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LUNG CANCER IN YOUNG ADULTS (< 35 YEARS)

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Abstract
Background and objective: Lung cancer in young adults has been differently described in publications from various regions of the world. In this paper literature data and results of our own study of lung cancer in 35 years old and younger patients are presented.
Method: A retrospective review of patients 35 years of age and younger with lung cancer treated at Department of Pulmonary Diseases and TB in Sarajevo University Clinical Center from 1995 to 2000 was done.
Results: There were 8 patients (5 male and 3 female). Mean age was 34 years (in range, 31-35). The predominant histologic type was squamous cell carcinoma in 5 cases (62,5%), including smoking and non- smoking patients.
Final histopathological diagnosis was made in 2 cases (25%) by combination of bronchoscopic techniques, in 2 cases (25%) by bronchial biopsy alone. Pleural punction and biopsy (25%) as well as thoracotomy (12,5%) were done in three cases with peripherally located tumors.
Almost all patients presented with advanced- stage disease, either stage III B (4 patients) or stage IV (3 patients). Only one patient had IIIA stage disease and underwent surgical resection and chemotherapy. Other treatments included chemotherapy and radiation therapy.
Five patients (62,5%) were followed up until death. Median survival of these patients was 17,4 months. There was only one 2- year survivor.
Three patients (37,5%) rejected follow up without known reason.
Conclusions: This study showed an undoubted risk of lung cancer among young persons in our population. Although males were commonly affected, females were also seen to have malignancy in a high ratio. The young with lung cancer presented with advanced- stage disease and curative treatment is rarely possible.
Key words: lung cancer, young adults, and radiology.

Introduction

Lung cancer (LC, also called bronchogenic carcinoma) is the most common malignancy among men and increasingly common among women throughout the world.

At the beginning of the 20th century, it was a rare disease, but its incidence and mortality have increased steadily over the past decades (1).

In 1990 Jensen et al. have been reported that LC accounts for 21% of all cancer cases among males and 4% among females in the European Community (2).

It is now the leading cause of death from malignancy in the United States and most industrialized countries for both men (34%) and women (21%), having surpassed breast cancer in women in recent years (3). Unfortunately, the 5 - year survival rate is below 15% in spite of the certain progress has been made in the diagnostic tools and the therapy for LC (4). When implemented for complete staging, about one third of patients will be in the stage of limited disease and two thirds in the stage of spread disease (5).

Four randomized, prospective controlled trials including 36,000 male smokers aged over 45 revealed no evidence to suggest that screening could reduce LC mortality (6,7). The Mayo Lung Project (6) and some other studies addressed the effect of regular screening with chest radiography. In these studies, screening led to improvements in stage distribution, respectability and survival. However, the disease- specific mortality showed no improvements. Based on these studies, mass screening for LC is not recommended.

There are also preliminary results for LC screening by spiral CT (computed tomography) with more accurate results and earlier detection compared with conventional chest radiography.
The majority of LC cases are patients of age between 55 and 65 years in both genders. The age and sex distribution for the various histological subtypes of LC has shifted during the past several decades (8).

LC is rare in patients 30 years of age or younger and there is very little published data on LC in this group. The young with LC present with advanced - stage disease and their cancers appear to be biological aggressive (9).

Although several case reports have been suggested that LC occurs more frequently in young patients who are human immunodeficiency virus (HIV) seropositive, some big retrospective studies revealed no increased incidence of LC from the pre – AIDS period (1976 - 1979) compared with the AIDS period (1987 – 1990) (10,11). Those results suggest that HIV seropositivity is not a risk factor for LC.
As well known, the lung cancer risk is strongly associated with exposure to cigarette smoking. Some investigators have concluded that smoking now accounts for 95% of LC in developed countries. The prevalence of smoking has been decreasing since about 1970, but has increased again since 1994, particularly among young people and women aged under 35 (12).

Exposure to environmental tobacco smoke (also called passive smoking) also causes LC. There is a dose - response relation between a non – smoker's risk of LC and the number of cigarettes and years of exposure to smoke, which adds weight to the

evidence that the association between environmental exposure and LC is causal (13,14,15).

There are a few known occupation–related causes of LC. Asbestos is the most common of them (builders, plumbers, electricians, metal plate workers are the largest high – risk groups). Radon is a naturally–occurring radioactive gas which emanates from uranium naturally occurring in the soil. For instance, radon exposure may increase the risk of LC among smokers 3– fold (16). Uranium, arsenic fumes, nickel, haloethers are some of carcinogens.

Dietary factors appear to influence the lung cancer risk as ingestion of beta-carotene or other retinoids (17).

An elevation in the risk of LC has been noted among some relatives.

Family studies have shown a two- or three - fold risk of LC among the non–smoking relatives of lung cancer patients compared with non–smokers without a family history of LC. The genetically determined ability to metabolize carcinogens may be one factor affecting the lung cancer risk (18).

The rising prevalence of marijuana or/and cocaine use among young adults in the United States prompted some investigators to investigate whether similar molecular and histopathologic alterations occur in habitual smokers of marijuana and cocaine who may or may not also smoke tobacco. Those findings suggest that smoking marijuana or/and cocaine, like tobacco smoking exerts field cancerization effects on bronchia epithelium, which may place smokers of these substances at increased risk for the subsequent development of LC (19).

Aim and objective

LC in young adults has been differently described in publications from various regions of the world, in respect of relative incidence, distribution of morphology and stages, and prognosis of the disease.

In this paper literature data and results of our own study of lung cancer in 35 years old and younger patients are presented.

Patients and Method

The study was designed as a retrospective review of lung cancer patients 35 years of age and younger referred to the Department of Pulmonary Diseases and TB in

Sarajevo University Clinical Center from 1995 to 2000. The source of information was Department's cancer register.

Out of 1593 patients 8 (0,5%) were = /< 35 years of age at the moment of lung cancer diagnosis was made.

According to clinicopathological features, all relevant data from medical history of these patients were analyzed, which included the age, gender, smoking habits, the various histological types of malignancy and the yield of various diagnostic techniques of lung cancer.

Results

Analysis comprised 8 patients during the five - year period, 5 male (62,5%) and 3 female (37,5%) with mean age being 34 years (in range 31- 35 years).

Four (50%) patients (3M, 1F) were found to be tobacco smokers and 2 of them were life–long smokers (15 years). While the minimum duration of smoking was 20 cigarettes per day during 3 years, the maximum duration for which two another patients had smoked was 30 to 40 cigarettes per day during 15 years. Four (50%) patients (2M, 2F) were non-smokers.

There were not data about drug addiction, AIDS or some other immunodeficiency disorders and about patient's close relatives with LC diagnosis as well. One male patient had previously established diagnosis of lung tuberculosis. Also, there were not data about professional exposure to asbestos or other known occupation- related risk factor.

The most common symptoms of disease were cough in 6 cases (75%) and chest pain on the tumor side in 5 cases (62,5%). Hemophtysis were noted in 3 cases (37,5%). The others included dyspnoea in 2 cases (25%), high body temperature and weight loss in 1 case (12,5%) both. The average duration of symptoms per anamnesis was 4,6 months, in range 3 days to 1 year.

Squamous cell carcinoma was found to be the most common type of malignancy in 5 (62,5%) patients (3M, 2F). Four of them were non- smokers and one was life-long smoker.

Adenocarcinoma was detected in 1 female patient (12,5%) who was 3- year smoker. One male patient (12,5%) was diagnosed as a case of small cell carcinoma. In 1 male patient (12,5%) diagnosis of large cell carcinoma was made (Table 1).

Table 1. Various histopathological types of LC among smokers and non-smokers.

	Diagnosis	Smokers (n)			Non-smokers (n)		
			M	F		M	F
1	Squamous cell carcinoma	1	1	0	4	2	2
2	Adenocarcinoma	1	0	1	0	0	0
3	Small cell carcinoma	1	1	0	0	0	0
4	Large cell carcinoma	1	1	0	0	0	0
	Total	**4**	**3**	**1**	**4**	**2**	**2**

In our study, in 2 cases (25%) the histological diagnosis of malignancy was made by all bronchoscopic techniques. In 2 cases (25%) diagnosis was made only by bronchoscopic biopsies, in 2 cases (25%) only by pleural punction and biopsy and 1 case (12,5%) needed explorative thoracotomy.

According to radiological methods, the first procedure for all persons was chest radiography and after that the spiral CT was done.

Seven patients (87,5%) were categorized as having an advanced stage of lung cancer (4 with stage III B, 3 with stage IV).

One patient (12,5%) had less advanced disease (stage III A) and only this patient was treated by operation and chemotherapy.

Three patients (37,5%) were treated by chemotherapy and radiation therapy, 2 patients (25%) by chemotherapy, 1 patient (12,5%) by radiation therapy and 1 patient (12,5%) rejected any therapy.

Out of 8 patients, 5 patients (62,5%) were followed up until death. The 2- year survival of these patients was 20% (in range 1- 2 years).

Three patients (37,5%) rejected follow up without known reason.

Discussion

As we expected, the study showed relatively low percentage of the young (0,5%) in our population of lung cancer patients.

It is very hard to compare the data about percentage and incidence of young LC patients, because there were different descriptions in various publications, in respect of age limit, total number of patients included into the investigation and the reviewing period of years.

For instance, our results could be the similar with results of restrospective study in Berlin (20). They were found 106/4939 patients were 40 years old or younger with LC during the 10- year period. The percentage of young group patients in that study was 2,1%.

The disease is known to be more common in males than females. In our study the ratio of males to females was 1,6: 1. The sex distribution showed relatively high percentage of female patients (37,5%), as we also expected according to literature (21,22).

The increase in LC among females follows the trend in cigarette smoking.

The percentage of female LC patients has increased from 6% to 15% in northern Finland during the last 20 years (23). The presented results suggest that in particular adenocarcinoma among females has increased during the past decades (24,20). Given the adenocarcinomas are less closely related to smoking, the increase of adenocarcinomas suggest additional risk factors that may play an important role in the etiology of lung cancer.

However, some surveys showed an increasing proportion of small- cell carcinomas rather than adenocarcinomas among the female population (25). A study from Minnesota, USA, showed an equal increase in all histological cell types of LC (26). A trend towards an increase of adenocarcinomas among females and non- smokers has also been reported (27, 28).

The percentage of tobacco smokers and non- smokers in our series of patients was equal. It makes the understanding of LC etiology more difficult. However, passive smoking was not recorded as well as other etiological factors in causing lung cancer.

The numerous case- control studies suggested a small but real risk for LC among non- smokers exposed to the tobacco smoke of others (29, 30).

The lack of statistical power may have been potential or additional limitation to our study. In our study, squamous cell carcinoma (62,5%) was the most common histopathological type of malignancy. These observations are very close to the observations reported in the past (31). It seems that squamous cell carcinoma remains the most frequent subtype in Europe.

The ratio of smokers to non- smokers in our patients with squamous- cell type was 1: 4. In various other studies squamous cell carcinoma was the commonest malignancy detected with the ratio of smokers being higher than the non- smokers (32, 33, and 34) were. The number of cases found in our study is two small for serious statistical evaluation, but this observation is very interesting and unexpected. However, the lack of additional information about lifestyle risk factors among the patients and their close family members restricted the interpretation of results of our study.

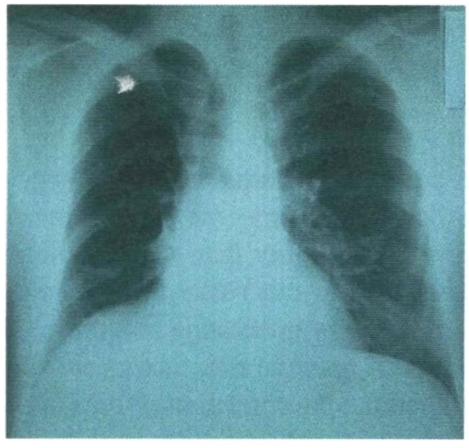
Adenocarcinoma was seen in very low percentage of our patients (12,5%). Large cell carcinoma accounts for 9% of all LC. In our study its incidence was 12,5%, as well as small cell carcinoma.

A specific histological cell type is obtained more often from the combination than from either technique alone (35). In our study, by combination of bronchoscopic techniques, final histopathological diagnosis was made only in 25% of cases. The equal percentage of diagnosis was made by bronchial biopsy. Pleural punction and biopsy (in 25%) as well as thoracotomy (in 12,5%) were done in three cases with peripherally located tumors.

To some extent, the clinical setting dictates us to, which of the bronchoscopic diagnostic methods will be most appropriate and most useful; but in most circumstances a combination of methods provides the best chance of making a specific diagnosis.

According to chest radiography and spiral CT findings, almost all our patients had advanced- stage disease at the time of presentation (Figure 1a,1b,2). In spite of that they were treated in accordance with standard stage- specific treatment guidelines.

Median survival among followed up patients (62,5%) was only 17,4 months and there was only one 2-year survivor. These observations are consistent with the most reports in the recent years (20, 21).



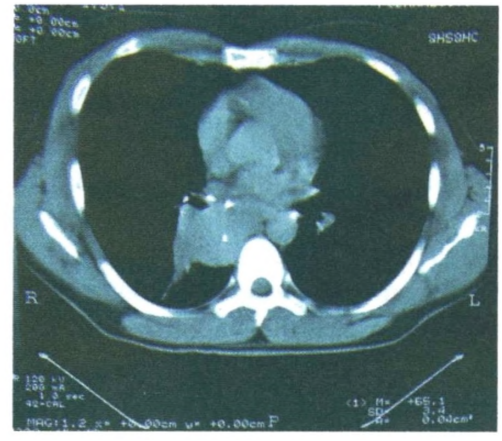


Figure 1a. Figure 1b.

Figure 1a,b. P-A chest film in a 34 – year old male smoker shows a right hilar mass with discrete lower lobe subatelectasis and lymphnode enlargement. PHD: Small - cell carcinoma.

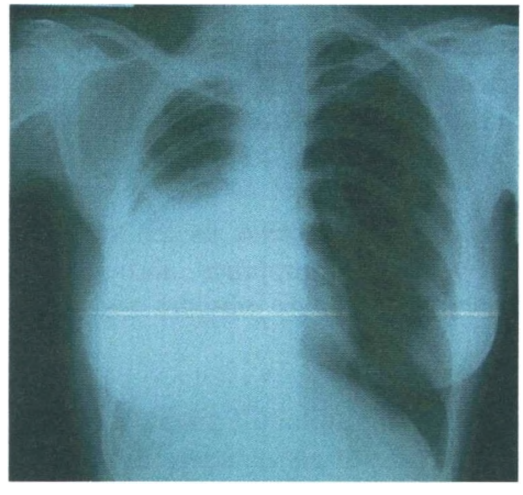


Figure 2.

Figure 2. A 34 – year old female non -smoker with massive right lower lobe atelectasis. Cytological examination of the associated right pleural effusion revealed adenocarcinoma.

Conclusions

This paper reports results from a hospital- based retrospective study showing an undoubted risk of lung cancer among young persons, especially smokers.

Although males were commonly affected, females were also seen to have malignancy in a high ratio.
Squamous cell carcinoma is the most common histological type of malignancy in our population including smoking and non- smoking patients.

Specific histological diagnosis was made by various bronchioscopic techniques, either alone or in combination.

In spite of relatively short duration of symptoms all our patients had advanced- stage disease at the time of diagnosis.

Apstrak

PLUĆNI KARCINOM U MLADIH OSOBA (< 35 GODINA)

Uvod i objekat: Plućni karcinom u mladih osoba je različito opisivan u publikacijama iz različitih regiona svijeta. U ovom radu su prezentirani podaci iz literature i rezultati naše vlastite studije o plućnom karcinomu u pacijenata starosti 35 godina i mlađih.

Metoda: Urađena je retrospektivna analiza pacijenata starosti 35 godina i mlađih sa plućnim karcinomom, liječenih na Klinici za plućne bolesti i tuberkulozu, KCUS od 1995. do 2000. godine.

Rezultati: Nađeno je 8 pacijenata (5 muških i 3 ženska). Srednja životna dob je bila 34 godine (u rasponu 31- 35). Dominantni histološki tip je bio planocelularni karcinom u 5 slučajeva (62,5%), uključujući pušače i nepušače. Konačna histopatološka dijagnoza je dobivana u 2 slučaja (25%) kombinacijom svih bronhoskopskih tehnika; u 2 slučaja (25%) samo sa bronhijalnom biopsijom. Pleuralna punkcija i biopsija pleure (25%) kao i torakotomija (12,5%) su učinjene u 3 slučaja (2+1) sa periferno lokaliziranim tumorima.

Skoro svi pacijenti su prezentirani sa uznapredovalim stadijem bolesti, bilo sa stadijem III B (4 pacijenta) bilo sa stadijem IV (3 pacijenta). Samo 1 pacijent je imao stadij III A i podvrgnut je hirurškoj resekciji i kemoterapiji. Ostali tretmani su uključivali kemoterapiju i iradijacionu terapiju.

Pet pacijenata (62,5%) je praćeno do smrti. Srednje preživljavanje ovih pacijenata je bilo 17,4 mjeseci. Samo 1 pacijent je preživio 2 godine. Tri pacijenta (37,5%) su odbili praćenje bez poznatog razloga.

Zaključci: Ova studija je pokazala nedvojben rizik od plućnog karcinoma među mladim osobama u našoj populaciji. Iako su muškarci češće zahvaćeni uočeno je da su i žene uključene u visokom procentu. Mladi sa plućnim karcinomom su prezentirani sa uznapredovalom bolešću, a kurativni tretman je rijetko moguć.

Ključne riječi: plućni karcinom, mlade osobe, radiologija.

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