

RESEARCH COMMUNICATION

Radiological, Bronchoscopic and Histopathologic Characteristics of Patients with Primary Lung Cancer in Turkey (2006-2009)

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Abstract

Aim: The aim of this study was to evaluate the radiological, bronchoscopic and histopathological features of patients with primary lung cancer. **Materials and Methods:** 485 patients who were hospitalized in our clinic between July 2006 and December 2009 and diagnosed with lung cancer (LC) were evaluated. **Results:** The final diagnoses, established using various methods, were small cell LC for 62 patients, NSCLC of undetermined cell type for 191, epidermoid carcinoma for 148 patients, adenocarcinoma for 81 patients, and large cell LC for 3 patients. The mass was identified to be centrally located in 283 cases (58.3%) and peripherally in 202 cases (41.7%), and was found in the right lung in 51.5% of cases and mostly in the upper lobes bilaterally on radiological examination. The rate of hilar fullness, consolidation and atelectasis were higher in SCLC and epidermoid carcinoma with radiological examination. Diagnostic FOB (fiberoptic bronchoscopy) was performed in 466 of 485 patients. Endobronchial pathology was not obtained 140 patients. Endobronchial mass lesion, mucosal-submucosal lesions and signs of external pressure were observed in 152, 186 and 140 patients, respectively. Diagnostic material was obtained in 274 of 466 FOB examinations. A total of 211 patients underwent TTNA (transthoracic needle aspiration) and diagnosis was established in 204 cases. Pleural biopsy and/or fluid cytology were/was positive (+) for malignancy in 25 of the 47 cases with pleurisy. One patient, who could not be diagnosed by any of FOB or TTNA was diagnosed by pleural biopsy. Diagnostic results were obtained by thoracotomy in six patients who could not be diagnosed by other methods. 137 (28.2%) of 485 patients were considered to be operable. **Conclusion:** NSCLCs (especially epidermoid) account for the majority of lung cancers in Turkey, gender and smoking influencing the histopathology. TTNA and FOB are diagnostic procedures providing best results, and more than 2/3 of patients are inoperable at diagnosis.

Keywords: Lung cancer - radiology - bronchoscopy - histopathology - Turkey

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Introduction

Lung cancer is a disease of increasing incidence due to various factors including smoking, and is one of the major health problems in our country in recent years, as well as all over the world. There is a slight decrease in mortality rate among men, whereas the mortality rate among women continues to rise rapidly in association with increased consumption of cigarettes (Lillington, 2003). More than 90% of the patients are symptomatic at presentation and diagnosis is usually done during the last stages (Beckles et al., 2003). Epidemiologic data shows that the incidence is decreased for epidermoid carcinoma and is increased for adenocarcinoma over the years. Histological types varies over time due to many factors such as decreasing number of smokers, changes in the structure and consumption of the cigarettes, changes in the exposure to environmental carcinogens, and changes in histopathological diagnostic criteria with the technological advances for the diagnosis of lung cancer (Yurdakul et al., 2002; Yoshimi et al.,

2003; Santoz-Martinez et al., 2005). In the United States, it was reported that 172,500 of 1,372,910 new cancer cases will be cases of lung cancer, and the total number of expected deaths associated with lung cancer will be 163,510, including 90,490 men and 73,020 women (Jemal et al., 2005). In our country, according to the statistics of Cancer Control Department of the Ministry of Health in 1999, lung cancer among men takes the first place of all cancers with rate of 29.38% and among women takes the fifth place with the rate of 4.07%, and the incidence of the lung cancer is 14.19/100.000 for men and 1.24/100.000 for women.

In our study, demographic, radiological and bronchoscopic characteristics of 485 patients with lung cancer diagnosed in our clinic, the histopathological type of tumor, and the diagnostic methods were investigated.

Materials and Methods

Four hundred and eighty five patients who were

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hospitalized in the Chest Diseases Clinic in Yedikule Chest Diseases Hospital between July 2006 and December 2009 and were diagnosed with lung cancer were enrolled our study. The relationship between patients' age, gender and the duration of smoking, the location of the tumor in the radiological examination, bronchoscopic characteristics and histopathological type of the tumor, and the methods used for diagnosis, and the relationship between the cell type of the tumor and smoking, gender, radiological and bronchoscopic findings were evaluated. With radiological examination, the lesions smaller than 3 cm were classified as nodules and the lesions larger than 3 cm were classified as mass lesions.

Bronchoscopic lesions were grouped as: 1 - Mucosal Findings: a) Tumor (mass), b) Infiltration 2-Submucosal Findings: Narrowing of the bronchi, loss of normal bronchial appearance, mucosal thickening, erythema, 3-Peribronchial (external pressure) (Çağlayan et al., 2005). While 20 to 22 gauge Spinocan needles were used for computerized tomography-guided transthoracic needle aspiration, 16 to 18 gauge tru-cut biopsy needles were used in some cases to get more enough examples.

Statistics

In statistical evaluations, "chi-square" test were used for the measurement of differences between the mean standard deviations, percent distributions and the inter-group percentages. p value of <0.05 was considered to be statistically significant. "Statistical Package for Social Sciences" software (SPSS-11.5) was used for the analysis of the data.

Results

The rate of all subtypes of lung cancer was higher in the group of smokers. Although it was not statistically significant, the most common tumor in smokers was non-small cell lung carcinoma (NSCLC) of undetermined cell type, followed by epidermoid carcinoma, whereas the most common tumor in non-smokers was non-small cell lung carcinoma (NSCLC) of undetermined cell type, followed by adenocarcinoma (Table 1).

Sixty two patients (% 12.7) were diagnosed with small cell lung carcinoma (SCLC), 191 patients (39.3%) were diagnosed with NSCLC of undetermined cell type, 148 patients (30.5%) were diagnosed with epidermoid carcinoma, 81 patients were diagnosed with adenocarcinoma (16.7%), and 3 patients (0.006%) were diagnosed with large cell carcinoma with

Table 1. Relationship between Tobacco Use and Histopathological Types of Lung Cancer

Cell Type	Smoker	Non-smoker	Total
Small Cell LC	61	1	62
Undetermined NSCLC	187	4	191
Epidermoid Carcinoma	148	-	148
Adenocarcinoma.	78	3	81
Large Cell Carcinoma	3	-	3
Total	477	8	485

histopathological evaluation.

The tumor was found to be most commonly located in right lung in bronchoscopic and radiological examination (51.5%), and especially in the upper lobes of both lungs (only in the right upper lobe (34.6%), and only in the left upper lobe (32.1%)). Radiological views were classified as mass appearance, hilar fullness, nodules, consolidation, atelectasis, cavity and effusion, and the relationship between these views and the histopathological type of tumor was investigated (see Table 2). Accordingly, although the mass appearance was not in statistically significant rates among the tumor types, the number of the cases having mass appearance was highest for NSCLC of undetermined cell type, followed by epidermoid carcinoma and adenocarcinoma, respectively. The mass appearance was also the most common radiological finding (A total of 450 patients, 92.7%). In general, there was no significant difference in the mass appearance between all the NSCLC groups (epidermoid carcinoma, adenocarcinoma, large cell carcinoma and NSCLC of undetermined cell type) and SCLC ($p > 0.05$). Hilar fullness was detected in 179 patients (36.9%) and was the second common radiological finding, and the rate of hilar fullness was highest in epidermoid carcinoma, followed by SCLC and NSCLC of undetermined cell type, respectively. The rate of the hilar fullness was statistically significantly higher in SCLC than all the NSCLC groups ($p < 0.001$). Consolidation was detected in a total of 135 patients (27.8%) and was the third common radiological finding, and the rate of consolidation was highest in epidermoid carcinoma, followed by SCLC. The rate of the consolidation was statistically significantly higher in SCLC than all the NSCLC groups ($p < 0.001$). Atelectasis was detected in a total of 124 patients (25.6%), and the rate of this appearance was highest in epidermoid and SCLC carcinoma. The rate of the atelectasis was statistically significantly higher in SCLC than all the NSCLC groups ($p < 0.001$). Pleural effusion was detected secondary to the mass in a total of 47 patients (9.7%). There was no

Table 2. Distribution of Radiological Findings by the Histopathological Types of Lung Cancer

Radiological Appearance	SCLC	Undetermined NSCLC	Epidermoid Carcinoma	Adenocarcinoma	Large Cell Carcinoma	Total	
Mass	60	177	138	19	3	397	(81.8)
Hilar Fullness	52*	48	62*	2	-	164	(33.8)
Consolidation	39*	34	50*	4	-	127	(26.1)
Atelectasis	40*	30	47*	2	-	119	(24.5)
Effusion	5	11	20	6	-	42	(8.6)
Cavity	-	11	10**	1	-	22	(4.5)
Nodule	-	3	2	5	-	10	(2.0)

* $p < 0.001$ and ** $p < 0.05$

statistically significant difference between SCLC and all the NSCLC groups ($p > 0.05$). The rate of the cavity was highest in NSCLC of undetermined cell type and epidermoid carcinoma (5.5%). There was no statistically significant difference between SCLC and all the NSCLC groups ($p > 0.05$). The rate of the nodule was highest in adenocarcinoma, followed by NSCLC of undetermined cell type (4.6%). However, there was no statistically significant difference between SCLC and all the NSCLC groups ($p > 0.05$). The tumor was classified as central in 58.3% of the patients and as peripheral in 41.7% of the patients. All of the patients with SCLC and 221 (52.2%) patients with NSCLC had central tumors, and 202 (47.8%) patients with NSCLC had peripheral tumors ($p < 0.001$). 108 (66.2%) of the epidermoid carcinomas were central tumors and 40 (33.8%) were peripheral tumors, 30 (27.6%) of the adenocarcinomas were central tumors and 51 (72.4%) were peripheral tumors, and 82 (42.9%) of NSCLC of undetermined cell type were central tumors and 109 (57.1%) were peripheral tumors.

Of 466 patients undergoing bronchoscopy, 152 had endobronchial mass lesion (32.6%), 186 had mucosal-submucosal lesions (39.9%) and 140 (30%) had the findings of external pressure. (As endobronchial mass lesions, mucosal-submucosal lesions and findings of external pressure can be seen in more than one patient, the total number of FOB can be perceived as more than 466). Endobronchial pathology was not observed in 140 patients (30%). The rate of endobronchial mass was highest in epidermoid carcinoma, followed by NSCLC of undetermined cell type and SCLC, respectively. There was no statistically significant difference between SCLC and all the NSCLC groups ($p > 0.05$).

The rate of submucosal lesions was highest in epidermoid carcinoma, followed by SCLC and NSCLC of undetermined cell type. The rate of the submucosal lesions was statistically significantly higher in SCLC than all the NSCLC groups ($p < 0.001$). The rate of the external pressure was highest in SCLC, followed by NSCLC of undetermined cell type and epidermoid carcinoma, respectively. The rate of the external pressure was statistically significantly higher in SCLC than all the NSCLC groups ($p < 0.001$). For definitive diagnosis, 466 patients underwent FOB examination, 211 patients underwent TTNA, 10 patients underwent pleural biopsy examination, 27 patients underwent cytological examination of pleural fluid, and 6 patients underwent thoracotomy. Bronchoscopic appearance of endobronchial mass and/or mucosal-submucosal infiltration were seen in 277 of 283 patients with central tumors, and the materials were diagnostic in 274 of these 283 patients (274/283, 96.8%). 7 patients with central tumors, who could not be diagnosed by FOB examination, were diagnosed by TTNA. 197 (97.5%) of 202 patients with peripheral tumors were diagnosed by TTNA alone and 3 (2.5%) were diagnosed by FOB examination. One patient, who could not be diagnosed by any of FOB or TTNA, was diagnosed by pleural biopsy. It was seen that the diagnostic values of FOB and TTNA are higher for central tumors and peripheral tumors, respectively, in accordance with the literature. Diagnostic thoracotomy was performed in

four patients with peripheral tumor and two patients with central tumor, who could not be diagnosed by both of these processes.

Discussion

Lung cancer is common in men, and although the incidence of lung cancer is lower in women, it shows more rapid increase in women than men. Lung cancer is most commonly seen between the ages of 40 and 70, and its incidence increases with age and reaches the peak value in 6th to 7th decades (Yurdakul et al., 2002; Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2002). The incidence of lung cancer is lower in young adults (around 5 to 10% under 50 years of age). This group of young adults usually has the family history of lung cancer, and adenocarcinoma is the most common type of lung cancer in this group (Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2006).

In France, a study investigating 355 patients with cancer have reported that the frequency of epidermoid carcinoma increases with the age, the frequency of adenocarcinoma is increased in women, and young women were diagnosed in the last stage of the cancer (Virally et al., 2006). In a study conducted in Poland, it was reported that, although epidermoid carcinoma is the most common type of cancer in men and women, it is two times more prevalent in men, the incidences of adenocarcinoma and small cell lung cancer (SCLC) are higher in women, as well as family history is more frequently recorded in women than men (Radzikowska and Glaz, 2000).

In a study including 3794 patients, which was conducted in Korea, epidermoid carcinoma was found to be most common lung cancer with the rate of 44.7%, followed by adenocarcinoma with the rate of 27.9% (Lee et al., 2000). In a study conducted in New York City, the rate of the family of the lung cancer was reported to be higher in female patients who had epidermoid carcinoma and were under the age of 57, and in the group of those who smoked less than 20 years (Ambrosone et al., 1993). Also in the study conducted in Germany, the rate of the family history was reported to be higher in young cancer patients, regardless of the histological type of cancer (Kreuzer et al., 1999). In a series of 1731 patients from Macedonia, lung cancer was found to be most common in males, and additionally epidermoid cancer was found to be common in males and adenocarcinoma was found to be common in females (Pavlovska et al., 2004). In a study conducted in Pakistan (Karachi), adenocarcinoma was reported to be most commonly seen in females (Bhurgrri et al., 2006). In a study including 73 patients, which was conducted in India, it was reported that male/female ratio is 4.2 /1 and adenocarcinoma is the most common type of cancer with the rate of 28.8% (Chhajer et al., 1999). In a study including 2216 patients, which was conducted in Turkey, The rates of the NSCLC, SCLC and the other malign tumors of undetermined cell type were found to be 77.7% , 15.5% and 6.8%, respectively, and epidermoid cancer was reported to be most common in males and adenocarcinoma was reported to be most common in females (Yurdakul et al., 2002). However,

in a study with the greatest number of the patients (n = 11,849) in our country, 90.4% of the patients were male and 9.6% were female, and age range was between 45 and 65 years. And the frequencies of epidermoid carcinoma, SCLC, adenocarcinoma and NSCLC were reported to be 45.4%, 20.5%, 20.2% and 9%, respectively (Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2002). In our study, the frequencies of NSCLC, epidermoid carcinoma, SCLC, adenocarcinoma and large cell carcinoma were found to be 39.3%, 30.5%, 12.7%, 16.7% and 0.006%, respectively. The comparison the histological type between males and females was not performed due to the relatively small number of female patients. In light of studies conducted, in general, while adenocarcinoma was detected most frequently in the United States and Japan, it was concluded that epidermoid carcinoma is still the most common type of cancer in Asian countries (Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2006). Further comprehensive epidemiological studies are needed to provide a conclusion about this issue in our country.

The relationship between lung cancer and smoking was proven with case-control based epidemiological studies conducted up to 1950, and the first findings supporting that smoking leads to lung cancer were published in 1962. The risk of developing cancer was increased by 24 to 36 fold in smokers when compared to nonsmokers. The risk of cancer is 3.5% in secondhand smoke (SHS) (Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2006). In the study conducted in Spain, epidermoid carcinoma was found to be most common type of lung cancer in male smokers (Santoz-Martinez et al., 2005). In a study conducted in Taiwan, while the incidence of epidermoid carcinoma and SCLC has been reported to be increased in male smokers, the incidence of adenocarcinoma has been reported to be increased in the young people, females and older male smokers (Perng et al., 1996). In the study conducted in Poland, it has been reported that lung cancer is 6 times more prevalent in males, epidermoid carcinoma is the most common type among all types of lung cancer, adenocarcinoma and SCLC is more common in young women than men, and the rate of the history of smoking is lowest in patients with adenocarcinoma (Radzikowska et al., 2002). The increase in the incidence of adenocarcinoma in recent years has also been observed in Sweden (Koyi et al., 2002), and higher rates of adenocarcinoma in non-smokers and females have been supported in various studies (Radzikowska and Glaz, 2000; Virally et al., 2006). In the study conducted in France, epidermoid carcinoma was found to be most common in male smokers, adenocarcinoma was found to be most common in females and non-smokers, and the increase in the incidence of adenocarcinoma was reported to be associated with changes in the cigarette composition and pattern of smoking (Chiriac and Gavrilita, 2002).

In a study conducted in Macedonia, 81% of men and 39% of women were smokers. There was a significant relationship between histopathological diagnosis and smoking, and SCLC and epidermoid carcinoma were found to be most common in smokers and adenocarcinoma was found to be most common in non-smokers (Pavlovska

et al., 2004). In the study conducted in India, epidermoid carcinoma was identified as the most common type of cancer in people with more than 20 packs / year history of smoking, and adenocarcinoma was identified as the most common type of cancer in non-smokers and in women (Chhaged et al., 1999). In our study, although very few number of non-smoker patients, NSCLC (non small cell lung cancer) of undetermined cell type and epidermoid carcinoma were observed as the most common types of cancer in smokers, and NSCLC of undetermined cell type and adenocarcinoma were observed as the most common types of cancer in non-smokers. All cases of epidermoid carcinoma were found to be smokers.

Lung cancer was found to be located more frequently in the right lung than left lung, and especially in upper lobes (Spiro, 1990). The study conducted in Macedonia has investigated 1731 patients, the tumor has been shown to be located mostly in the right and left upper lobes (Pavlovska et al., 2004). In our country, the study conducted by Atıcı et al (2004) has reported that 52% of lesions located on the right, 48% located on the left and 91% of the lesions were centrally located mass. In another report in our country, it was reported that the most frequent location of tumor was right upper lobe with the rate of 24.4% and the most frequent appearance was mass appearance, and epidermoid carcinoma was found to be most common tumor with the rate of 42.8%, followed by the SCLC with the rate of 17.6% (Sevgi et al., 1997). In the study of Bulbul et al. (2002) epidermoid carcinoma was found to be most common tumor with the rate of 60.6% among 218 patients, followed by SCLC with the rate of 18.1%, and tumors were found to be most frequently located especially in the upper lobes and right lung. The study conducted in Arabia reported that the most frequent location of tumor was the right lung, and right and left upper lobes were the most frequent sites of involvement (Alamoudi, 2010). In the study conducted in South Africa, the tumor was reported to be involved more frequently in the right lung than the left lung, and 43.6% of the tumors were centrally located and 46.6% were peripherally located (Nanguzgambo et al., 2011). The study conducted in Spain emphasized that 88.7% of the tumors were centrally located and 11.3% were peripherally located, and hilar fullness was seen more frequently in SCLC (Martinez Moragon et al., 1994). In our study, 58.3% of the tumors were found to be centrally located and 41.7% were peripherally located, and hilar fullness was observed in all cases with SCLC. 51.5% of the tumors located in right lung, 48.5% located in left lung, and 34.6% located in the right upper lobe and 32.1% were located in the left upper lobe. The most common radiological finding in our study was mass appearance as in some studies in our country (Demirtaş et al., 1995; Sevgi et al., 1997). This supports that that the tumor locates in the right lung, especially in upper lobes, and the rate of centrally located masses was higher than the others in our study, as in the other studies.

The fiberoptic bronchoscopy (FOB) developed and used first by Ikeda in the 1960s is a very valuable method for diagnosis and staging of lung cancer. 95% of tumors that are endobronchial, infiltrating and narrowing the bronchial lumen and 68% of submucosal tumors can

be diagnosed by FOB (Kargı and Veral, 1999). In our study, 466 of 485 cases underwent FOB, and diagnostic materials were obtained from 274 (58.7%) of these 466 patients. Endobronchial tumors were detected in 152 patients and mucosal-submucosal lesions were detected in 186 patients. No endobronchial pathology was found in 140 patients (It has been reported that there may not be any bronchoscopic finding in peripheral lung cancers). 140 patients had the signs of external pressure. There was bronchoscopic appearance of endobronchial tumor in 152 of centrally located tumors with radiological appearance of hilar fullness and mass. Epidermoid carcinoma is seen as polypoid masses in large bronchi, adenocarcinoma is usually seen as peripheral parenchymal masses, and SCLC is seen as the lesions infiltrating the bronchial wall without forming an intra-bronchial mass in large bronchi (Carr et al., 1994). In our study, a higher incidence of endobronchial tumors has been observed in epidermoid carcinoma and NSCLC-undetermined type, respectively.

Transthoracic fine-needle aspiration (TTNA) biopsy has a higher diagnostic value for peripheral masses than FOB examination (Kowalewski et al., 2004). The specificity of this procedure, which is guided by computed tomography, ranges 96 to 100% and sensitivity ranges 89 to 92% (Turkish Thoracic Society, Lung and Pleural Malignancies Study Group, 2006). In the study conducted in Poland, TTNA was identified to have high specificity (93.1%), moderate sensitivity (73.9%) for malign lesions, and diagnostic value by 50.6% for NSCLC and by 11.1% for SCLC (Kowalewski et al., 2004). The study conducted in Korea reported that TTNA is very important in adenocarcinoma in particular (Lee et al., 2000). In of the studies conducted in our country, the diagnostic value was found to be 94.6% (Demirtaş et al., 1995). In our study, 211 patients were underwent TTNA and 204 were diagnosed by this procedure, and the success rate with this approach was 96.6%.

In the study conducted in Korea, two thirds of patients with NSCLC were reported to be inoperable at diagnosis, and the rate of inoperable patients was 74.1% in the study conducted in India (Chhajed et al., 1999; Lee et al., 2000). Only 137 (28.2%) of 485 patients in our study were operable and 71.8% of the patients were found to be inoperable, as in the above-mentioned studies. This shows that there is a delay between the application to the hospital and the time of diagnosis.

In conclusion, it was seen that NSCLC (especially epidermoid) generates the majority of lung cancers, gender and smoking are effective on the histopathology of the tumor, all lung cancers are seen especially in the upper lobes with radiological examination, bronchoscopic findings of endobronchial tumor are mostly seen in epidermoid carcinoma, mucosal-submucosal infiltration is mostly seen in epidermoid carcinoma and SCLC, findings of external pressure are mostly seen in SCLC, SCLCs are seen as centrally located with radiological examination, TTNA and FOB together have a diagnostic value of 98.5%, and more than 2/3 of patients have inoperability criteria at diagnosis.

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