Subclassification of Bronchogenic Carcinomas on Transbronchial and Transbronchial Fine-Needle Aspiration Cytopathology of Lung Tumors; A Retrospective Study of 227 Cases with Cyto-Histopathological Correlation

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INTRODUCTION

Cytopathological subtyping of not only small cell lung cancer (SCLC) but also non-small cell lung cancer (NSCLC) has an increasing clinical relevance due to the diverging differences in medical treatment between squamous and nonsquamous tumors (Nizzoli et al). In the past, management protocols did not require the histologic distinction of NSCLCs. However, recently, changes in the therapeutic modalities (e.g., targeted therapy with EGFR inhibitor) have increased the demand for subclassification of NSCLCs (e.g., adenosquamous) as well as biopsy specimens (Toschi et al).

In 1986, Maneth et al was the first to diagnose lung carcinoma by fine needle aspiration (FNA) Cytology tomography (CT) guidance for FNA is preferred for small lesions that are not well delineated in fluoroscopy, hilar and mediastinal masses, thoracic inlet lesions, parotid masses which are juxtaparotid in location, and in superior vena cava syndrome (Arslan et al). The aim of this study was to evaluate the diagnostic accuracy of transbronchial (TTFNA) and transbronchial (TBFNA) FNA and bronchial lavage (BL)/materials in establishing the specific cell type in primary lung cancer.

MATERIAL-METHODS

To examine the performance of our pulmonary cytopathology practice, a retrospective analysis of data from 227 cases who received a paracardial or subsequent histodiagnostic diagnosis on endoscopic-transbronchial biopsy (ETBX) or resection within the last 3 years (2008-2010) was carried out. TTFNA was performed by 22-gauge needle with the preextraction/prebiopsy cases were categorized according to the primary cytopathologic diagnosis (righ malignancy cells, suspicious for malignancy cells, negative malignancy diagnosis) and the precise classification of the neoplasm (e.g., adenocarcinoma) when given. The positive (malignant) cases did not include those that were diagnosed as “atypical cells”. The positive-malignant cases that did not receive a precise classification had been given a general diagnosis such as NSCLC-NOS.

Cytopathological interpretations were made by the same author (SÖ) without knowing ETEB results. Immunocytochemistry were not used for cytopathological subtyping on cytologic materials.

For each procedure, the frequency of positive (malignant) diagnosis was determined and correlated with the ETEB/resection diagnosis, and the histodiagnostic procedures were considered the gold-standard.

Metastatic carcinomas and uncommon NSCLCs such as salivary gland type carcinomas were excluded from the statistical analysis. The sensitivity, specificity, accuracy, negative and positive predictive values of CT-guided TTFNA, TBFNA and BL were calculated for all 227 lesions. Statistical analyses were performed using the Chi square test.

RESULTS

Over the study period, 1182 TTFNAC and TBFNAC and 662 BL only cytologic samples were obtained from patients with suspicious intrathoracic lesions. The present study included 227 patients (162 females 159 males; age mean 62.4 years(range 3-84); underwent ETBx/Resection.

The overall sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of TTFNA, TBFNA and BL are illustrated on Table 1. Among the 227 patients, cytopathological diagnoses of primary NSCLCs(67 on TTFNA and 53 on TBFNA/BL) and 11 SCLCs on TBFNA/BL was obtained. The PPV of TTFNA-TBFNA in subtyping NSCLC was much higher for adenosquamous(TFBNA, 87.5%) than ADC(46.9% and SCCs(60%)). The diagnostic yield also differs in terms of different cytologic material. The PPVs of TTFNA for ADC and SCC were 96.7% and 63.3%, and those of TBFNA were 60%, 25%, respectively.

BSs were less effective; but they occasionally contributed a positive (malignant) diagnosis in cases that fell short by ETEB.

<table>
<thead>
<tr>
<th>Cytologic material</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTFNA</td>
<td>100%</td>
<td>75%</td>
<td>97.3%</td>
<td>97.1%</td>
<td>100%</td>
</tr>
<tr>
<td>TBFNA</td>
<td>90.2%</td>
<td>50%</td>
<td>75%</td>
<td>88.9%</td>
<td>33.3%</td>
</tr>
<tr>
<td>BL</td>
<td>55.9%</td>
<td>94.7%</td>
<td>68.8%</td>
<td>95%</td>
<td>54.5%</td>
</tr>
<tr>
<td>Overall</td>
<td>81.6%</td>
<td>81.1%</td>
<td>81.5%</td>
<td>94.7%</td>
<td>51.8%</td>
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DISCUSSION

Transbronchic (TTFNA) and transbronchial (TBFNA) FNA are invasive procedures and should therefore be subject to regular review.

The diagnostic sensitivity of TTFNA for malignant lesions has been reported to range from 76% to 97%. The usefulness of this procedure has been limited by its relatively low yield for specific bronchogenic disorders. It has been suggested that TTFNA should be supported by other diagnostic methods because TTFNA has false negative results and inadequate samples. The most common cause of inadequate results are extensive tumor necrosis, inappropriate biopsy, and inadequate sampling (Arslan et al). The rate of inadequate sampling was 15.9% in our series. These were no false positives for malignancy in the present series.

Despite the best efforts, the lesionous or the most representative area of the neoplasm may not be obtained in some cases due to sampling issues. Even when the tumor is sampled, poor tumor differentiation or insufficient characteristic features in the tumor sample may result in the diagnosis of malignancy without a specific histologic designation (Toschi et al).

Transbronchial needle aspiration (TBFNA) was initially started in 1949 by Schieppati. After its adaptation to the flexible bronchoscope in 1978 by Holt et al, this technique has given first indications in the diagnosis and staging of lung cancer, in peripheral pulmonary nodules and masses; in the evaluation of endobronchial masses; in the diagnosis of submucous, benign diseases, i.e., sarcoidosis and mediastinal cysts and abscesses (Ganitho et al).

TBFNA has been proven to be accurate in staging lung cancers, identifying inoperable carcinomas, and diagnosing a variety of lung diseases (Dasgupta et al).

Sensitivity analysis confirmed that the sensitivity of TBFNA depends critically on the prevalence of mediastinal metastasis. In populations with a lower prevalence of mediastinal metastasis, the sensitivity of TBFNA is much lower than reported in recent lung cancer guidelines (Holt et al).

Improvements in the diagnostic yield of TBFNA aspirates, and increasing knowledge of predictors of a positive aspirate, has reduced the need for mediastinoscopy, and occasionally thoracotomy, with benefits in terms of reduced healthcare costs and improved patient welfare (Rajamani et al).

Cytopathologists who examine TBFNA cytology specimens understand this procedure, its limitations, and ways that it may be optimized (Coppiello et al).

CONCLUSIONS

TTFNA and TBFNA continues to be effective tools in our cytopathology practices assessing lung lesions with good performance for subtyping NSCLC. In poorly differentiated and doubtful cases, the use of ancillary techniques, such as immunocytochemistry, as we have recently applying when needed, may be applied to improve the diagnostic yield.

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REFERENCES


Figure 1: Well differentiated squamous cell carcinomas: Diffuse sheet with oval to most squamous cell carcinoma (H&E, ×400).

Figure 2: Poorly differentiated squamous cell carcinomas: cytodiagnostic as nodose, cohesive mass of cells with a clear cytoplasmic border and pleomorphic nuclei (Papanicolaou stain, ×400).

Figure 3: Hippel-Lenard section of the same case (H&E, ×200).

Figure 4: Adenosquamous cell carcinoma: Neoplastic cells with excentrically placed nuclei and presence large mucous vacuoles (H&E, ×400).

Figure 5: Adenosquamous carcinoma of the MAC subtype: Crowded sheets of the tumor cells with intracellular and extracellular present present in one (H&E, ×400).

Figure 6: Adenosquamous, Epithelial (all along with akan plasmic arrangement (H&E, ×400).

Figure 7: Poorly differentiated adenosquamous: Pisschomag granulertumor cell with excentrically placed nuclei (H&E, ×400).

Table 1: The sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of MAC, TBFNA, and BL, respectively.