Small Cell Lung Carcinoma Associated with Progressive Systemic Sclerosis

Kaushik SAHA; Arnab SAHA; Prabodh PANCHADHYAYEE; Mrinmoy MITRA; Tara Sankar MALIK; Pratik BARMA; Santanu GHOSH

aDepartment of Pulmonary Medicine, Burdwan Medical College, Burdwan, West Bengal, India

ABSTRACT

The association between progressive systemic sclerosis (PSS) and malignancy is uncommon. The possibility of development of small cell carcinoma lung (SCLC), among all the reported lung malignancies in PSS patients is lowest. A fifty-five year old non-smoker female diagnosed as PSS for 1 year presented to our outpatient department with dry cough for 2 months, shortness of breath for the last 1 month and progressive facial and right upper limb oedema for the last 15 days. Chest X-ray showed homogenous opacity in the right upper and mid zones of lung and the obliteration of both costophrenic angles. High resolution computed tomography (CT) of the thorax revealed a right upper lobe lung mass with bilateral minimal pleural effusion and the presence of bilateral reticular opacities, with basal predominance, associated with septal thickening, suggestive of interstitial lung disease of non-specific interstitial pneumonia pattern. CT guided fine needle aspiration cytology (FNAC) from the right upper lobe mass was suggestive of small cell carcinoma. Patient was improved after 6 cycles of chemotherapy with carboplatin and etoposide.

Keywords: interstitial fibrosis, progressive systemic sclerosis, small cell lung carcinoma

INTRODUCTION

Progressive systemic sclerosis (PSS) is a systemic connective tissue disorder; characterized by symmetric thickening, tightening, and induration of the skin of the fingers and skin proximal to the metacarpophalangeal or metatarsophalangeal joints. PSS is manifested by Raynaud’s phenomenon, fibrosis of various organs such as kidney, lung, heart, gastrointestinal tract and skeletal muscles (1). PSS is usually benign in case of isolated involvement of skin but if there is associated renal, cardiac or lung involvement, five year survival rate decreases to about 70% (2). Pulmonary manifestations usually include interstitial fibrosis and pulmonary hypertension; these may be present separately or combined (2).

Small cell lung carcinoma (SCLC) accounts for 15% of the lung cancers. Most cases of small cell lung carcinomas are due to smoking, although other causes can contribute as well. This type of lung cancer is more common in men than in women. Small cell lung cancer
SMALL CELL LUNG CARCINOMA ASSOCIATED WITH PROGRESSIVE SYSTEMIC SCLEROSIS

grows rapidly; the vast majority of patients already have extensive stage disease at the time of diagnosis.

The association between PSS and malignancy is uncommon. For the first time, in 1944, Hale and Schatzki showed a possible relationship between PSS and lung malignancy (3).

We are reporting a case of SCLC in a non-smoker female with PSS complicated with interstitial lung fibrosis.

CASE REPORT

A fifty-five year old non-smoker female was diagnosed 1 year ago with progressive systemic sclerosis on the basis of sclerodactyly, suggestive history of Raynaud’s phenomenon, digital ulcerations of both hands, skin thickening, raised titre of anti nuclear antibody (1:340) and strongly positive anti scl70 antibody. Nifedipine 30 mg / day was introduced after the diagnosis. The patient presented to our outpatient department with dry cough for 2 months, shortness of breath for the last 1 month, and progressive facial and right upper limb oedema for the last 15 days; no hemoptysis or weight loss were noted.

The physical examination revealed the presence of pallor, clubbing, thickening with tightening of facial and palmar skin suggestive of PSS (Figure 1a and b), facial puffiness, non-pulsatile engorged neck veins, and tortuous dilated superficial thoracic veins with the venous flow directing towards the umbilicus suggestive of superior vena cava obstruction. Examination of the respiratory system showed dull percussion note, diminished vocal resonance and diminished breath sounds over the right upper anterior thoracic and upper posterior thoracic areas suggestive of a space occupying lesion in the upper lobe of the right lung. We also observed velcro-like fine end inspiratory crackles over bilateral infra axillary and infracapular area suggestive interstitial lung disease. Rest of the examination was considered normal.

Blood investigations revealed normocytic normochromic anaemia with haemoglobin 9.0 g/dl. Her blood tests, glycaemia, renal and liver function tests, were normal. Echocardiography didn’t reveal any pulmonary hypertension. The chest X-ray showed homogenous opacity in the right upper and mid zones of the lung and obliteration of both costophrenic angles. High resolution computed tomography (HRCT) of the thorax revealed a right upper lobe lung mass with bilateral minimal pleural effusion and the presence of bilateral reticular opacities, with basal predominance, associated with septal thickening suggestive of interstitial lung disease of non-specific interstitial pneumonia pattern (Figure 2A). Pulmonary function test showed restrictive pattern (forced expiratory volume in one second (FEV1) / forced vital capacity (FVC) 92%, FEV1 80% and FVC 65%). Ultrasonography (USG) guided pleural fluid analysis showed lymphocytic exudative pleural effusion with presence of malignant cells. CT guided fine needle aspiration cytology (FNAC) from the right upper lobe mass lesion showed malignant cells in dispersed pattern with focal clustering adherent to vascular fragments, fine granular chromatin and occasional nuclear moulding suggestive of small cell carcinoma (Figure 2B). Fiber-optic bronchoscopy revealed a constricted right upper lobe bronchus due to compression from outside without any intraluminal growth. The diagnosis was confirmed by immunohistochemistry staining of the specimen, which was positive for cytokeratin and epithelial membrane antigen and negative for thyroid transcription factor 1. The patient was treated with a chemotherapy regimen consisting of carboplatin and etoposide. After 6 cycles of chemotherapy there was clinical improvement with a decrease in lung mass on chest x-ray.

DISCUSSION

In 2001 Yang et al showed that the most frequent type of lung cancer among the PSS patients is adenocarcinoma or bronchioalveolar cell carcinoma (BAC) when they reviewed 96

FIGURE 1. Face examination of the patient showing fish mouth opening, glistening of skin and engorged jugular vein (A). Hand examination of the patient showing tightening of the skin with digital pitting (B).
reported cases of systemic sclerosis associated with lung cancers (4). The possibility of development of small cell carcinoma amongst all the reported lung malignancies in PSS patients is lowest as in our case (5). There are few studies which have shown that lung cancer can occur in the presence of pulmonary fibrosis as the fibrosis is responsible for the subsequent malignant transformation (6,7). Our patient also had interstitial fibrosis which may be the inducing factor for the development of SCLC. The possible pathophysiology is the atypical proliferation of alveolar epithelium which usually occurs near the fibrotic lung tissue (8). Indeed, lung cancer may be associated with interstitial fibrosis, but in the presented case, both the duration and the severity of fibrosis are not as supposed. The diagnosis of PSS is only one year (we may estimate that the duration for the mass formation and the SVC syndrome may be similar in time) and also the pulmonary function test is roughly normal when considering that there is also atelectasis.

Although the linkage between lung fibrosis (either idiopathic / PSS or post tuberculosis) and lung cancer was demonstrated in large series of patients, the mechanisms are still intriguing, being considered either due to the non-specific inflammation (the potential pathogenic mechanisms indicate that recurrent injury and inflammation result in genetic alterations that predispose to lung cancer) or to more specific factors (like metal exposure in pneumoconiosis or active / passive smoking associated) (9).

Most of the lung cancers which are associated with interstitial pneumonia usually develop in heavy smokers and are located in the peripheral lung field. In our patient, lung cancer was also associated with interstitial lung disease, but she was non-smoker and the lung mass was centrally located. Bronchoalveolar carcinoma is the most common histological type of lung cancer associated with PSS, followed by squamous cell carcinoma, small cell carcinoma, anaplastic carcinoma and mesothelioma (9). A small cell lung carcinoma is thus a rare entity in PSS.

Chemotherapy alone or combination of chemotherapy and radiation therapy is the mainstay of treatment of small cell lung cancer (10). In a study by Ohe Y et al, presence of pulmonary fibrosis on chest x-ray was mentioned as a risk factor for radiation therapy related death in lung cancer patients (11). There is no concurrent data available in literature regarding the risks of using radiation therapy for lung cancer treatment in patients having interstitial lung disease. We avoided radiation therapy in our patient due to presence of pulmonary fibrosis in her chest radiography and considered treatment with chemotherapy alone.

CONCLUSION

Survival in case of PSS is dependent on multiorgan involvement. Small cell lung carcinoma is a rare entity in a PSS patient. Radiation therapy was avoided in our patient due to presence of pulmonary fibrosis in her chest radiography and chemotherapy was safe and efficient. A complete surgical resection was not considered due to both the histologic type of cancer and mediastinal extension.

Conflict of interests: none declared.
Financial support: none declared.
REFERENCES