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<td>Author(s)</td>
<td>Lam, B; Lam, WK; Lam, CL; Ooi, GC; Ho, JCM; Wong, MP; Tsang, KW</td>
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Adenocarcinoma of the lung in Chinese patients: a revisit and some perspectives from the literature

B Lam, W K Lam, C L Lam, G C Ooi, J C M Ho, M P Wong and K W Tsang

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Adenocarcinoma of the lung in Chinese patients: a revisit and some perspectives from the literature

B Lam, W K Lam, C L Lam, G C Ooi, J C M Ho, M P Wong, K W Tsang

Abstract

Aim—To establish an updated clinical profile of adenocarcinoma of the lung. Design—Retrospective review of clinical charts, chest radiography, and computed tomography of consecutive patients who attended Queen Mary Hospital in Hong Kong between June 1995 and December 1997. Results—In the 115 patients studied, 13% were <40 years of age (33.3% ever smokers). Haemoptysis is more common among patients with early disease, while finger clubbing was detected more commonly among smokers and ex-smokers. Most (98.3%) patients had abnormal chest radiology including presence of mass lesion, pleural effusion, collapse/consolidation, and effusion. Patients with adenocarcinoma were significantly more likely to be younger, female, in advanced disease (stage IIIIB and IV), non-smoker, and symptomatic on presentation (p<0.05) than those with squamous cell lung cancer (n=128). Conclusion—The clinical profile of Chinese adenocarcinoma patients should help clinicians in the diagnosis and management of these patients. (Postgrad Med J 2001;77:708–712)

Keywords: lung cancer; adenocarcinoma; clinical profiles

Lung cancer is the commonest lethal malignant disease worldwide and many cases are already at advanced stage on presentation.²³ Despite considerable medical advances, the five year survival for patients with lung cancer is merely 14%.² In Hong Kong, lung cancer accounts for more than 40% of all cancer deaths, and is the commonest lethal cancer in both genders. Adenocarcinoma has surpassed squamous cell carcinoma as the commonest histological type of lung cancer in many localities including Hong Kong.²³ Since the establishment of the Hong Kong Cancer Registry in 1990, adenocarcinoma has been consistently found to be the commonest histological lung cancer type, and has accounted for 30% of newly diagnosed lung cancer from 1990 to 1996. Although there have been some published series on the clinical profiles of patients with lung cancer over the last three decades,²³ four recent studies had addressed this increasingly important and common type of lung cancer in a systematic manner. We have, therefore, performed this review on Chinese patients with adenocarcinoma of the lung in Hong Kong. We aimed to establish an updated clinical profile of this disease with particular emphasis on presentation, symptomatology, and clinical staging, and compare these characteristics with patients with squamous cell lung carcinoma. Our experience with this series of patients should help clinicians have further insights into the clinical characteristics of those with adenocarcinoma of the lung.

Methods

SUBJECTS

The clinical charts, chest radiographs, and (whenever available) thoracic computed tomography of all patients with a final diagnosis of adenocarcinoma of the lung admitted to the Department of Medicine of the University of Hong Kong, between June 1995 and December 1997, were reviewed. Our institution is the largest teaching hospital in Hong Kong SAR and is a tertiary referral centre for all respiratory diseases including lung cancer. Inclusion criteria included histological or cytological evidence of adenocarcinoma of the lung and fulfilment of other diagnostic criteria.¹ These included the presence of the following: compatible plain chest radiograph and/or thoracic computed tomography; clinical features of bronchial carcinoma including appropriate symptoms and signs; compatible clinical or radiological metastatic lesions with or without cytological or histological evidence; and absence of other known malignancies or diseases that would otherwise explain the overall clinical picture. The presence of a possible non-pulmonary primary adenocarcinoma was excluded in each case by detailed symptomatic inquiry, full physical examination (including breast examination for women, testicular examination for men, and rectal examination), and appropriate investigations in the presence of appropriate systemic symptoms (including gastroscopy, colonoscopy, abdominal and pelvic ultrasound or computed tomography, and thyroid isotope scan).

CLINICAL FEATURES

Relevant clinical data were extracted from the charts of eligible patients. These included smoking history, presenting symptoms; presence or otherwise of constitutional symptoms (weight loss, lethargy, and malaise), respiratory symptoms including persistent cough (defined as daily coughing for more than week weeks), sputum production, haemoptysis, dyspnoea, chest pain, recurrent or unresolved pneumonia, hoarseness of voice, neck masses, bone pain, or other systemic symptoms. The abnormal signs found on initial physical examination of the respiratory and other systems were also recorded.

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Adenocarcinoma of the lung in Chinese patients

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stage II or less. The youngest patient was a
were therefore only six (5.2%) patients who
(63.5%) patients who had stage I, II, IIIA, IIIB,
TNM classification, there were one (0.9%),
less at the time of presentation. Based on the
cohort was 58 (22–87) years. A previous or
current history of cigarette smoking was
ex-smokers were reclassified
and contrast computed tomography using
standard criteria.11

DATA ANALYSIS
Summary statistics of the presenting clinical
and radiographic features were obtained by
cross tabulations. Ex-smokers were reclassified
as smokers. Patients were arbitrarily classified
as “young” if their age at presentation was 40
years or less, and as “early” presenters if the
TMN staging was II or less. Comparison of
data between groups of patients was by
chi-squared tests, Fisher's exact tests, and Mann-Whitney U test
where appropriate. Where appropriate statisti-
cal analysis was performed to determine if
“early” presenters of the disease would be
identified on the basis of information obtained
at presentation. A p value of <0.05 was taken as
indicative of statistical significance. The analy-
sis was performed using the Statistical Analysis
System package.

Results
SUBJECTS WITH ADENOCARCINOMA
From June 1995 to December 1997, a total of
354 consecutive new cases of primary cancer of
the lung were diagnosed in our centre. Of
these, 115, 128, 12, 74, and 25 patients were
histologically classified as adenocarcinoma,
squamous cell, large cell, non-small cell, and
small cell lung cancer. Among the patients with
adenocarcinoma of the lung, there were 40
women who had never smoked, who was 22
years of age on presentation with stage IV dis-

PRESENTING FEATURES OF ADENOCARCINOMA
The presenting features of these patients are
summarised in table 1. Five patients were
entirely asymptomatic at time of presentation
and were found to have abnormal lesions on
incidental chest radiographs. All these five
patients had unresectable (TNM stages IIIB or
IV) disease. Thirty seven, 47, and 25 patients
had one, two, and three or more symptoms at
presentation respectively. The commonest pre-
senting symptoms were persistent cough,
haemoptysis, malaise, and weight loss. Weight
loss was a common presenting feature (28.7%)
but it occurred largely in association with other
symptoms and was, therefore, not a specific
indicator of disease. Persistent cough and hae-

Table 1 Clinical symptoms at presentation in patients with adenocarcinoma of the lung

<table>
<thead>
<tr>
<th>Presenting features</th>
<th>No (% of patients</th>
<th>Mean duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>5 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Persistent cough</td>
<td>56 (48.7)</td>
<td>66.6</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>35 (30.4)</td>
<td>106.0</td>
</tr>
<tr>
<td>Malaise and weight loss</td>
<td>33 (28.7)</td>
<td>58.2</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>29 (25.2)</td>
<td>42.3</td>
</tr>
<tr>
<td>Chest pain</td>
<td>21 (18.3)</td>
<td>74.9</td>
</tr>
<tr>
<td>Neurological</td>
<td>9 (7.8)</td>
<td>47.2</td>
</tr>
<tr>
<td>Bone pain</td>
<td>8 (7.0)</td>
<td>38.5</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>7 (6.1)</td>
<td>25.9</td>
</tr>
<tr>
<td>Neck mass</td>
<td>5 (4.3)</td>
<td>82.2</td>
</tr>
<tr>
<td>Unresolved pneumonia</td>
<td>2 (1.7)</td>
<td>2.0</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>8 (7.0)</td>
<td>49.0</td>
</tr>
<tr>
<td>Signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>25 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>37 (32.2)</td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node</td>
<td>30 (26.1)</td>
<td></td>
</tr>
<tr>
<td>Clubbing-HPO</td>
<td>20 (17.4)</td>
<td></td>
</tr>
<tr>
<td>Collapse/consolidation</td>
<td>17 (14.8)</td>
<td></td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>8 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td>7 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Superior vena cava obstruction</td>
<td>5 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>6 (5.2)</td>
<td></td>
</tr>
</tbody>
</table>

HPO = hypertrophic pulmonary osteoarthropathy.
commonly found among previous or current smokers than those who had never smoked (p<0.005). Taken together, other than haemoptysis, there was no particular pattern of presenting symptoms, physical signs, and imaging findings that would distinguish between the “early” from the “late” presenters. There was no significant difference in the presenting symptoms between adenocarcinoma patients who were never or ever smokers (p>0.05, table 2).

OTHER INVESTIGATIONS IN ADENOCARCINOMA
Chest radiographs and computed tomography were available for review in 113 and 73 patients respectively (table 3). The commonest abnormality at presentation was a mass lesion, followed by pleural effusion. Computed tomography had positively identified a greater percentage of lesions compared with the chest radiographs (table 3). Diagnostic bronchoscopy was performed on 69 patients in whom 54 (78.3%) showed centrally located, that is, macroscopically visible, tumours. Concomitant presence of pleural effusion and abnormal cervical lymph nodes occurred in 58 (50.4%) cases.

Discussion
In this study, 13% of our adenocarcinoma patients were younger than 40 years of age on presentation and only 33.3% of these had ever smoked. Most of the female patients (80%) had never smoked. The presence of persistent cough and haemoptysis occurred in 64.3% of patients. Most patients had mass lesion or pleural effusion on the presenting chest radiograph. There were significantly more patients presenting with haemoptysis in early disease (TNM less than II) compared with more advanced TNM staging (p<0.001). Finger clubbing was found significantly more commonly among patients who had been smokers (p<0.005). However, there was no significant difference in the presenting features, physical or imaging findings between those who were 40 years or younger and those who were over 40. Unfortunately, all the patients who had adenocarcinoma diagnosed from incidence chest radiographs had advanced diseases as had the majority (89.3%) of cases who had a normal physical examination.

Most Western studies have consistently showed a low incidence of lung cancer in non-smokers and young subjects less than 40–50 years of age.12–14 However, our results show a preponderance of young female adenocarcinoma patients who have never smoked (table 3). This directly contrasts the results reported by the Edinburgh Lung Cancer Group, which reported that only 2% of 3070 patients had never smoked.14 The Edinburgh study also reported that adenocarcinoma and small cell lung cancers (predominantly adenocarcinoma) were significantly older than their counterparts (75.4 ± 68.0 years),14 although there was no such significant age difference in our adenocarcinoma patients (54 ± 50 years; table 2). In fact, our patients with adenocarcinoma were significantly younger than their counterparts who had squamous cell lung cancer (58 ± 69 years; table 2). There are also another nine studies, conducted in the 1960s and 1970s, on non-smoking Caucasian patients who had lung cancer.14–22 These showed that adenocarcinoma, squamous cell and small cell lung cancers accounted for 31%–69%, 6%–32%, and 7%–42% of all lung cancer types respectively. The characteristics of patients in the aforementioned studies do not correspond with those of the Chinese patients. A recent pathological survey in Hong Kong, which was not accompanied with analysis on clinical and radiological features, showed that adenocarcinoma accounted for 37.3% of all lung cancers and 50% of these cases were under 40 years of age.23

Although the association between smoking and lung cancer has been well established,24 a higher proportion of the patients with bronchial adenocarcinoma are non-smokers.14–22 The smoking rates for the general population in

Table 3 Imaging findings in 115 patients with adenocarcinoma of the lung

<table>
<thead>
<tr>
<th>Finding</th>
<th>No (%) having chest radiography (n=113)</th>
<th>No (%) having computed tomography (n=73)</th>
<th>No of findings detected only by computed tomography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>2 (1.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mass</td>
<td>81 (71.9)</td>
<td>55 (75.3)</td>
<td>11</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>45 (39.1)</td>
<td>28 (38.4)</td>
<td>7</td>
</tr>
<tr>
<td>Collapse/consolidation</td>
<td>18 (15.6)</td>
<td>18 (24.7)</td>
<td>11</td>
</tr>
<tr>
<td>Metastases</td>
<td>9 (7.8)</td>
<td>5 (7.8)</td>
<td>8</td>
</tr>
<tr>
<td>Mediastinal lymph node</td>
<td>7 (6.1)</td>
<td>39 (53.4)</td>
<td>34</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 (1.7)</td>
<td>3 (4.1)</td>
<td>2</td>
</tr>
</tbody>
</table>

†Indicates p<0.001 when compared with smokers who had the same histological type of lung cancer.
Adenocarcinoma of the lung in Chinese patients

Hong Kong were recently reported to be 2.9% for women and 27.1% for men respectively.\textsuperscript{24} In this study, 43.9% of the adenocarcinoma patients had never smoked and there were significantly more women than men who had never smoked (81.0% vs 12.8%), although there appears to be more female smokers in our cohort than in the general population. The high incidence of adenocarcinoma of the lung among non-smoking young Chinese women in Hong Kong also sharply contrasts that reported from Europe and North America.\textsuperscript{14–22}

The aetiologic factors for the high incidence of bronchial adenocarcinoma in women in Hong Kong, who are largely non-smokers, remain obscure.\textsuperscript{25} Studies of passive smoking in Hong Kong have given inconsistent results,\textsuperscript{26} and studies on other environmental inhaled agents such as fumes from kerosene stoves and insect burners have also been negative.\textsuperscript{27} Similarly, HLA antigen analysis and genetic studies to date have not been able to define the aetiologic factors.\textsuperscript{28–30}

The long duration of symptoms before diagnosis reflects a possible low index of suspicion of lung cancer among doctors and also the non-specific nature of many of the presenting symptoms. This was probably also perpetuated by the traditional clinical teaching of a remote probability of lung cancer among non-smokers. Although emergence of symptoms is usually indicative of advanced disease status and poor prognosis, carcinoma of the major bronchi might present early. Abnormalities were found in the presenting chest radiographs in 98.3% of the patients. This suggests that, although not being cost effective as a screening tool, chest radiography is a sensitive and cost effective initial investigation for patients with suspected disease. Our results therefore suggest that Chinese patients, particularly women, irrespective of their risk factor profiles, should undergo routine investigation for patients with suspected lung cancer.

We have also compared the clinical profiles of our patients with a concurrent cohort of patients with squamous cell lung cancer (n=128; 23 women; stages I, II, IIIA, IIIB, and IV were 1.6%, 3.1%, 20.3%, 39.1%, and 35.9% respectively). Patients with adenocarcinoma were significantly more likely to be younger (p<0.0001), of female gender (p=0.03), never smokers (p<0.001), in advanced disease, that is stage IIIB and IV (p=0.001), but less likely to be asymptomatic (p=0.001) when compared with their counterparts with squamous cell lung cancer (table 2). There were, otherwise, no significant difference in the presenting features for patients with adenocarcinoma and squamous cell lung cancer (p=0.05). A previous history of smoking was not associated with any significant difference in the staging of lung cancer on presentation in both histological types of lung cancer (p>0.05, table 2). Smokers with squamous cell lung cancer were significantly more likely to be asymptomatic at presentation than their counterparts with adenocarcinoma (p=0.003, table 2), although there is no obvious explanation.

Adenocarcinoma of the lung is an increasingly more prevalent lung malignancy and our experience shows that it predominantly affects women who have never smoked and are symptomatic on presentation with advanced disease. Our explanation on this series of patients should help clinicians in the evaluation of patients, particularly Chinese females, with lung cancer.

7 Hong Kong Cancer Registry. Cancer incidence and mortality in Hong Kong. Hong Kong: Hong Kong Cancer Registry, 1999.

Medical Anniversary

Sir William James Erasmus Wilson, 25 November 1809

Sir William James Erasmus Wilson (1809–84) was born in Marylebone High Street, London, the son of an Aberdeen naval surgeon who settled as a surgeon in Dartford, Kent. He was educated at Epsom College and St Bartholomew’s (1831), became a lecturer in anatomy and physiology at the Middlesex Hospital, assistant editor of the *Lancet* (1840), surgeon to St Pancras Infirmary, FRS (1845), President of the Medical Society of London (1878), President of the Royal College of Surgeons (1881), and was knighted in 1881.

He had a successful consulting practice as a dermatologist; it was said that when he entered a room those present would start scratching themselves. His numerous benefactions included restoring Swanscombe church, rebuilding the headmaster’s house at Epsom College, founding a scholarship at the Royal College of Music, and endowing a chair of dermatology at the Royal College of Surgeons. He paid £10 000 to transport Cleopatra’s Needle from Alexandria to the Victoria Embankment, London and £30 000 for a new wing and chapel to the Margate Seabathing Infirmary.

He died at his home in Westgate on 7 August 1884 leaving £200 000 to the Royal College of Surgeons. —D G James