Non-Small Cell Lung Cancer: Disease Spectrum and Management in a Tertiary Care Hospital

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Abstract

Objectives: To review the spectrum of presentation and the surgical management of Non Small Cell Lung Cancer (NSCLC) and the role of various diagnostic modalities in predicting the post-operative stage and the correlation of the post-operative stage with the chances of recurrence.
Settings: The Aga Khan University Hospital, Karachi - a tertiary care referral center in Paksitan.
Methods: This is a retrospective study of medical records of all the patients who were managed at the Aga Khan University Hospital (AKUH) between 1988 and 1998. The patients with a diagnosis of lung cancer were identified using the ICD-9-CM coding system and the data was analyzed for patients with NSCLC only.
Results: A total of 773 patients were admitted with a diagnosis of lung cancer at AKUH over 10 years period. Out of these 21(2.71 %) underwent staging niediastinoscopy and 20 (2.58%) patients underwent exploratory thoracotomy and biopsy without any resection, as the disease was found to be unresectable. Only 18(2.32%) patients underwent surgical resection. There were 15 males and 3 females and the mean age was 53 years. Mean duration of symptoms was 12 months and cough and haemoptysis were the main presenting symptoms. Most of the tumors were located on the right side. CT scan and mediastinoscopy were mainly used to stage the disease. Complete surgical resection including en-bloc resection of adjacent structures was attempted, when possible. Median follow up was 24 months and the recurrence rate was 39%. There was no significant correlation between post-op stage and recurrence.
Conclusion: It is concluded that most of the patients present at the advanced stage and resection is possible only in a small number of patients. The size of primary tumor and local extension should not contra-indicate surgery in patients with negative mediastinal nodes and without distant metastasis as it can be performed safely. All pulmonary lesion in the adults must be thoroughly investigated as early diagnosis and complete resection is the only key to cure and long term survival (JPMA 50:330, 2000).

Introduction

Lung cancer is a major health problem. It consists of about 14% of all newly diagnosed cancers in males and 13% in females and is the most frequent cause of cancer-related deaths in both sexes, The overall best 5-year survival rate is l3-14%[1]. This is because advanced disease or cardiopulmonary impairment preclude surgical intervention in all but 20-25% of the patients[2].
The present study focuses on the non-small cell lung cancer (NSCLC) only. Small cell lung cancer is usually not amenable to surgical resection except in highly selected cases. Non-small cell lung cancer comprises about 75-80% of all lung cancers and the survival in these cases is closely related to the stage of the disease[3]. As a general statement, it is fair to say that there has been relatively little improvement in the cure rate for primary lung cancer during the past 30 years, but it is the area of 'selection' and preoperative staging that significant advances have been made[4]. Surgical resection still offers the best chance of cure in appropriately 'selected' cases. Surgical resection remains the treatment of choice for the physiological fit individuals presenting with NSCLC localized to pulmonary parenchyma, with or without contiguous broncho pulmonary lymph node involvement (stage I or II disease)[5]. Selected patients with isolated ipsilateral meditational nodal involvement (stage IIIa) may also benefit from surgery[6] Approximately 40% of the individuals undergoing a curative resection for a

presumably resectable cancer (all stages) will survive 5 years.
The basic objective of this study was to review the spectrum of presentation and the surgical management of NSCLC at AKUH and to analyze the role of various diagnostic modalities in predicting the post-operative stage and its correlation with chances of recurrence.

Material and Methods

The medical records of all the patients who were admitted between January, 1988 to December, 1998 with a diagnosis of NSCLC were retrieved, using the ICD-9-CM coding system. The data was collected for patients who underwent surgical resection for an operable lung cancer and the variables reviewed included demographic features, clinical presentation, diagnosis, management and outcome. The patients, who underwent thoracotomy and biopsy only, without any other surgical intervention, were excluded from the study. Percutaneous line needle aspiration biopsy and bronehoscopy was used to get a tissue diagnosis white CT scan and niediastinoscopy were used to stage the disease. The data were analyzed using the student t test for continuous data and the Fischer Exact test for categorical data with the Epi-info software package.

Results

A total of 773 patients were admitted with a diagnosis of lung cancer and out of these, 607 patients (78.5%) were diagnosed to have NSCLC. After evaluation, only 39 patients (6.4%) were found to be eligible for surgical resection. Twenty-one (3.45%) patients underwent a thoracotomy and biopsy only, as the disease was unresectable at surgery and only 18 (2.3%) patients underwent a curative surgical resection. There were 15 males and 3 females. The mean age at presentation was 53 years with a range of 40 to 65 years. Twelve patients had a history of smoking while one was asthmatic. There was no history of occupational exposure. Amongst the medical comorhids, 3 patients were diabetic and 2 were hypertensive. One patient had a prior coronal)' artery bypass grafting and had to undergo a coronary angiograni for proper risk stratification.
The mean duration of symptoms was 12 months with a range of 1-30 months. Persistent cough was the most common symptom at presentation, being present in 12 patients. Other symptoms included chest pain in 8, haemoptysis in 7 and dyspnoea in 5 patients. Systemic features like weight loss and fever were present in 8 and 7 patients respectively. About 50% of the patients had physical findings like reduced air entry or coarse crepitations on the affected side. The tumor was located in right lung in I 3 patients and left lung in 5 patients.
Percutaneous fine needle aspiration biopsy (PFNAB) was used to establish the histopathological diagnosis in 8 patients. The diagnosis was accurate in 7 patients, while one patient. initially diagnosed to have adenocarcinoma, was ultimately found to have small cell lung cancer on final histopathology report. All the remaining patients underwent a bronchoscopy for tissue diagnosis. CT scan and mediastinoscopy were used to assess the nodal stage of the disease. CT scan was done in all cases and revealed a sensitivity of 40% and specificity of 42% in predicting the nodal stage. Mediastinoscopy was done in 7 patients and only one patient was found to have N2 disease, which was considered amenable to curable resection and the patient underwent surgery.
Ultimately 6 patients preoperatively were labeled as stage I and 7 patients as stage II. The remaining 5 patients were found to have stage lila disease with involvement of adjacent chest wall structure. These included involvement of upper lobe with adjacent 3 ribs (2 cases) sternum, clavicle and upper 3 ribs (I case) and part of brachial plexus and adjacent ribs (case). Involvement of lower lobe with adjacent parts of diaphragm and pericardium was found in I case.
All the patients underwent surgical resection with a curative intent. The procedures performed included lobectomy in 6, bilobectomy in 5 and pneumonectomy in 2 patients. The remaining 5 patients with stage lila disease underwent a lobectomy with en bloc resection of adjacent structure. The chest wall defect in these cases was repaired by using mersilene mesh (Table 1).

Table1. Types of surgical procedures.
Surgical resection (n = 18)

Procedures	Patients
Lobectomy	6
Bilobectomy	5
Pneumonectomy	2
Lobectomy and en-bloc resection	5
a Lobectomy + parts of sternum and clavicle + 1-3 ribs	1
b. Lobectomy + 1-3 ribs	2
c. Lobetomy + part of brachial plexus+1-4 ribs	1
d. Lobectomy + parts of diaphragm and pericardium	1

The histopathology revealed squamous cell carcinoma in 8, adenocarcinoma in 7 and large cell carcinoma in 2 cases. One patient was postoperatively diagnosed to have small cell carcinoma and was referred to the oncologist. All 5 patients with involvement of chest wall structures and one patient with N2 disease were given postoperative radiotheraphy

There was no 30-days mortality but postoperative complication were identified in S patients. They included atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, recurrent nerve injury and transient vagus nerve damage in one case each. The follow up was available upto a median duration of 24 months with a range from 6 to 48 months.

The recurrence was seen in 7 patients and all were systemic. The sites included brain in 4, opposite lung in 2 and liver in! patient .Two patients died of disease at 7 and 9 month after resection. Three of the seven patients had their recurrence within three months and the remaining cases two years after surgical resection. All the early inetastases were to the brain and the patients had either adenocarcinoma (2) or small carcinoma (1). There was no significant correlation of the postoperative anatomical stage with the recurrence (p value 0. 11), as well as the histopathology with the recurrence (p value 0.13) (Table 2).

Table 2. Correlation of histopathalogy and stage with recurrence.

Characteristics	Recurrence	No recurrence	P-value
No. of patients	7	11	
Histologic type			
a. Squamous cell carcinoma	3	5	
b. Adenocarcinom	3	4	0.13
c. Large cell carcinoma	0	2	
d. Small cell carcinoma	1	0	
Anatomical stage			
a. Stage I	4	3	
b. Stage II	1	4	0.11
c. Stage IIIa	2	4	

Discussion

Lung cancer is the most common cause of death by malignancy in both men and women. Moreover, the age-adjusted death rate for lung cancer increased steadily from 1930 to 1990 and the rate of increase does not seem to be abating [7]. This is because most of the patients present late in the course of disease and are not a candidate for surgical resection. As in this series, only 2.3% of the patients diagnosed to have lung cancer underwent surgical resection.

• In international literature, about 15% of all the patients with non-small lung cancer are candidates for surgery[8]. The rate of surgical resection is very low in this series, as the patients and physicians often ignore the symptoms or attribute them to tuberculosis. The mean delay between the onset of the symptoms and diagnosis in this study was 12 months with a range of 1-30 months. It is important that respiratory symptoms should not be ignored and thoroughly investigated especially in smokers more than 40 years of quite separate from it[10]. MR imaging is better than CT in diagnosing chest wall involvement by the tumor[11] 1 Similarly, CT and MR have a poor yield in the nodal staging of the lung cancer. Using Icentimeter size of the lymph node as the criteria for abnormality, one finds a range of the sensitivity of 29-95% and specificity of 46-94% in various studies[12].

The role of various diagnostic modalities also remain controversial. Percutaneous fine needle aspiration biopsy (PFNAB) and bronchoscopy are often used to get a histhopathological diagnosis of the disease, but they are not completely reliable. The sensitivity of PFNAB in diagnosing malignancy is variable in different studies, ranging from 64-97%, but cytologic-histologic correlation is around 80%9 As in this study, one patient was labeled as having adenocarcinoma on PFNAB, but the postoperative histopathology revealed it to be a small cell carcinoma. Preoperative bronchoscopy is done routinely, but it may not be possible to reach the peripherally located lesion.

CT and MRI are usually used to stage the disease. CT scan is poor in the assessment of the chest wall involvement in most cases, but still it may clearly demonstrate that a mass which appears to be contagious with the chest wall on the plain chest radiograph, is actually.

Since there is ample evidence to support the correlation of the preoperative stage with the survival, mediastinal lymph node staging by mediastinoscopy has been recently used to properly stage the disease. Thus, the status of the mediastinal nodes may mean the difference between a potentially curable therapy, palliation, or no therapy at all [13]. Many surgeons recommend the advisability of the surgical resection to be based upon the histological evidence of nodal status.

The presence of the distant metastatic disease in NSCLC is associated with a poor prognosis and surgical resection at the primary site is contra-indicated. A large proportion of the patients clinically regarded as having resectable disease and potential cure may actually have occult metastatic disease. Clinically undetected metastasis has been reported in 30% of the cases that underwent postmortem examination after curative surgical resection[14]. Interval development of the extra- thoracic metastatic disease accounts for approximately 75% of the 'early mortality' in these surgically treated cases[6]. Normal hematological and biochemical serum markers do not reliably rule out the presence of metastatic disease. Brain is the commonest site of extra-thoracic metastasis and Grant et al[15] reported metastatic disease in 13%of the asymptomatic patients in whom CT scan of the brain and abdomen were employed in preoperative staging. This risk is more significant with adencarcinoma, as all the patients who developed early metastasis in this series had either adencarcinoma or small cell carcinoma. An extensive preoperative metastatic work-up including CT scan of the brain is recommended in these cases.

Survival in NSCLC is closely related to the stage of the disease. Little controversy exists regarding the advantage of surgery in the treatment of stage I and II lung cancer. For advanced stages, surgery continues to offer the best long-term survival and with complete resection, 5-year survival of upto 40% has been achieved in some studies. However, complete resection is possible in only about 2O% of the cases. In our study, a complete resection was possible in all patients with histological proven negative nodes by mediastinoscopy, should not contra-indicate surgery, as this offers the only best chance for survival in these cases.

Non-small cell lung cancer has a dismal outlook and outcome with a poor survival. Extended surgical resection can be performed safely in locally advanced but lymph node negative cancer without any added morbidity or mortality. There is a need for the development of a proper screening and staging system to evaluate and manage the disease at an early stage. The development of a novel chcmotherapeutic or immune-modulating agent may change the ultimate outlook.

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