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Bronchogenic Carcinoma in a Scleroderma Patient with Multiple Metastases: One Case Report

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Introduction

The association between pulmonary interstitial fibrosis and the development of bronchogenic carcinoma in a patient with scleroderma has been reported rarely[1]. It is hypothesized that intense epithelial proliferation that is accompanied by the fibrotic process increases the occurrence of carcinomatous changes[2]. We report the case of a patient who presented with 3-year history of Raynaud's phenomenon, gradual tightening of the skin which was ignored by the patient and her family members, and a 2-week history of severe respiratory distress with left shoulder and upper back pain followed by the development of paraparesis. After a series of examinations, the patient was diagnosed with scleroderma and simultaneously with bronchogenic carcinoma and multiple distant metastases.

Case Report

A 45-year-old, Hindu female, who had one 14-year-old son, presented to us with shortness of breath. The patient also complained that 3 years ago she had episodic severe lower extremity cramping pain followed by typical Raynaud's phenomenon in both the upper and lower limbs and that the severity of the symptoms had gradually increased. She was treated for her symptoms by a local physician, but no further evaluation was performed. One year ago she experienced a bout of severe respiratory distress accompanied by cough, sputum, and high fever and was admitted to another hospital where she received antibiotics and underwent further examination, including an HRCT scan of the chest, which was remarkable for the interstitial ground glass appearance and fibrosis (Fig.1). The patient was discharged without a diagnosis and there was no follow-up.

The patient presented to our institution with complaints of high fever and severe respiratory distress lasting for 2 weeks, which was preceded by left shoulder pain, swelling and a dull aching pain in the upper part of the back. Her oxygen saturation was 92%; therefore, oxygen and antibiotics were given. The patient was anemic and had skin tightness in the face and fingers with pigment changes in the

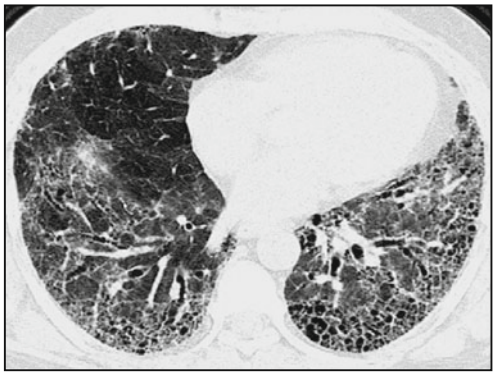

Fig.1. HRCT scan of chest showing bilateral interstitial ground glass appearance and fibrosis.

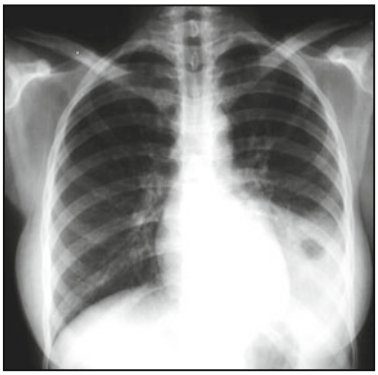

Fig.2. The chest x-ray (PA view) showing shrinking lung volume with bibasilar patchy opacities and a homogeneous opacity in the left lower lobe.

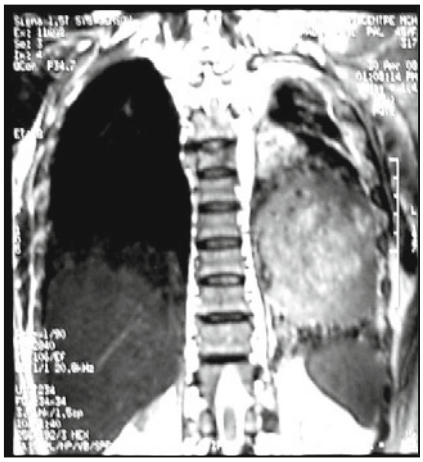

Fig.3. T2-weighted coronal view of MRI of the chest with abdominal screening, showing a fairly large mass at left lower lobe with irregular margins and a heterogenous signal change. Thoracic-5 vertebra shows compression collapse along with a right paravertebral soft tissue mass.

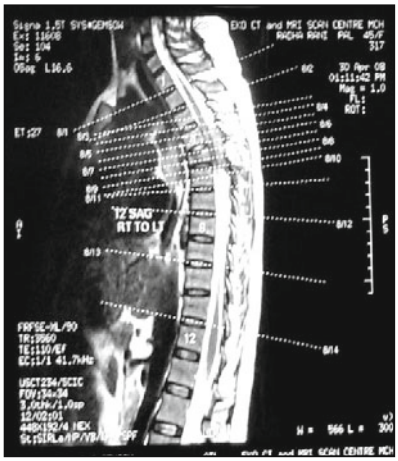

Fig.4. MRI of the vertebral column (saggital view) shows altered signal intensity of thoracic-4 and 5 vertebra with spinal chord compression.

skin, typical of scleroderma. There was digital resorption of the finger pulps. She had a palpable lymph node in the left supraclavicular area, a respiratory rate of 40/min, bilateral crepitation with bronchial breath sounds at the base of left lung, and concurrently an erythematous, hot, tender and swollen left shoulder joint.

Laboratory studies showed PMN leukocytosis (80% of TLC-15500/cm), increased alkaline phosphatase (1076 IU/L, normal 53-128 IU/L), normal renal function, increased LDH (1044 U/L), positive ANA with a titer > 1 : 640 in a homogeneous fine speckled pattern, and strongly positive Anti Scl-70. Chest X-ray showed (Fig.2) decreased lung volume with bibasilar patchy opacities and a homogeneous opacity in the left lower lobe of the lung. The left shoulder joint shown in the same X-ray showed evidence of bony erosion near the head of the humerus. The patient responded partially to antibiotics, but one day she suddenly complained of paraparesis with pain in the back. Physical examination revealed spastic paraparesis at the thoracic-5 level. An MRI scan was performed which revealed the following (Figs.3 and 4): *i*) A large mass in left lung; *ii*) A paravertebral soft tissue mass around Thoracic 5-6 with collapse of the vertebrae and intraspinal encroachment; *iii*) An enlarged right suprarenal gland; *iv*) Soft tissue mass in the left shoulder.

CT-guided FNA of the left lung mass, the paravertebral soft tissue mass and of the soft tissue mass in the left shoulder showed features of lung carcinoma (small cell variant) with metastases at multiple sites. As a result, CT-guided FNA of the enlarged right suprarenal gland was not performed. Unfortunately, we did not have ample time to formulate a definitive management plan since the general condition of the patient deteriorated quickly, and because the patient died before definitive results from pathologic examination became available.

Discussion

Scleroderma is a chronic autoimmune multisystem disorder with unknown etiology[3]. It is a sporadic acquired disease affecting all races and is prevalent all over the world. Scleroderma, like other connective tissue diseases, exhibits prevalence in females, mostly in those of childbearing age and declines after menopause. Prevalance of lung complications in systemic sclerosis (SSc) are 65% and 50% in diffuse cutaneous SSc and limited cutaneous SSc, respectively[3]. The major pulmonary complications of systemic sclerosis are interstitial lung disease and PAH. Additional pulmonary complications of SSc include aspiration pneumonia, pleural disease,

spontaneous pneumothorax, drug induced pneumonitis, pneumoconiosis and cancer[3]. The coincidence of scleroderma and malignancy has been described, including the occurrence of lung carcinoma with long-standing interstitial pulmonary disease[1]. In one series of incidence of lung cancer in systemic sclerosis, the relative risk of lung cancer in patients with scleroderma was 16.5[1]. Most of the patients with the disease die of cardiopulmonary complications. Prognosis is worse in males, and the disease is diffuse as well. A twofold increase in the incidence of lung carcinoma has been documented in patients with systemic sclerosis, compared with that in the normal healthy population. A population based follow-up study carried out in 233 patients with scleroderma from the 6-county Uppsala health care region of Sweden for a period from 1955 to 1984 showed that among 233 patients in which 144 were female and 89 male, 22 patients developed cancer. The types of neoplasia in these patients were the following: lung cancer in 5 cases, breast cancer in 2, ovarian cancer in 1, lymphatic and hematopoietic cancer in 3, and non-Hodgkins lymphoma in 2. Of the 5 lung cancer patients, squamous cell carcinoma was in 3, adenocarcinoma in 1 and carcinoma not otherwise specified in 1[4]. Of note there was not a single case of small cell lung cancer reported in this study. But in our study it was a small cell carcinoma which is unique. Another study performed on 123 patients with scleroderma demonstrated that 14 cases had malignancies, and there were 3 cases of CREST syndrome with lung cancer and anti-centomere antibodies[5].

Metastasis to various extrathoracic sites had been observed (vertebrae, adrenal glands etc.) from primary lung cancer[6]. Bronchogenic carcinoma commonly metastasizes to areas outside the thorax, such as to the brain, liver, or skeletal bones is common and the incidence of > 95% of patients with small cell cancer of lung[6]. Bone is a common metastatic site for bronchogenic carcinoma. Usually, these metastases induce pain and other symptoms as it was in our study, which suggest a bony metastasis that requires radiologic examination of the suspected area for confirmation. Our patient also had adrenal metastases which observed in 20%-45% of cancer patients depending on the localization of the primary cancer[7]. Up to 40% of non-small cell lung cancer patients develop unilateral or bilateral adrenal metastases as the carcinoma progresses[8]. Our patient had small cell lung cancer. Lung and breast cancer have been frequently included in autoimmune diseases by recent epidemiological studies. Patients with systemic scleroderma should be examined carefully and attentively for these risks.

Pulmonary fibrosis presenting in scleroderma may increase the risk of lung cancer. Accurate systematic microscopic examination of lung scar tissue has shown areas of epithelial hyperplasia surrounding the fibrosis, and this in turn may be associated with unexpected carcinomatous change. The pathogenesis of the relatively small proportion of lung scar tissue in which a malignancy develops is not well understood and in many cases smoking history may be highly important. Growth factors implicated in fibrosis may be mitogenic in many cases and may excessively increase cellular division, resulting in malignant transformation[9]. On the other hand, the behaviour of normal cells may be affected by the changes in the extracellular matrix, which in turn plays an important part in cell growth and differentiation[10].

There is an association between malignancy and autoimmune disease though it is very rare. Various autoimmune phenomena have been found in malignancies, and conversely, malignant tumours are detected more frequently in autoimmune diseases. Though interstitial lung disease and PAH are the major significant complications of SSc but some studies including our study suggest that lung malignancy is not uncommon in patient of SSc. So we should remain vigilant regarding this fact during evaluation of patient with SSc. Proper evaluation and early initiation of therapy may alter the life expectancy of these patients.

Conflict of interest statement

No potential conflicts of interest were disclosed.

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