

Is the cytologic confirmation of malignancy sufficient for decision making in treatment of patients with non-small cell lung cancer?

Malignite varlığının sitolojik doğrulanması küçük hücreli dışı akciğer kanserli hastaların tedavisine karar vermede yeterli midir?

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We read with interest the paper by Cömert et al.^[1] which was designed to compare the sensitivity, specificity, and diagnostic accuracy of positron emission tomography-computed tomography (PET-CT) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the diagnosis of malignant mediastinal/hilar lymph nodes (LNs). We congratulate them on their good results with the sensitivity, specificity, and diagnostic accuracy along with their negative and a positive predictive values of EBUS-TBNA (94.3%, 100%, 95.8%, 85.9%, and 100% respectively).

They reported that 96 of the 102 lung cancer patients had non-small-cell lung carcinoma (NSCLC) and the frequency of mediastinal lymph node (LN) metastasis (N₂ and N₃) was detected at a rate of 79% in both adenocarcinoma and squamous cell cancer and 69.6% in NSCLC, for which subtypes can not be determined. However, we did not find any information about the specific type of NSCLC that was established by the EBUS. If this procedure was used as a diagnostic tool for advanced staged patients (stage 4), the authors should have made a distinction between the cases of adenocarcinoma and squamous cell carcinoma. This is important when we are choosing chemotherapeutic agents because adenocarcinoma histology has improved outcomes with pemetrexed therapy and squamous histology can be accompanied by a life-threatening hemorrhage with bevacizumab

therapy. In addition, adenocarcinoma histology and nonspecified NSCLC should be tested for epidermal growth factor receptor (EGFR) mutations. When these are present, patients have responded well to tyrosine kinase inhibitors. Moreover, cytology alone is usually not sufficient for identifying these mutations.^[2] A mediastinoscopy may be the best diagnostic method for patients with EGFR mutations since it provides a sufficient sample if the location of the LNs is accessible.

These diagnostic tools should aid in the choice of treatment for N₂ positive NSCLC patients because of the extremely heterogeneous diseases which may be encountered, such as occult metastasis in one LN or bulky metastasis in multiple LNs. In fact, multiple- or single-level LN metastasis is one of the major prognostic factors for these particular patients. Therefore, systematic LN sampling and on-site evaluation of needle aspirates by a cytopathologist are very important for determining the proper course of treatment for those with N₂ positive NSCLC. We believe that specimen cross-contamination is inevitable when the sampling of N₂ nodes takes place after the N₃ nodes. When we consider that skip metastasis is not rare in patients with NSCLC, it is easy to see how patients with single LN metastasis could be misdiagnosed as having multiple LN metastasis, which would cause a change in treatment strategies and a misestimation of the prognosis.

Lastly, we should not use the terms “less invasive” or “more invasive” when discussing EBUS, mediastinoscopies and video-assisted thoracic surgery (VATS). The European Society of Thoracic Surgeons (ESTS) guidelines for preoperative LN staging for NSCLC recommended that the invasive staging techniques be divided into invasive surgical technique and invasive non-surgical technique subgroups.^[3]

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Author's Reply

Dear Editor,

We would like to thank our readers for showing interest in our article and expressing their views on this topic.^[1] As you mentioned, endobronchial ultrasound (EBUS) was used as a diagnostic tool for advanced stage non-small-cell lung cancer (NSCLC) patients (stage 4), but it was not possible to discriminate between adenocarcinoma and squamous cell carcinoma in all of our cases. However, according to our observations, as the pathology department gains more experience regarding the cytopathology of subtypes of lung cancer, the results should improve. Esterbrook et al.^[2] reported that EBUS-transbronchial needle aspiration (TBNA) samples, made into cell blocks and subjected to a panel of immunohistochemical stains, returned adequate tissue for cytological analysis in over 97% of cases. They also determined that cytology specimens are adequate for epidermal growth factor receptor (EGFR) mutation testing in over 88% of cases.^[2] Navani et al.^[3] also reported in a large, multicenter study that cytology samples obtained from EBUS-TBNA in routine practice are suitable for the subtyping of NSCLC and EGFR mutation analysis and that the use of immunohistochemistry reduces the rate of NSCLC that is otherwise not specified.

Since we do not have on-site pathology, we sample all of the lymph nodes (LNs) for staging one by one systematically; hence, we do not stop the sampling when we find metastatic LNs. Cross-contamination may only be important in patients with single station N₂ metastasis. To avoid cross-contamination of LNs suspected of this type of metastasis, a new needle could be used, but this would be very expensive.

In addition, EBUS and endoscopic ultrasound are mentioned as being “minimally invasive” nonsurgical techniques in the European Society of Thoracic Surgeons (ESTS) guidelines for preoperative LN staging for NSCLC.^[4]

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