 100%), benign thymus (0%, 100%), and indeterminate (100%, 90%) (Table 2). There was a lack of concordance between the FNAC and corresponding surgical pathology in 17 out of 77 (22%) cases as listed in Table 3.

The sensitivity and specificity of FNAC in the different locations within the mediastinum were respectively as follows: anterosuperior mediastinum (80%, 98%), posterior mediastinum (33%, 95%), middle mediastinum (100%, 100%), and mediastinum, NOS (79%, 99%) (Table 4).

4. Discussion

Only a scant amount of literature deals with FNAC of mediastinal masses, and these papers have different methods of reporting data and/or only publish data collected by specific techniques such as FNAC, Core Needle Biopsies, and Endoscopic Ultrasound-Guided FNAC [1-6].

A study by Morrissey et al. found similar results to our study. It included 65 mediastinal FNACs and reported a diagnostic accuracy of 77%. In addition, the diagnostic accuracy was higher for carcinoma cases (88%) than non-carcinoma cases (69%) [4].

In a study by Petranovic et al. CT guided FNAC was performed in 52 patients with anterior mediastinal masses. The percentage of FNACs with diagnostic material were as follows: overall (60%), metastatic lesions (80%), germ cell tumors (67%), primary pulmonary neoplasms (86%), thymic neoplasms (82%), and lymphomas (36%) [1].

The overall FNAC sensitivity in our study (78%) was higher than the overall diagnostic yield noted in the study by Petranovic et al. (60%). In particular, the sensitivity for lymphoma in our study (84%) was much higher than the FNAC diagnostic yield for lymphoma noted in the other study (36%). Both studies had a similar number of lymphoma cases; our study had 19 cases of lymphoma including 6 cases of Classic Hodgkin Lymphoma and the other study had 22 cases of lymphoma including 8 cases of Classic Hodgkin Lymphoma. In the other study, the diagnostic yield for specific types of lymphoma were all well below the sensitivity found in our study: Hodgkin Lymphoma (25%), Non-Hodgkin Lymphoma (43%), B-Cell Lymphoma (55%), Gray-Zone Lymphoma (0%), and T-Cell Lymphoblastic Lymphoma (0%). Possible reasons for

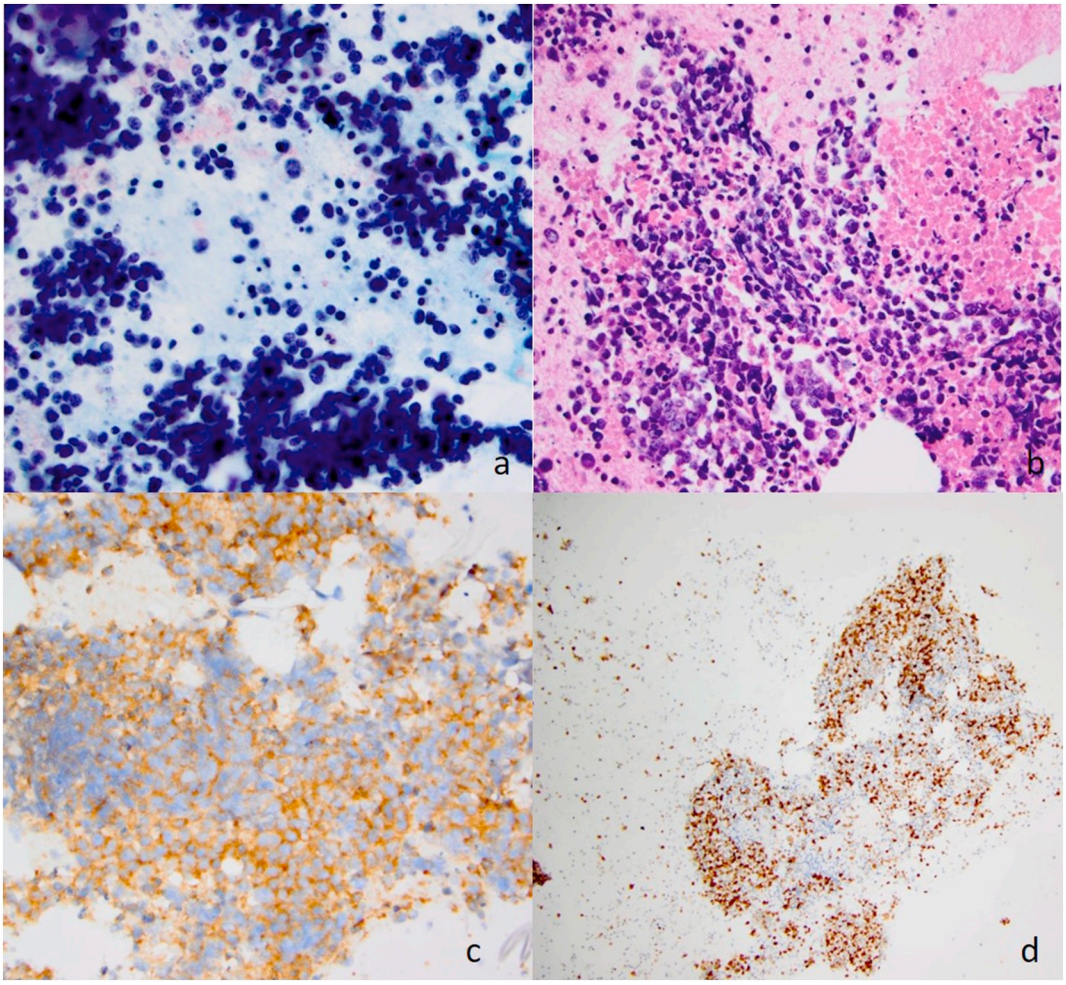

Fig. 2. These images are of a small cell carcinoma. Fig. 2a is a small cell carcinoma stained with Diff-Quik (40×). Fig. 2b shows the cell block of the small cell carcinoma stained with hematoxylin and eosin (20×). Fig. 2c shows that the small cell carcinoma is positive for the immunohistochemical stain Synaptophysin (20×). Fig. 2d shows that the small cell carcinoma has an elevated Ki67 index (10×).

this discrepancy include differences in techniques used to obtain the biopsies and differences in diagnostic interpretation.

Our investigation determined that overall FNAC is a fairly sensitivity (78%) and very specific (98%) procedure for mediastinal masses. Furthermore, the sensitivity of FNAC in the categories with the most cases, lymphoma (25% of cases), metastatic carcinoma (19% of cases), and thymoma (19% of cases), was higher than the overall sensitivity; the sensitivity was 84% for lymphoma, 93% for metastatic carcinoma, and 87% for thymoma.

The majority of cases in this study were either located in the anterosuperior mediastinum (49/77) or the mediastinum, NOS (24/77) and the minority were located in the posterior mediastinum (3/77) and middle mediastinum (1/77). The sensitivities of the anterosuperior mediastinum (80%) and the mediastinum, NOS (79%) were similar to the overall sensitivity (78%). It is difficult to draw conclusions about the sensitivity of FNAC in the posterior mediastinum and middle mediastinum because of the low number of cases in our study found in these locations.

The overall sensitivity in our study may have been underestimated because only cases with concurrent or subsequent surgical pathology were used in its calculation.

A number of the diagnostic categories in our study, such as cysts, soft tissue tumors, paraganglioma, germ cell tumors, thymic carcinoma, benign thymus, and benign thyroid, and locations, such as posterior mediastinum, contained only a small number of cases. This may be a contributing factor as to why they suffered from low sensitivity. If a study set contained more cases, then the sensitivity for some of these groups may improve.

The surgical pathology and FNAC discrepancies were predominantly due to inadequate diagnostic material. The discrepant cases of granuloma, thyomoma, carcinoma involving a lymph node, and thymic carcinoma were likely the result of sampling. The discrepant cases of Classic Hodgkin lymphoma, bronchogenic cyst, and thymic cyst were likely the result of these lesions containing only a scant amount of diagnostic cells. The diagnostic sensitivity of FNAC can be influenced by many factors, but it can be improved by techniques such as rapid on-site evaluation, radiographic guidance, ancillary tests, and sampling different parts of the mass [7-9]. In our study, all of the FNAC were performed using radiographic guidance and with the assistance of rapid on-site evaluation.

The minority of the surgical pathology and FNAC discrepancies, namely the paraganglioma and thymic hyperplasia, were most likely due to misinterpretation. One of these misinterpretations may have been avoided by noting the location of the tumor. Paragangliomas typically arise from the para-aortic (middle mediastinum) or para-vertebral (posterior mediastinum) sympathetic chain ganglia and germ cell tumors typically occur in the anterior mediastinum [10-12].

It should be noted that 34/107 (32%) of the masses undergoing

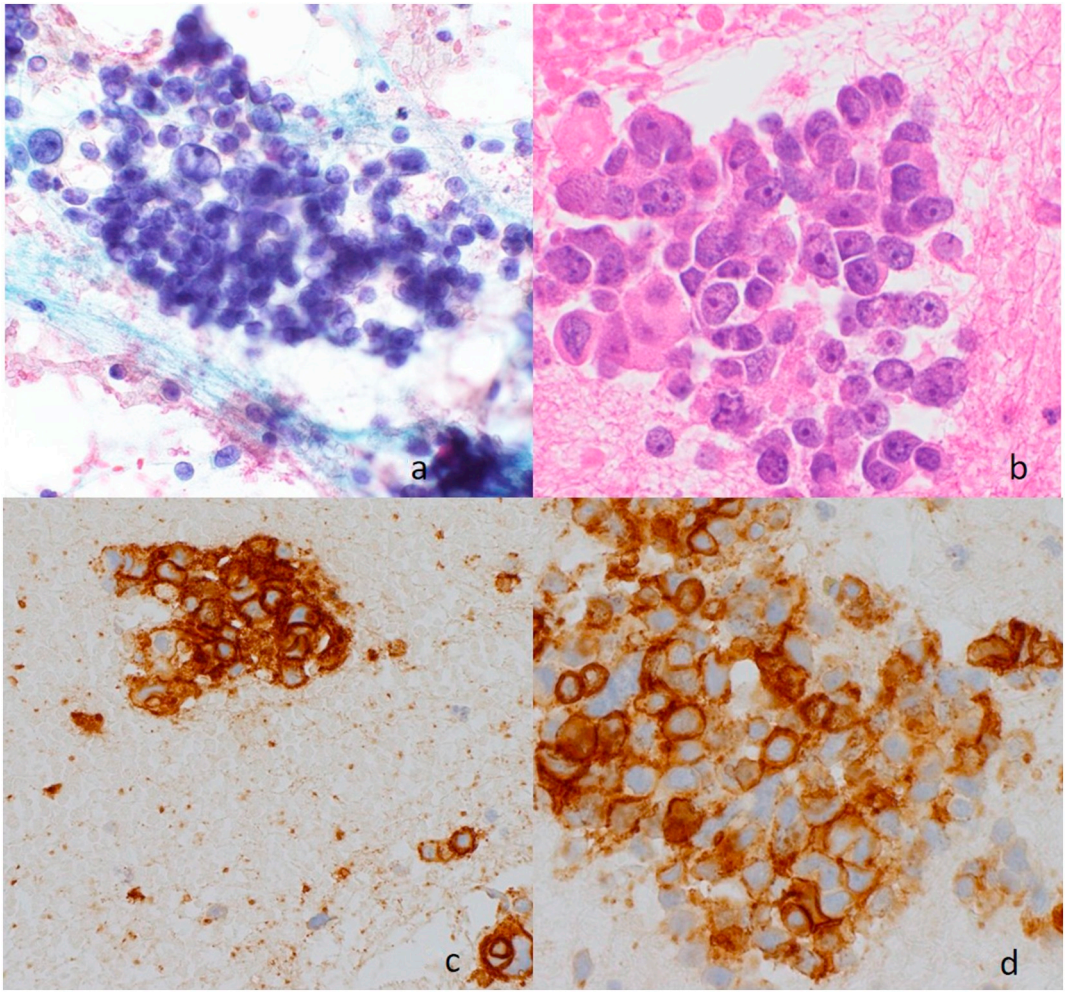

Fig. 3. These images are of a thymic carcinoma. Fig. 3a is a thymic carcinoma stained with Papanicolaou stain (40×). Fig. 3b shows the cell block of the thymic carcinoma stained with hematoxylin and eosin (40×). Fig. 3c shows that the thymic carcinoma is positive for the immunohistochemical stain CD5 (40×). Fig. 3d shows that the thymic carcinoma is positive for the immunohistochemical stain CD117 (40×).

Table 1
Number of cases with fine needle aspiration cytology (FNAC) and surgical pathology.

Category	FNAC	Surgical pathology
Infectious/Inflammatory	7	6
Metastatic carcinoma	24	15
Lymphoma	20	19
Cyst	6	4
Soft tissue tumor	5	3
Paraganglioma	2	2
Germ cell tumor	2	2
Thymoma	20	15
Thymic carcinoma	6	5
Benign thymus	2	1
Indeterminate	12	5
Benign thyroid	1	0
Overall	107	77

FNAC were simply designated as occurring only in the mediastinum without a more precise location. As demonstrated above, in the mediastinum it is important to know the exact location of a lesion because the differential diagnosis depends on this information. Therefore, it would be prudent to identify the exact location of a mediastinal mass before rendering a diagnosis.

Table 2
Sensitivity and specificity: For each diagnostic category and overall.

Diagnostic category	Sensitivity	Specificity	Total number of cases
Infectious/Inflammatory	33%	99%	6
Metastatic carcinoma	93%	100%	15
Lymphoma	84%	97%	19
Cyst	25%	100%	4
Soft tissue tumor	100%	100%	3
Paraganglioma	50%	100%	2
Germ cell tumor	100%	99%	2
Thymoma	87%	94%	15
Thymic carcinoma	60%	100%	5
Benign thymus	0%	100%	1
Indeterminate	100%	90%	5
Overall	78%	98%	77

In conclusion, FNAC is a relatively non-invasive technique that can yield a rich amount of information through smears, thin-layer liquid-based preparations, cytospins, and other preparations as well as through ancillary techniques such as immunohistochemistry, flow cytometry, and molecular assays. Our study shows that mediastinal FNAC is both fairly sensitive and very specific and is a valuable technique in the diagnosis of mediastinal masses.

Table 3
Surgical pathology vs fine needle aspiration cytology (FNAC) discrepancies.

Surgical pathology diagnosis	FNAC diagnosis
Granuloma	Atypical lymphocytes
Granuloma	Lymph node
Granuloma	Bronchial cells and cartilage
Granuloma with acid fast Bacilli	Lymph node
Thymoma, type AB	Atypical lymphocytes
Thymoma, type B2	Nondiagnostic
Non-small cell lung carcinoma involving left level 4 lymph node	Reactive lymph node
Classic Hodgkin lymphoma	Favor thymoma
Classic Hodgkin lymphoma	Favor thymoma
Classic Hodgkin lymphoma	No lymphoma or thymoma
Bronchogenic cyst	Nondiagnostic
Bronchogenic cyst	Degenerated material
Thymic cyst	Nonspecific, proteinaceous material and cartilage
Thymic Carcinoma, focal squamous cell carcinoma with thymoma	Favor thymoma with spindle cell features
Thymic Carcinoma, Not otherwise specified	Favor thymoma
Paraganglioma	Germ cell tumor, favor dysgerminoma
Thymic hyperplasia	Low grade neuroendocrine neoplasm

Table 4
Sensitivity and specificity: for each location within the mediastinum and overall.

	Sensitivity	Specificity	Total number of cases
Anterosuperior	80%	98%	49
Posterior	33%	95%	3
Middle	100%	100%	1
Mediastinum, Not otherwise specified	79%	99%	24
Overall	78%	98%	77

Declarations of interest

None.

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