

LUNG CANCER AMONG YOUNG MALAYSIANS

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SUMMARY

1. *The findings in 48 young patients with lung cancer are presented.*
2. *Sixty-two percent were non-smokers.*
3. *Adenocarcinoma was the commonest histological subtype.*
4. *Only one was operable at diagnosis.*
5. *Avoidable delays in diagnosis occurred in 17%, including 10% who were initially given antituberculosis therapy.*
6. *This report aims to increase awareness of lung cancer in the young, to suggest aggressive pursuit of a definitive diagnosis, and to point out the danger of unwarranted therapeutic trials and delays in diagnosis in this setting.*

INTRODUCTION

The prevalence of lung cancer has increased rapidly in the last three decades to the point where it is currently the leading cause of cancer death in the United Kingdom, Europe as well as the United States of America.^{1,2,3,4} Recent reports suggest a similar trend in Asian countries like Singapore, Hong Kong, Taiwan and Japan^{4,5} and in Malaysia.⁶

Being mostly a disease of middle aged and elderly smokers, it is in this group that doctors

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harbour a high index of suspicion. This report reviews experience with the condition in young adults seen at the University Hospital, Kuala Lumpur, and discusses its implications.

MATERIALS AND METHOD

In a previous study on lung cancer at the University Hospital,⁷ it was noted that a small proportion was relatively young, and we have continued periodically to see such patients aged forty years and below. For this study, forty years was adopted as the upper limit, as was done in the study by Ganz, Vernon and Preston,⁸ and this report is based on adult patients seen between 1967 and 1987.

Patients suspected to have lung cancer were hospitalised for workup, diagnosis and assessment, and reviewed during weekly chest rounds. Hospital records of admissions for lung cancer were scrutinised to ensure that no patient in this age group was missed, and the appropriate details were extracted from the case files and radiographs. Patients in whom there was a possibility that the lesions were metastatic, and those who had other specific types of neoplasms were excluded. Forty eight young patients were diagnosed to have lung cancer during this period. The diagnosis was based on clinical and radiological features with histological confirmation in forty four. Tissue diagnosis was not possible in the following four patients:—

1. A 35 year old male smoker (16 daily for 20 years) with two months of cough and right sided neck swelling due to hard enlarged lymph nodes. The chest x-ray (CXR) revealed a mass in the right upper lobe. He discharged himself against advice.
2. A non-smoking male age 39 with a month of cough, dyspnoea, chest pain and fever.

His CXR showed a right upper lobe mass lesion, and hilar prominence. He was in a terminal state and died before tissue diagnosis. Autopsy was refused.

3. A 40-year old male, heavy smoker (60 cigarettes daily) with cough, haemotysis, dyspnoea and chest pain for four months. He had a massive bloody pleural effusion on the right side and died suddenly. Autopsy was refused.
4. A 37 year old smoker (20 cigarettes daily for 25 years) with cough, dyspnoea, hoarseness and weight loss for three months. He had superior vena caval (SVC) obstruction, and CXR showed collapse/consolidation of the right upper lobe, hilar prominence and diaphragmatic palsy. He absconded.

A fifth patient, a 31 year old male non-smoker, with nine months of headache and fits died in hospital of cerebral metastases. He had a pneumonectomy elsewhere three years earlier for proven lung cancer, the exact histological type of which could not however be traced.

Clinical features at presentation were classified according to the symptomatic groups described by Feinstein,⁹ into (i) primary, due to the local effects of the tumour, (ii) systemic or general and (iii) metastatic symptoms, including those representing direct spread beyond the primary site.

The anatomic extent of disease was classified as described by the American Joint Committee for cancer staging and results reporting (1974)¹⁰ into stages I, II and III.

RESULTS:

1. Age:

The youngest patient was 20 years old; the age distribution within the group is shown in Figure 1. As might be expected, patient numbers were larger at the older end of the scale. The average age of all our patients with lung cancer in our previous study was 60 years.⁷

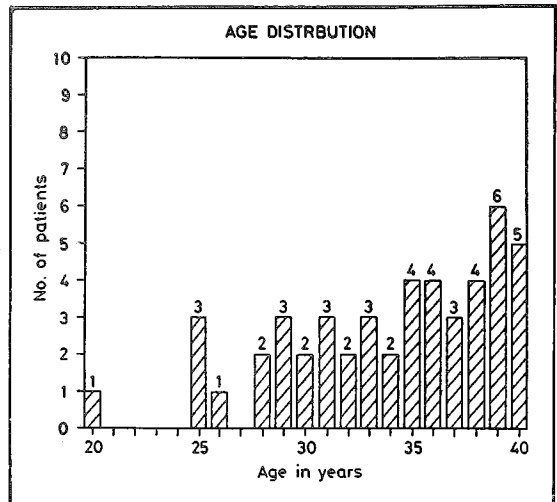


Figure 1

2. Sex:

Seventy-two percent (35 patients) were male, giving a male to female ratio of 2.7 :1, essentially similar to what was found in our patients of all ages.⁷

3. Smoking:

Information on smoking habits was not available in one male patient. Of the rest, 62% (29 patients) were non-smokers. Half of the males, and one of thirteen women smoked. These figures contrasted with the preponderance of smokers (78%) in our patients with lung cancer as a whole.⁷

4. Race:

The ethnic distribution in the forty-eight compared to all patients from the previous study is shown in Table I. Although Chinese formed the largest group, this ethnic predominance was less marked in the young.

5. Clinical Features

(a) Duration of Symptoms: Two patients were asymptomatic and discovered accidentally, one during appendicitis and one following a routine chest film for asthma. Sixty-four percent had symptoms less than six months, and seventy-nine

TABLE I
ETHNIC GROUP:
YOUNG GROUP vs. ALL PATIENTS (7)

Ethnic Group	% Patients	
	Young	All Patients
Chinese	65	82
Malay	25	11
Indian	8	5
Others	2	2

TABLE II
DURATION OF SYMPTOMS

duration in Months	No. of Patients
Unknown (asymptomatic)	2
< 1	3
1 - 3	14
3 - 6	14
6 - 12	7
12 - 24	5
> 24	3
Total	48

percent less than a year (Table II). This was similar to the duration of symptomatology in our patients of all ages.¹

(b) Clinical Features at Presentation

The incidence of the various symptom classes and features are shown in Table III. More than one class of symptoms were present in many. The commonest symptoms were cough 73%, weight loss 56%, haemoptysis 35%, dyspnoea 33%, fever 31%, chest pain 29% and malaise 21%. The number of patients presenting with the various symptom classes or combinations thereof are shown in Table IV. Seventy-nine percent had primary, 56% general, and 41% had symptoms or features suggesting inoperability.

TABLE III
PRESENTING CLINICAL FEATURES

Clinical Feature	% Patients
I Asymptomatic	4
II Primary	
cough	73
haemoptysis	35
dyspnoea	33
chest pain	29
III General	
weight loss	56
fever	31
malaise weakness anaemia	29
clubbing	10
hypertrophic osteoarthropathy	2
neuromyopathy	2
IV Metastasis and Spread	
(a) local spread	
hoarseness	8
SVC obstruction	88
dysphagia	6
pericardial tamponade	4
Pancoat tumour	2
(b) Distant spread	
nodes	23
hepatomegaly	13
bone pains	10
bony swellings/lumps	10
skin lumps	8
intracranial space occupying lesion	6
proptosis	2

TABLE IV
SYMPTOM CLASSES AT PRESENTATION

Presenting Classes or Combinations	% Patients
Primary only	25
Primary + General	29
Primary + General + Metastatic	18
Metastatic + General	10
Primary + Metastatic	8
Metastatic only	6
No symptoms	4
Total	100 %

6. **Radiological Features at Presentation** and their frequency are set out in Table V. The lesion was right sided in 26 patients (54%), and on the left in 17 (35%). Of the remaining five, four had bilateral abnormalities including two with alveolar cell carcinoma, and one with haemoptysis and pericardial effusion died suddenly before bronchoscopic evaluation. The commonest abnormalities were pleural effusion 40%, hilar prominence 31%, consolidation/collapse 27% and a mass lesion 25%. Solitary pulmonary nodules (coin lesion) and cavitation were uncommon features, being seen only in one patient each.

TABLE V
RADIOLOGICAL FEATURES

Feature	% Patients
Pleural effusion	40
Hilar mass	31
Consolidation / collapse	27
Mass lesion	25
Mediastinal widening	23
Bony lesions	15
Mass + hilar enlargement	13
Phrenic palsy	6
Infiltrate / pneumonitis	4
Pericardial effusion	4
Coin lesion	2
Cavity	2

7. Diagnostic methods, histology and staging

Methods employed for tissue diagnosis and their yield were as follows: effusion cytology 25%, bronchoscopy 23%, thoracotomy 18%, sputum cytology 18%, lymph node biopsy 16%, pleural biopsy 12%, needle biopsy 12%, biopsy of skin nodule 7%, biopsy of bony metastatic lesion 7%, bone marrow biopsy 5%, liver biopsy pericardiocentesis, and craniotomy 2% each.

This histopathological type and their frequency in the young group as opposed to all patients from the previous study⁷ are shown in Figure 2. The

most obvious feature was a higher incidence of adenocarcinoma in the younger group. This was true both for smokers (44%) and non-smokers (42%). The proportion of smokers in each histological group of young patients was: adenocarcinoma 37%, squamous 38%, large cell 57%, small cell two of three patients, anaplastic/undifferentiated: none.

One patient had stage I disease at diagnosis but refused surgery. One had stage II disease, but was unfit on account of coexisting renal failure. Ninety-six percent had stage III or clearly inoperable disease, very similar to what was seen in all our patients.¹

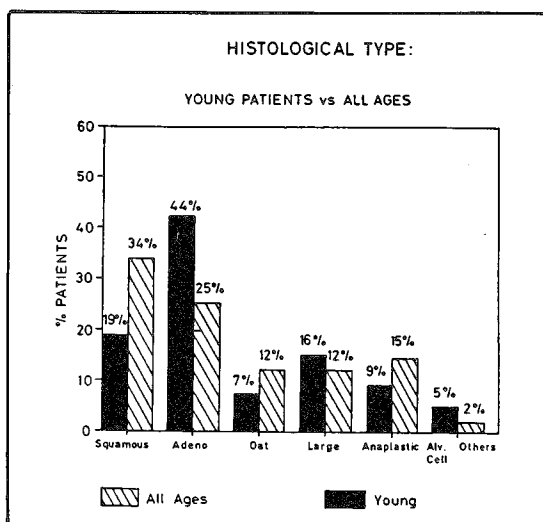


Figure 2

8. Some Pertinent Observations

The group which included three non-smoking doctors with inoperable adenocarcinoma, were being seen at an extremely advanced stage of the evolution of their diseases as evidenced by the staging at diagnosis and the fact that eight of the 48 died during their first admission here. Five were previously treated elsewhere as tuberculosis on clinical and radiological grounds without bacteriological evidence before being diagnosed as lung cancer. In three patients, delays in diagnosis were due to their initial refusal to have invasive investigations. Two of these patients

who were probably operable at first consultation returned later, clearly inoperable. Two absconded before completion of diagnostic workup.

Some findings with respect to the diagnostic methods and their yield merit comment. The low positive yield from bronchoscopy and sputum cytology were linked to underutilization of these procedures (38% and 56% of patients respectively). In the case of bronchoscopy, this was probably on account of the relatively less ready availability of the facility in earlier years. These investigations, and fine needle aspiration have been used regularly wherever appropriate since. The significant contribution to tissue diagnosis from the other methods reflect advanced disease.

DISCUSSION

Malignant solid tumours commonly known to affect the young include neuroblastoma, Wilm's tumour, sarcoma, nasopharyngeal carcinoma, lymphoma and embryonal cell carcinoma;⁷ lung cancer on the other hand, while being the commonest cancer in many communities,^{1,2,3,4} is predominantly seen in the sixth and seventh decades of life.^{3,12} There have however, been isolated reports of its occurrence in children ranging from ten months to thirteen years of age¹² and figures quoted for the proportion of patients below forty years of age vary from 1.7 to 6.1%,¹³ our experience being 5%.⁷

Several authors have found an increased number of women, and a lower male to female ratio in the young as opposed to all patients with the conditions,^{8,14,15,16,17,18} an observation that was not seen in this group. The percentage of Chinese in this group was lower than we found in all our patients in general.⁷

A notable finding in our young patients is that 62% were non-smokers, while at least 78% of all our lung cancer patients had smoked.⁷ Of relevance also is the increased percentage of adenocarcinoma, and the smaller numbers with the squamous variety; links with smoking are weakest for the former type, while the latter is seen almost exclusively in smokers.³ This pattern

of histopathology in the young has been noted by other authors,^{8,13,14,17,18,19} and the lower number of squamous cancers has been attributed to the longer induction period for this type.²⁰

Whereas there is little doubt about the importance of smoking as an aetiological factor in lung cancer,^{21,22} its role in the young where the duration of carcinogen exposure is likely to be much shorter, has been the subject of discussion.²³ Doll and Hill²¹ estimated that the carcinogenic effects of smoking generally appear after the age of forty five years, but emphasized later the importance of the age at the onset of smoking, the duration of the habit, and the number of cigarettes smoked.²⁹ In other series on young patients the percentage who were smokers ranged from 87 to 95,^{8,15-19,23} the overall impression being that heavy smoking was an important causative factor. This was also likely in some of our patients who had begun smoking early, and done so heavily for a relatively prolonged period. Nevertheless, in the non-smoking majority of this group the aetiology is unexplained, and could include genetic factors and individual susceptibility to environmental or other factors.²⁵ It is interesting in this connection that 50% of young patients with lung cancer reported by Larrieu et al¹⁸ had a family history of cancer.

There were no distinctive clinical or radiological features that set the young apart from other patients, except for the rather more frequent finding of fever (31%) in this group as opposed to 5% in patients of all ages. Through the common clinical features in our young patients were very similar in nature and frequency to comparable groups described by others, some have described a more advanced and virulent disease with a poorer prognosis in the young,^{14,16,18,19} possibly linked to age related factors. Relevant to this are published observations of the more aggressive behaviour of melanoma and breast cancer in the young,²⁰ and of the slower tumour growth rate, and the reduced frequency and extent of metastatic disease in elderly patients with lung cancer.²⁶ The poorer prognosis in the young may also be due to the

occurrence of more unfavourable histological types and the lack of aggressive diagnostic evaluation.²⁰ In our experience, both age groups had advanced disease at presentation as shown by their staging at diagnosis, but survival figures for our patients are unavailable as many were not followed up here. It would seem that the young patients did not differ much in clinical features; a higher index of suspicion for cancer in this age group may therefore be important for the earlier detection of a disease that has become so much commoner and yet remains usually fatal²⁴ despite the medical and technological advances of the last two or three decades.

The lung cancer patient familiar to most doctors is the elderly smoker, and moreover some standard textbooks on pulmonary disease^{27,28} quote forty as an age above which the likelihood of cancer gets proportionately higher, and below which it is less so, in the context of solitary pulmonary nodules. The doctor faced with a lung lesion may hence have a false sense of security when dealing with a young patient, compounded by features like fever and weight loss that may lead to inappropriate management such as a therapeutic trial for tuberculosis, losing valuable time.

Despite the generally poor prognosis, an earlier diagnosis is most important. The results of surgery in young patients with limited disease have not been more unfavourable than in all patients,^{17,18} and some groups^{18,19} have shown increased survival in young patients even with more extensive disease who were operated on, compared to those not treated surgically. Better fitness, relative freedom from intercurrent diseases common in older ages, and greater tolerance for radical surgery are factors that may allow a more aggressive approach in younger patients, and a lower operative mortality has been recorded in younger patients undergoing radical surgery.²⁹

It is suggested that in young patients with unusual lung lesions, every attempt be made to identify the disease. Heightened awareness of the occurrence of lung cancer among the young in

our community should prompt a greater sense of urgency and a more aggressive approach. Timely and appropriate utilisation of facilities like fiberoptic bronchoscopy, sputum cytology, fine needle aspiration of lung lesions, and if needed thoracotomy may yield a greater number who are resectable and better able to withstand surgery than their older counterparts.

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