
The impact of ultrasonography-guided fine needle aspiration of no palpable supraclavicular lymph nodes on diagnosis and staging in advanced lung cancer

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ÖZET

İleri evre akciğer kanserinde palpe edilemeyen supraklaviküler lenf nodlarının ultrasonografi eşliğinde iğne aspirasyonunun tanı ve evrelemeye etkisi

Acığer kanserinin doğru tanı ve evrelemesi hastalığın prognozunu etkilemede ve uygun küratif veya palyatif tedavinin seçiminde esas rolü oynamaktadır. Bu amaçla çeşitli invaziv ve noninvaziv teknikler uygulanmaktadır. Bu çalışmada, bilgisayarlı tomografide mediastinal lenf nodu olan akciğer kanserli hastalarda palpe edilemeyen supraklaviküler lenf nodlarının sıklığını ve ultrasonografi eşliğinde iğne aspirasyonunun tanı ve evrelemeye etkisini araştırmak amaçlanmıştır. Bu çalışmada, palpe edilen supraklaviküler lenf nodu bulunmayan ve bilgisayarlı tomografide en az 2 istasyonda genişlemiş lenf nodu bulunan akciğer kanserli hastalara supraklaviküler ultrasonografi uygulandı. Supraklaviküler lenf nodu bulunması halinde ultrasonografi eşliğinde ince iğne aspirasyonu yapıldı. Çalışmaya alınan 40 hastanın 16 (%40)'sında ultrasonografi eşliğinde ince iğne aspirasyonu ile supraklaviküler lenf nodu metastazı sitolojik olarak gösterildi. Bilgisayarlı tomografide üst paratrakeal lenfadenomegali varlığı supraklaviküler metastazlı grupta anlamlı olarak yüksek bulundu. Uzak metastaz varlığı, hücre tipi ve evre yönünden supraklaviküler metastazlı grup ile supraklaviküler metastaz bulunmayan grup arasında istatistiksel fark bulunmadı. Üç hastada ultrasonografi eşliğinde ince iğne aspirasyonu tek tanı yöntemi idi. Patolojik boyutta mediastinal lenf nodu olan akciğer kanserli hastaların üçte birinden daha fazlasında supraklaviküler lenf nodu metastazı tespit edildi. Ultrasonografi eşliğinde ince iğne aspirasyonu, mediastinal lenf nodu olan akciğer kanserli hastalarda basit, güvenli, standart tanı yöntemlerine göre daha az invaziv prosedür olarak görülmüştür.

Anahtar Kelimeler: Acığer kanseri, supraklaviküler lenf nodu, ince iğne aspirasyonu, evreleme.

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SUMMARY***The impact of ultrasonography-guided fine needle aspiration of no palpable supraclavicular lymph nodes on diagnosis and staging in advanced lung cancer***Gülcihan ÖZKAN¹, Mehmet TUTAR², Mehmet BAYRAM¹, Dilek BAKAN¹, Aygün GÜR¹, Güngör ÇAMSARI¹¹ Clinic of Chest Diseases, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, Istanbul, Turkey,² Clinic of Radiology, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, Istanbul, Turkey.

Diagnosis and accurate staging of lung cancer is essential for selection of appropriate curative or palliative therapy and affects patient prognosis. Both invasive and non-invasive procedures are used for this purpose. We aimed to assess the frequency of no palpable supraclavicular lymph node metastases in lung cancer patients with enlarged mediastinal lymph nodes, and their impact on diagnosis and staging using ultrasound in this study. Lung cancer patients with no palpable supraclavicular lymph nodes and at least 2 enlarged mediastinal lymph nodes on computerized tomography underwent supraclavicular ultrasound examination. Ultrasound-guided fine needle aspiration (US-guided FNA) was performed when enlarged lymph nodes were present. Supraclavicular lymph node metastasis was confirmed cytologically via US-guided FNA in 16 (40%) of 40 patients. Upper paratracheal lymphadenomegaly was significantly higher in patients with supraclavicular metastases than in those without. No statistical significant differences were observed in the stage, cell types, and metastases of patients with or without supraclavicular metastases. In 3 patients US-guided FNA was used for diagnosis. More than one-third of lung cancer patients with enlarged mediastinal lymph nodes had supraclavicular lymph node metastases in present study. US-guided FNA is an easier, safer, and less invasive procedure than standard techniques used to diagnose lung cancer patients with enlarged mediastinal lymph nodes.

Key Words: Lung cancer, supraclavicular lymph node, fine needle aspiration, staging.

Lung cancer is the leading cause of cancer death for both men and women world-wide (1). In a recent study, 86.7% of lung cancer patients were in the advanced stage (2). Both invasive and non-invasive procedures are used for lung cancer diagnosis and staging. Although, thorax computerized tomography (CT) and positron emission tomography (PET) are non-invasive techniques used to detect lymph node involvement, histological sampling of lymph nodes is often required. Thus, invasive techniques like transbronchial needle aspiration (TBNA), needle aspiration by endobronchial ultrasound (EBUS), and mediastinoscopy are frequently used to take histological samples from lymph nodes (3). Since patients often have poor general condition or severe hypoxemia due to co-existing disease (COPD, heart failure, etc.) it may not be possible to use invasive procedures for diagnosis and staging in some of lung cancer patients.

In lung cancer TNM staging, supraclavicular lymph node involvement is indicative of N3 disease and the presence of stage IIIB lung cancer, and suggests inoperability (4-6). CT examination is less sensitive than ultrasonographic examination for the detection of no palpable supraclavicular lymph nodes, because the vascular structures are crowded in this region (7). Some ultrasound (US) studies have indicated that this technique can be used to examine lung cancer patients with no palpable cervical and supraclavicular adenopathy (8,9). Supraclavicular US is a sensitive and simple procedure for detecting supraclavicular lymph node involvement (10). Since the distance from the lymph node to the skin is < 3 cm, US-guided fine needle aspiration (US-guided FNA) of supraclavicular lymph nodes is both simple and safe (7). It provides information for both diagnosis and staging, helping clinicians to avoid many invasive procedures for lung cancer.

In this study, we evaluated the presence of supraclavicular lymph nodes by US and detect supraclavicular lymph node involvement by US-FNA in lung cancer patients with multiple enlarged mediastinal lymph nodes detected by thorax CT.

MATERIALS and METHODS

Between April 2004 and April 2005, consecutive patients with suspected lung cancer and at least 2 enlarged mediastinal lymph nodes on CT were enrolled in the study. All patients gave written informed consent. Patients were recruited from inpatient services and outpatient referrals from non-specialized physicians. The inclusion criteria for the patients were the presence of suspected lung cancer with no palpable supraclavicular lymph nodes, no prior diagnosis of malignancy, and the presence of lymph nodes ≥ 1 cm by thorax CT in at least 2 stations on mediastinum.

Patients with no palpable supraclavicular lymph nodes and at least 2 enlarged mediastinal lymph nodes detected by CT underwent SC US examination. The thorax CT images of all patients were evaluated by the same radiologist. US examination was made using a 5-7.5 MHz linear probe on a Shimadzu SDV-450 machine. Examination was limited to a B scan and no Doppler imaging was conducted. Transverse and sagittal images were obtained from the carotid bifurcation to the sternoclavicular area inferior and lateral to the acromioclavicular joint. The number and location of the enlarged lymph nodes, including whether they were ipsilateral, contralateral, or bilateral with respect to the dominant lung lesion and their short- and long-axis, transverse node dimensions were documented. Additional informed consent was obtained for FNA of the enlarged supraclavicular lymph node. If the short axis was > 5

mm, no echogenity was detected on the hilus of the lymph node, and the long axis/short axis ratio was < 2 , the lymph node was called pathological and FNA was performed. US-guided FNA procedures were performed by 2 pneumologists. The patients were placed in a supine position with their necks hyperextended. Enlarged nodes were aspirated with fine 20 gauge needles. Patients were divided in 2 groups: group I; patients with supraclavicular lymph node involvement and group II; patients without supraclavicular lymph node involvement.

The chi-square test was used for statistical analysis.

RESULTS

Clinical characteristics of the patients are shown in Table 1. Supraclavicular lymph nodes were detected in 18 (43%) of 42 patients by US (Figure 1). It was not technically possible to perform either US guided FNA or surgical biopsy in 2 patients because of the proximity of their lymph nodes to vascular structures. It's not able to know if these lymph nodes were involved or not. Thus, these 2 patients were excluded from the study. FNA was performed in 16 (40%) of 40 patients and supraclavicular lymph node involvement was confirmed cytologically in all patients. The FNA reported atypical cells in 2 cases, so it was performed again, after which malignant cells were confirmed. No complication due to FNA was observed. The mean short-axis dimension of the 16 malignant supraclavicular lymph nodes was 19 ± 6.1 mm (range, 10-30 mm). In 15 patients supraclavicular lymph node involvement was ipsilateral to the primary tumor and in one patient whose primary tumor was on the right upper lobe, supraclavicular lymph node involvement was

Table 1. Clinical characteristics of the patients.

	Supraclavicular metastasis (+)	Supraclavicular metastasis (-)
n	16	24
Age (mean)	56.1	58.3
NSCLC	15	17
SCLC	1	7
Presence of distant metastasis	6	4

NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer.

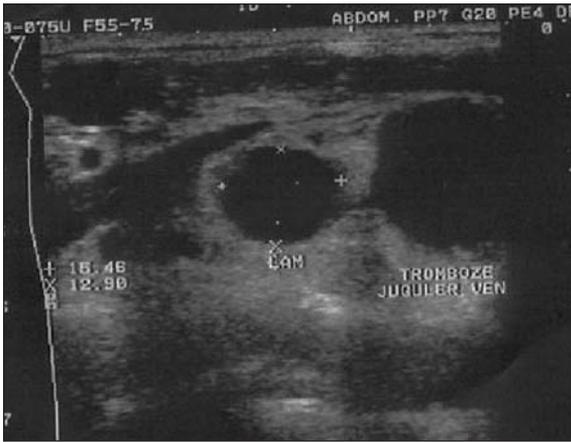


Figure 1. Pathologically enlarged lymphadenomegaly was seen by US examination of supraclavicular region.

shown on the left side. No statistical significant differences were observed in age, cell type, and presence of distant metastases between group I and group II ($p > 0.05$) (Table 2).

The presence of upper paratracheal (2R, 2L) lymphadenomegaly (LAM) was significantly higher in group I than group II ($p < 0.001$) (Table 3).

No statistical significant differences were observed between the groups in the regional count of mediastinal LAM. Two patients were upstaged

from IIIA to IIIB since they had positive FNA, so no further investigation was conducted for these patients (Table 2). In 2 patients, bronchoscopy and TTNA were non-diagnostic and in 1 patient for whom invasive diagnostic methods could not be performed because of severe hypoxemia, US-guided FNA was the unique diagnostic method.

DISCUSSION

Lymph node involvement is important for treatment and prognosis of lung cancer. Non-invasive techniques to detect cancerous involvement of lymph nodes rely on either lymph node size (CT) or metabolism (PET). While non-invasive tests can identify lymph nodes that are suspicious for cancer, they do not provide definitive tissue diagnosis, preventing the use of non-surgical treatment for inoperable patients. Thus, invasive tests, including TBNA, EBUS, TTNA, mediastinoscopy, and mediastinotomy are often required to make a further assessment of non-resectability (4). These are expensive invasive and often unavailable in some centers.

In lung cancer staging supraclavicular lymph node involvement refers to N3 disease, indicates the presence of IIIB lung cancer, and suggests that

Table 2. Outcome of patients with supraclavicular metastasis.

Patient	Diagnosis before FNA	Diagnosis of FNA	Clinical stage	Stage after FNA
1	NSCLC	Epidermoid carcinoma	T4N3M1	T4N3M1
2	NSCLC	Epidermoid carcinoma	T4N2M0	T4N3M0
3	Epidermoid carcinoma	Epidermoid carcinoma	T4N3M0	T4N3M0
4	SCLC	SCLC	T4N2M1	T4N3M1
5	No diagnosis	SCLC	T2N3M0	T2N3M0
6	NSCLC	NSCLC	T4N2M1	T4N3M1
7	Epidermoid carcinoma	Epidermoid carcinoma	T3N2M0	T3N3M0
8	NSCLC	Epidermoid carcinoma	T1N2M1	T1N3M1
9	NSCLC	Epidermoid carcinoma	T4N3M0	T4N3M0
10	Adenocarcinoma	Adenocarcinoma	T4N2M1	T4N3M1
11	Adenocarcinoma	NSCLC	T4N2M0	T4N3M0
12	Adenocarcinoma	Adenocarcinoma	T4N3M0	T4N3M0
13	No diagnosis	Epidermoid carcinoma	T2N2M0	T2N3M0
14	No diagnosis	Epidermoid carcinoma	T4N2M0	T4N3M0
15	NSCLC	NSCLC	T2N2M1	T2N3M1
16	NSCLC	NSCLC	T3N3M0	T3N3M0

NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer.

Table 3. Relation between upper paratracheal lymph node enlargement on CT and supraclavicular metastasis.

		SC metastasis (+) (%)	SC metastasis (-) (%)	Total	p
2R,2L	Present	14 (%93.3)	10 (%40)	24 (%60)	0.001
	Absent	1 (%6.7)	15 (%60)	16 (%40)	

the patient is inoperable. Supraclavicular lymph nodes were previously evaluated by palpation alone, such that patients with no palpable nodes in examination were thought to have no supraclavicular lymph node involvement. In the last 20 years, however, studies of patients with head and neck carcinomas, esophagus carcinomas, and malignant melanomas showed that palpation was not reliable enough to detect supraclavicular and neck lymph node involvement. The use of non-invasive imaging techniques like CT and US was recommended in place of palpation (7,11-14).

The sensitivity of palpation, CT, and neck US in detecting supraclavicular LAM was reported as 33%, 83%, and 100%, respectively (15).

The specificity and sensitivity of US-FNA is higher than 90% in patients with head and neck cancers (16). This procedure is minimally invasive and is thus applicable to all patients with suspected lung cancer. Gupta et al. determined that the sensitivity, specificity, and PPV of US-FNA were 92.7%, 98.5%, and 98.5%, respectively in 218 patients with palpable supraclavicular LAM (11). We did not confirm the FNA by surgical biopsy so it's not possible to specify the sensitivity, specificity and accuracy rates. We determined lymph node involvement in 16 of 18 patients who had pathologic lymph node in US examination. Patients in our study minimal metastatic lymph node size is 10 mm and mean size is 19 mm. So it's not seems to be very surprising that supraclavicular lymph node involvement was confirmed cytologically in all patients in our study. High diagnostic rate in this study is comparable with previous studies (11,16).

Some studies have shown a relationship between mediastinal LAM on CT and supraclavicular metastases in lung cancer patients. Overhagen et al. detected supraclavicular metastasis using the sa-

me procedure in 30 (26%) of 117 consecutive patients with lung cancer. They also reported that 28 (93%) of 30 patients with supraclavicular metastases have enlarged mediastinal lymph nodes on N2 and N3 stations on thorax CT. The presence of distant metastases was reported in 12 (40%) of 30 patients (15). In a similar study, Futz et al. investigated supraclavicular metastases by supraclavicular US and CT in patients with potentially operable lung cancer. They reported that 17 (31%) of 55 patients had supraclavicular metastases and concluded that there is a high frequency of supraclavicular metastases in patients with mediastinal adenopathy and distant metastases (17). In a recent study, Ohno et al. conducted supraclavicular lymph node biopsy and mediastinoscopy in 123 non-small cell lung cancer (NSCLC) patients with no evidence of distant metastasis or palpable supraclavicular lymph nodes and concluded that the frequency of supraclavicular metastasis is higher in patients with bulky N2 involvement (18). Kumaran et al. conducted supraclavicular US examination in lung cancer patients with enlarged mediastinal LAM by thorax CT. Strikingly, in 61 of 101 patients, supraclavicular LAM was detected by US examination and in 46 patients (45.5%) supraclavicular metastases were also proven histological. No invasive procedures were needed in 43 patients and 10 patients were upstaged from IIIA to IIIB (19). In another study focusing on supraclavicular US-guided FNA, Alan et al. reported that 2 (4%) of 50 potentially operable NSCLC patients were upstaged to IIIB. As a result of this upstaging saved them from unnecessary surgery (20).

US-guided FNA of supraclavicular lymph nodes is a simple and safe procedure that can usually be performed by a single operator (17,21). These nodes are nearly always superficial (most are less than 3 cm from the skin) at US. No complication in our study was compatible with literature (17,21).

In this report we assessed the frequency of no palpable supraclavicular lymph node involvement and its impact on diagnosis and staging using US in lung cancer patients who had enlarged mediastinal lymph nodes on thorax CT. We found a high incidence of supraclavicular lymph node metastases in patients with enlarged mediastinal lymph nodes on thorax CT in the 2R and 2L stations. Two of the patients were upstaged from IIIA to IIIB, requiring no further investigation.

Our study also illustrated that US-guided FNA was the unique diagnostic method in 3 patients whose cancer could not be diagnosed using any invasive procedures. In 2 of these patients bronchoscopy and TTNA were non-diagnostic and in the third patient no invasive diagnostic method could be performed due to COPD induced severe hypoxemia. These findings revealed that US-guided FNA is an effective diagnostic method in patients with advanced stage cancer and co-existing conditions like COPD.

US-guided FNA is a simple, safe, non-invasive procedure and is applicable in outpatients. So far no complications associated with US-guided FNA have been reported (7,15,20). Thus, US-guided FNA might be considered as an additional tool before other invasive diagnostic and staging procedures in suspected lung cancer patients with enlarged mediastinal lymph nodes (especially upper paratracheal) on thorax CT.

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