Case Report

A Rare Case of Concurrent Multiple Primary Lung Cancer of Different Histological Types

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ABSTRACT

Occurrence of concurrent multiple primary malignancies with different histopathological presentations of the same organ at the same time is often not diagnosed and rarely reported in the literature. We present a case of multiple primary lung cancers with hepatic metastasis where the patient had a moderately differentiated adenocarcinoma of the right lower lobe and a moderately differentiated squamous cell carcinoma of the right upper lobe.

[Indian J Chest Dis Allied Sci 2011;53:181-183]

Key words: Multiple primary lung cancer, Lung cancer, Chronic arsenicosis, Adenocarcinoma, Squamous cell carcinoma.

INTRODUCTION

The incidence of multiple primary malignancies has shown an increasing trend in the recent years.[1] Primary lung cancer is commonly accompanied by malignancies of the lung, upper respiratory tract, breast, oesophagus, colon, rectum, stomach and cervix.[2] However, the diagnosis of concurrent multiple primary malignancies with different histopathological presentations in the same organ is often overlooked and missed if the patient is not thoroughly evaluated. We present a case of multiple concurrent primary lung malignancies of different histological types with metastasis.

CASE REPORT

A 45-year-old male presented with complaints of pain over the right hypochondrium, cough with intermittent scanty haemoptysis for three months and irregular low-grade fever for last one-and-a-half months and loss of appetite. He had noticed a small swelling over the right hypochondrium which was firm in consistency and tender. He was diagnosed to have pulmonary tuberculosis about 22 years back for which he was adequately treated. He was an employee of an oil mill and has been smoking around 20 to 25 *bidis* per day for the last 20 years. There was no history of alcohol abuse or any other addiction.

On physical examination, the patient was afebrile and had pallor and clubbing. There was no cyanosis, oedema or lymphadenopathy. Pulse rate was 90 per minute, blood pressure was 130/80mmHg and respiratory rate was 24 per minute. He had numerous hypomelanotic macules with characteristic "rain-drop-pigmentation" all over the body and a few palmo-plantar keratotic papules suggestive of chronic arsenicosis (Figure 1). On examination of chest, breath sounds were diminished in intensity over the right mammary, infra-axillary and infra-scapular areas without any associated adventitious sounds. Abdominal examination revealed tender hepatomegaly.

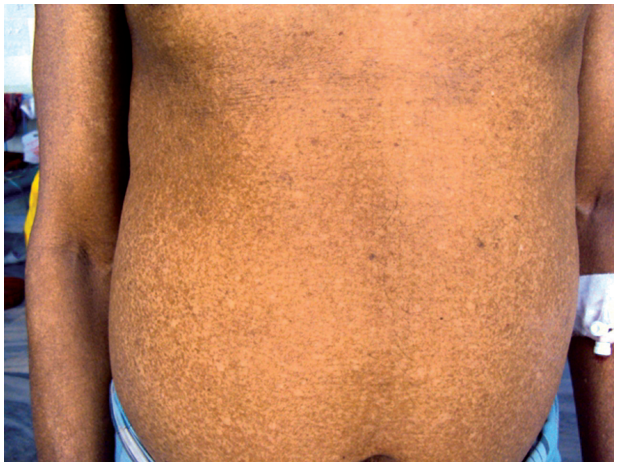

Figure 1. Numerous hypomelanotic macules over the trunk and upper extremities suggestive of chronic arsenicosis.

[Received: September 23, 2010; accepted after revision: January 25, 2011]

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Laboratory investigations revealed a haemoglobin of 9.8g/dL and there was mild neutroplilic leukocytosis. Blood sugar, liver and kidney function tests were within normal limits and the test for human immunodeficiency virus (HIV-1 and HIV-2) was non-reactive. Estimation of arsenic content of hair (normal: up to 0.8µg/g) and nail (normal: up to 1.2µg/g) was done by the 'weight digestion method' and was found to be 0.42µg/g and 0.98µg/g, respectively. Chest radiograph (postero-anterior view) showed a nodular lesion over the right mid zone and a thick-walled cavity over right lower zone (Figure 2). Sputum for

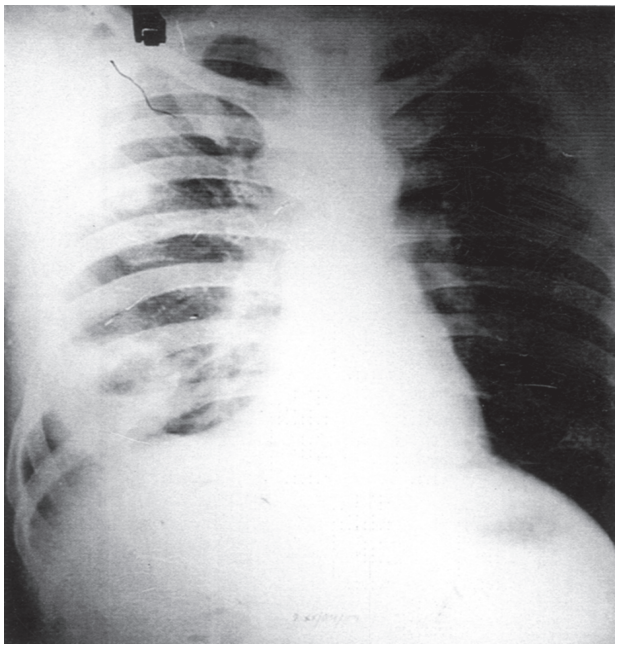

Figure 2. Chest radiograph (postero-anterior view) showing a nodular lesion over the right mid zone and a thick-walled cavity over the right lower zone.

acid-fast bacilli was negative in two consecutive samples. A computed tomography (CT)-guided fine needle aspiration cytology (FNAC) was done from the cavitating mass situated in the right lower lobe revealing features those were consistent with a moderately differentiated adenocarcinoma (Figure 3).

On fibreoptic bronchoscopy, deposits of fleshy reddish growth on both the sides of the carina and an irregular intra-luminal growth in the right upper lobe bronchus were seen. Biopsy specimens from the latter lesion showed features of invasive moderately differentiated squamous cell carcinoma (Figure 4). Ultrasonography of abdomen showed two heterogeneous space occupying lesions the in liver, the larger one measuring approximately 9.6cm x 6.5cm and the smaller one about 3.8cm x 5.1cm.

Sonography-guided aspirates from both the SOLs were done, which on examination were found to be metastatic deposits from adenocarcinoma. Upper gastrointestinal endoscopy and colonoscopy

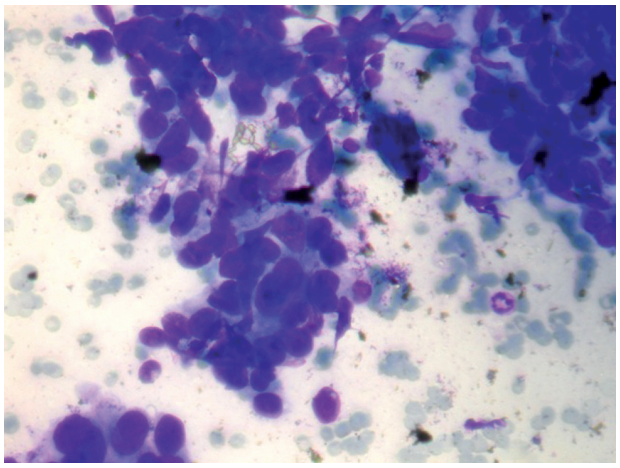

Figure 3. Computed tomography-guided fine nedle aspiration cytology from the right lung SOL shows clusters and discreet pleomorphic malignant cells having large hyperchromatic nuclei and variable amount of cytoplasm consistent with diagnosis of moderately differentiated adenocarcinoma (May-Grunwald×400).

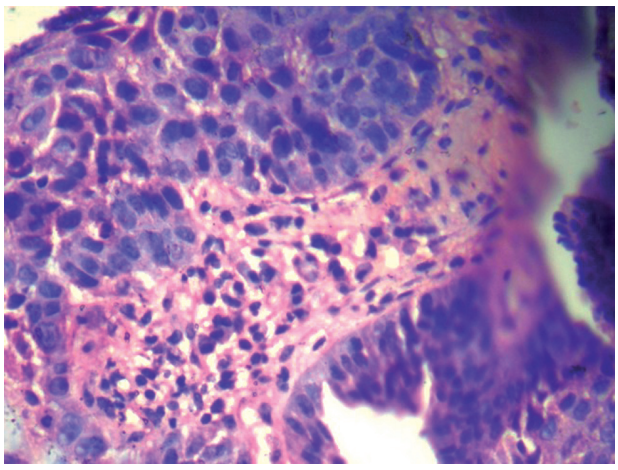

Figure 4. Bronchial biopsy from the right upper lobe endobronchial mass shows atypical pleomorphic epithelial cells with inappropriate keratinisation consistent with diagnosis of invasive moderately differentiated squamous cell carcinoma (Haematoxylin-Eosin×400).

examinations were not remarkable. Being inoperable, the patient was prescribed chemotherapy with cisplatin and etoposide. The patient has completed four cycles of chemotherapy and is doing well.

DISCUSSION

The occurrence of concurrent multiple primary bronchogenic carcinomas of different histopathological patterns is commonly appreciated but may become increasingly prevalent as early detection techniques and cancer therapy improve. The incidence of multiple lung cancers in the reported clinical series[3] ranges from 1% to 7% and autopsy studies[4] have revealed a higher incidence of 3.5% to

14%. It has been found that 10% to 32% of patients surviving resection for carcinoma of the lung may go on to develop a second primary tumour.[5,6] The lungs have been reported to have multi-centric, systemic, dually located primary cancers, just like any other paired organs, such as breasts and ovaries.[7] Among patients with multiple primary lung malignancies, synchronous presentation is less frequent than metachronous presentation.[7,8]

In cases of multiple synchronous lung tumours, it is often difficult to differentiate between multi-centric lung cancers, a single lung cancer with intra-pulmonary metastasis, or pulmonary metastasis from primary cancer in other organs, especially when multiple tumours are found in the same lobe. There are no specific clinical or radiological features that can differentiate multiple primary lung cancers and intra-pulmonary metastases. Establishing the diagnosis of multiple primary bronchogenic carcinomas requires demonstration of histologic, anatomic or temporal separation of the tumours. The diagnosis of multiple primary lung cancers was established in our case according to the criteria defined by Martini and Melamed,[9] which are in agreement with most of the studies in the literature describing second primary lung cancers. If the tumours are present at the same time, they must be separate and the histology must be different. If both tumours are histologically same, these are located in different lungs, lobes, or segments with no common lymphatics. There are no distant metastases present and these are considered to be two independent primary tumours. The most frequent pathologic associations are between squamous carcinoma and squamous carcinoma, squamous carcinoma and small-cell carcinoma and squamous carcinoma and adenocarcinoma.[8]

Environmental risk factors including smoking and exposure to asbestos, radioactive dust and chemical carcinogens are thought to be important factors in the pathogenesis of multiple primary lung malignancies.[10] Arsenic exposure at various levels has been linked to the development of lung cancer in many studies,[11-13] though the evidence is not conclusive.

Multiple methods of management, mainly resection combined with chemotherapy or radiotherapy should be adopted according to the staging, histologic types and biologic characters of the tumours (synchronous or metachronous; located unilaterally or bilaterally). The average survival was found to be 29 months in synchronous patients and 26.2 months in metachronous patients in one large study by Wu *et al*.[7]

The incidence of multiple synchronous primary lung malignancies may be more than reported. The key to early diagnosis of multiple primary lung cancers lies in clinical suspicion, detailed examination of the respiratory tract and regular follow-up of those who have undergone initial resection of a primary lung cancer.

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