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TRANSTHORACIC FINE-NEEDLE ASPIRATION BIOPSY CYTOLOGY OF PULMONARY LESIONS

Vural Gürcan, M.D.

Assist. Prof., Cytopathologist and Pathologist, Okan University Hospital Pathology Department and Sitonet Cytopathology Center, Şişli, İstanbul, Turkey

İmamoğlu Tamer, M.D.

Assist. Prof., Pathologist, Beykent University Pathology Department, İstanbul.

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ABSTRACT

The transthoracic fine-needle aspiration (TFNA) biopsy specimens from 147 cases were reviewed. The material was inadequate in 15 of them. Benign diagnoses were given in 31 cases. In the remaining 101 cases, malignant cells were found. Among the malignant cases, 42 were primary and 35 were metastatic tumors. There were 21 malignant cases of unknown origin. Of 3 cases interpreted as “suspicious”, 2 proved to be malignant on follow-up. There were no false-positive diagnoses of malignancy and only 4 false-negative results by sampling error.

An error in typing of the neoplasm occured in 4 cases. However, the distinction between small-cell carcinoma and non-small-cell carcinoma was accurate in 8/9 cases.

For the diagnosis of cancer, TFNA cytology had a specificity of 100% and a sensitivity of 86,6. TFNA cytology is a rapid and reliable method to obtain a microscopic diagnosis.

Keywords: Transthoracic FNAB; Cytology; Lung carcinoma; Thorax; Mediastinum

INTRODUCTION

Lung carcinoma is the most frequent visceral malignancy in males; also in women it has increased to become a major cause of death.[1] It is important to clinically to establish a definite diagnosis and, if possible, to type the lung carcinoma prior to treatment.

As a complement to exfoliative cytology from the airways (sputum, bronchial washings and brushings), transthoracic FNAB offers another method for diagnosing lung tumors. This method is particularly applicable for peripheral tumors of the lung, where exfoliative cytology often is not representative. [2,3]

Cytologic sampling from the lung tumors used at the Memorial Hospital for Cancer and Allied Diseases, New York, in the 1930s.[4-5] It was not broadly accepted, however, until after the monograph by Dahlgren and Nordenström,[6] and after publication of Söderström’s [7] results in 1966.

Since then it has been shown in several studies that transthoracic FNA cytology is a rapid and accurate diagnostic tool in the hands of an experienced cytopathologist.[2,8-10]

In this article we have reviewed a 12 years material of insend TFNA biopsies to Sitonet Cytopathology Center, from differant hospitals and radiology centers in Istanbul in order to highlight pitfalls and sources of false cytologic diagnoses.

MATERIAL and METHOD

During the period from January 2008 till the end of December 2019, the Sitonet Cytopathology Center received transthoracic fine-needle aspirates from 147 patients who had x-ray evidence of suspicious pulmonary infiltrate. Of these 147 patients, 43 had been treated for a primary malignant tumor in another organ than the lung. The remaining 104 patients had no history of a previous malignancy in

any organ. In 4 cases the aspirations were performed under biplanar fluoroscopic guidance. In 12 cases aspirations were performed with guidance of ultrasonography and in 131 cases with guidance of computerized axial tomography. The tumors were visualized by a radiologist and aspirations were done in close cooperation with a qualified cytopathologist. Aspirates were obtained using a 21gauge needle attached to a 20 ml syringe in a Cameco handle. One or two air-dried slides were stained at once with Diff-Quick for immediate microscopic evaluation of the representitivity of the material. If the cellular material was not adequate, a new aspiration was peformed. The smears were either air-dried or fixed in 95% ethanol. The air dried smears were stained according to May-Grünvald-Giemsa and ethanol fixed smears according to Papanicolaou method. Material for cell block was also collected for immunohistologic staining. The number of slides in each case was between 4 and 15. The stained cellular material was evaluated and classified by a senior cytopathologist. TTF-1, CK7,CK20, Chromogranin, P40 and P63 immunostaining was performed regularly to the cases which was obtained sufficient cell block.

Based on the final cytologic diagnosis, all cases were classified into one of four diagnostic categories:

a) Consistent with malignancy.
b) Atypical or suspicious of malignancy.
c) Cells consistent with benign lesion.
d) Non-diagnostic, inadequate for any cytologic diagnosis.

Cytology slides, histologic sections and clinical files of all cases which showed discrepancy were reevaluated by the authors.

RESULTS

In the twelf year period, there were 251 aspiration biopsy cytology samples, including transbronchial and bronchoscopic biopsy cytology, submitted to our laboratory from local hospitals. In all 147 cases: 101 malignant tumors, 31 benign lesions or nontumorous lesions and 15 cases with inadequate aspirations. There were 94 males and 53 females with an average age of 63,5 years (males 65,7 years, females 60.8 years).

Cytopathologic diagnoses are listed below.

Group A:

Among 147 cases, a definite cytologic diagnosis of malignancy was given in 98 (66,6%) cases. In this group, we have found 42 primary lung carcinomas. The cytologic typing of these primary lung carcinomas is shown in Table 1. Of the 147 patients, 43 had a previously known primary malignant lesion in another organ than the lung. Of these 43 cases, TFNA cytology revealed malignant cells consistent with a metastatic tumor in 36 cases. The metastatic tumors are summarized in Table 2.

Table 1. TFNA Diagnosis of 147 lung lesions.

Lesions	Number	Percent
Primary Lung Carcinoma		
Squamous Ca	13	8.0%
Adeno Ca (Figure 1)	12	8.2%
Small Cell Ca	8	5.4%
Undiff. Ca	9	6.1%
Secondary Lung Carcinoma	35	23.8%
Ca of unknown origin	21	14.3%
Suspicious of malignancy	3	2.1%
Benign	31	21.0%
Inadequate	15	10.3%

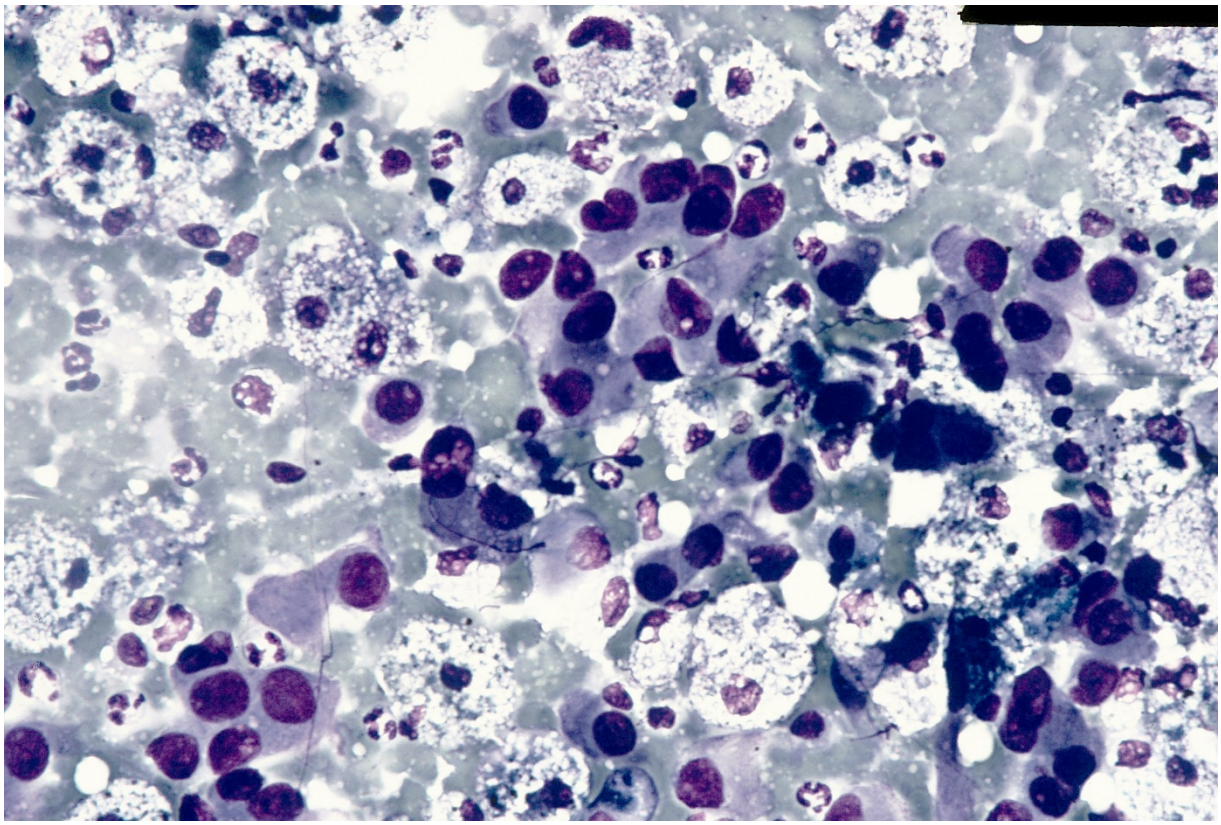

Figure 1. Adenocarcinoma of the lung, May-Grünvald-Giemsa stain, X40

The correlation between the preoperative TFNA cytology tumor diagnoses and the histopathologic diagnoses of surgical biopsies from the lung tumors and diagnoses other than histology (repeated cytology, clinical data) is shown in Table 3.

Table 2. TFNA Diagnosis of 36 Secondary Lung Tumors

Metastases from	Number	Percent
Adenocarcinom NOS	12	37.6%
Squamous ca	6	16.8%
Sarcoma NOS	2	5.6%
Breast ca	2	5.6%
Malignant Melanoma	2	5.6%
Urothelial ca	2	5.6%
Ovarial ca	2	5.6%
Mesothelioma	2	5.6%
Prostat ca	2	5.6%
Endometrial ca	1	2.8%
Undiff. ca	1	2.8%
Leiomyosarcoma (Figure 2)	1	2.8%
Lymphoma	1	2.8%
Total	36	99.8%

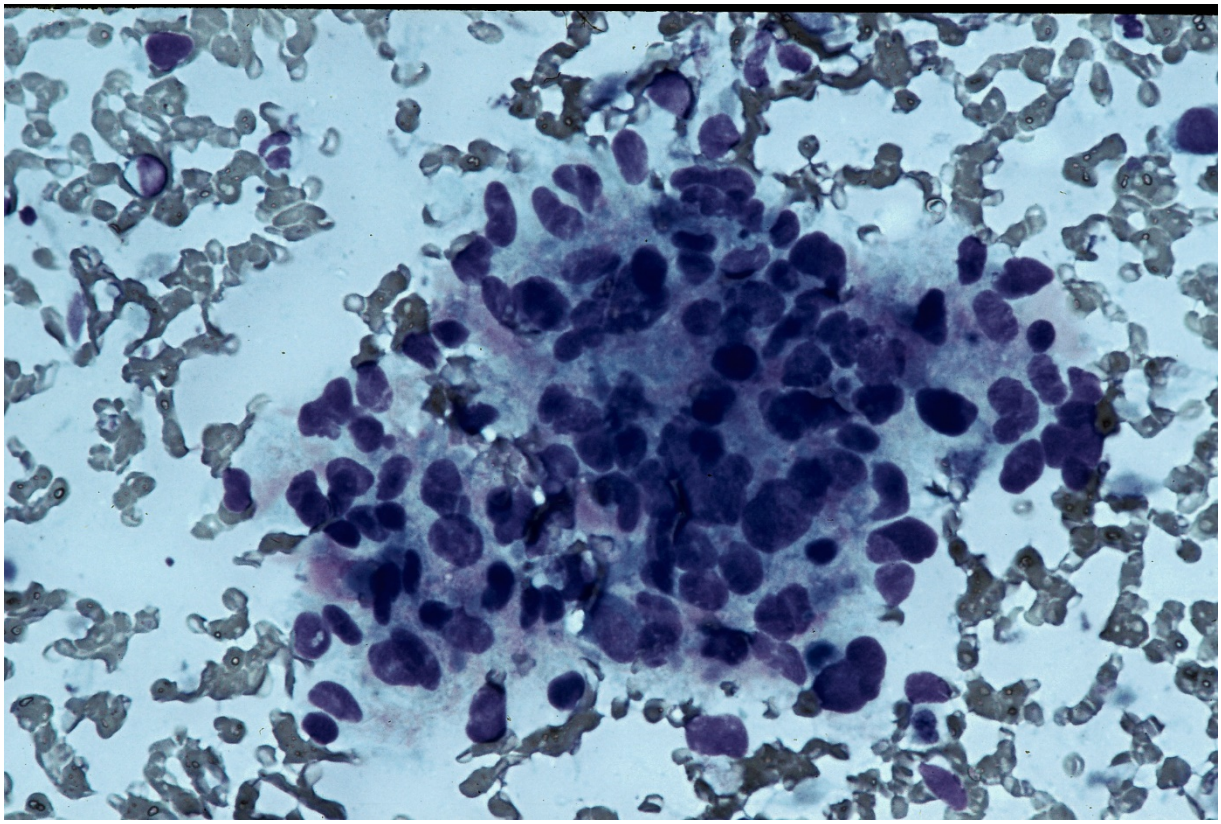

Figure 2. Lung metastasis of leiomyosarcoma of the uterus, May-Grünvald-Giemsa stain. X40

Group B:

Of the 147 cases studied, 3 cases were diagnosed as “suspicious of malignancy”. Of these 3 cases, one did not reveal malignant diagnoses by repeated cytologic examinations. In the remaning two cases, the following histopathologic diagnoses were given: squamous cell carcinoma and undifferentiated carcinoma.

Table 3. The correlation between TFNA diagnoses and histopathologic diagnoses or other follow-up in 65 cases.

Cytologic Diagnosis	Histopathologic Diagnosis			Other follow-up (Cytology, Clinic, Hospital Registrations)		
	true (+)	true (-)	false (-)	Malignant	Benign	Total
True (+) with right typing						
Primary Adeno Ca Squam.Ca Undiff.Ca Small cell	 4 4 3 3			 3 3 1 5		 7 7 4 8
Metastasis	8			9		17
Benign Cyt.		4			10	14
True (+) with rong typing	4					4
False (-)			4			4
Total	26	4	4	21	10	65

Group C:

There were 31 cases diagnosed as benign (Table 4), 13 of which revealed only normal lung cytology. Chronic inflammation was found in 9 patients. Hamartoma was diagnosed in one patient and Schwannoma in one patient.

In 7 patients open surgery was performed after TFNA cytology diagnosis. While the histopathologic diagnoses were consistent with cytology in 4 cases (two cases with normal lung parenchyme, one case with fibrosis and one case with granulomatous inflammation-tuberculosis), there were 3 discrepant cases summarrized in Table 5. One case was acellular (Group D), while the other ones were not representative of the lesion.

Table 4. Summary of 31 TFNA's with benign diagnoses and comparison of cytologic and histopathologic diagnoses in 7 cases.

Cytologic Diagnosis	No	Histopathologic diagnosis
Benign lung cytology	13	--
Chronic inflammation	9	--
Hamartoma	1	--
Schwannoma	1	--
Benign lung cytology	2	Lung parenchyme, no atypia
Fibrosis	1	Fibrosis
Tuberculosis	1	Tuberculosis
False -negatives	3	Malignant tumor diagnoses (Table 5)
Total	31	

Group D:

In the study group, 15 cases were found inadequate for any cytologic diagnosis. The slides from these cases were extremely hypocellular and/or haemorrhagic. In this group, 4 patients had been treated for

a previous malignancy (one carcinoma case in each localization: uterine cervix, rectum, ovary; in addition, there was one case of lymphoma).

By later follow-up, lung malignancy was excluded in 10 patients. Follow-up was not satisfactory in the remaining 5 patients.

Table 5. Discrepancy between cytologic and histopathologic diagnoses in 3 cases.

Age	Sex	Cytologic Diagnosis	Histopathologic Diagnosis
69	M	Benign lung cytology	Squamous cell ca
51	M	Benign lung cytology	Adenocarcinoma metastasis
67	M	Inadequate	Adenocarcinoma

Table 6. Discrepancy of the tumor type in 3 cases

Cytological Diagnosis	Histopathological Diagnosis
Squamous cell carcinoma	Metastasis of adenocarcinoma
Small cell carcinoma	Adenocarcinoma
Undifferentiated carcinoma	Squamous cell carcinoma

DISCUSSION

TFNA biopsy cytology has been increasingly used in the last 25 years.[2,10-15,19,22,23,25-32] This biopsy method is usually undertaken for peripheral lung lesions where bronchoscopy, bronchial washings and brushings, and sputum cytology are not able to prove or disprove malignancy. The main advantages of TFNA, compared to other biopsy methods, are to avoid i) a major trauma to the patient (this is very important in the case of a patient with a poor respiratory function and/or a patient with an advanced disease), ii) thoracotomy in the case of benign disorders, iii) the expense of thoracotomy or open lung biopsy.

On the other hand, high specificity is a necessity because this technique is usually applied when other diagnostic methods fail or are unsuitable .[11] There was no false positive diagnosis of malignancy in this series. The occasional false positive diagnoses from literature are: pleural fibroma [12], chondroid hamartoma [13], lipoma, inflammatory lesions and lesions associated with alveolar cell hyperplasia. [14-16]

The number of histopathologically confirmed cases in this study was 30. There were additionally 31 cases with clinical follow-up and a repeated confirmatory cytologic sample. The reason for the relatively small number of histologic biopsies was that most of the patients with malignancy diagnosis were treated either by radiotherapy and/or chemotherapy or died before any histologic confirmation.

In this series, we found a good correlation between the cytologic and histologic typing of the pulmonary tumors. Among 26 cases positive for malignancy, there was an error in typing of the neoplasms by TFNA cytology in 3 (11,5%) cases. Discrepancies usually occured with poorly differentiated carcinomas and we have noticed two erroneously given undifferentiated carcinoma diagnoses (Table 6). This is similar to the observation of Sprun and co-workers. [17]

Even where the error rate for typing the neoplasm is relatively high, the distinction between small cell carcinoma and non-small cell lung carcinoma was accurate in all cases except one (8/9 cases of small lung carcinoma). This is clinically the most important information, since the therapy of small cell lung carcinoma is primarily not surgical.

Recently, because of the heterogeneous phenotype of the lung cancer and several different classifications, the clinical utility of classifying lung cancer has been questioned.[18] Lung carcinoma can exhibit multidirectional differentiation (f.ex. adenosquamous carcinoma, subtypes of small cell

carcinoma), including the neuroendocrine type. Immunohistochemistry and/or electron microscopy can be helpful to differentiate multidirectional and neuroendocrine differentiation.[19]

In several TFNA studies authors have reported rather high specificities of 97% to 100%.[19-22] This series showed the specificity of 100% as the previous study from by Crosby and co-workers.[23] The sensitivity of TFNA cytology was 86,6% in this series. The false negativity rate was due to failure to obtain diagnostic samples.

TFNA biopsy requires a good technique and a skillful and experienced aspirator. Close co-operation between the cytopathologist and the radiologist is valuable to minimize the number of inadequate samples.

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