Case Report

Synchronous squamous cell carcinoma of lung and adenocarcinoma of esophagus in a patient with progressive systemic sclerosis: A case report and review of literature

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ABSTRACT

We report an extremely rare case of synchronous metastatic squamous cell carcinoma of lung and adenocarcinoma of esophagus in a 32-year -old, non-smoker, Asian male with progressive systemic sclerosis. The short history and rapid progression of both the malignancies and systemic sclerosis in our patient suggested the possibility that systemic sclerosis may represent a systemic manifestation of malignancy.

Key words: Adenocarcinoma esophagus, squamous cell carcinoma lung, systemic sclerosis

INTRODUCTION

Systemic sclerosis (SSc) is a connective tissue disorder, characterized by fibrosis of the skin and visceral organs due to collagen deposition. According to the results of international studies and several reports, it is frequently associated with neoplastic diseases, particularly lung and breast malignancy, but whether there is a causal relationship, or not, that is still controversial. Here, we report a very rare case of synchronous metastatic squamous cell carcinoma of lung and adenocarcinoma of esophagus in a 32-year-old, non-smoker, Asian male with progressive SSc. To the best of our knowledge, this is the first ever reported case of SSc associated with synchronous lung and esophageal malignancy.

CASE REPORT

A 32-year-old, non-smoking, Asian male, presented with complaints of gradually progressive dysphagia to solids for last 2 months, and pain in his left shoulder for last 1 month. He had no family history of cancer. The diagnosis of systemic sclerosis (SSc) had been established 6 months earlier by skin biopsy. He was positive for anti-centromere and anti-topoisomerase-I antibody. At the time of presentation with dysphagia, he also had arthralgia, dryness and thickening of skin and Raynaud's phenomenon, which were aggravated for last 1 month. He had undergone an upper gastrointestinal endoscopic (UGIE) examination, which revealed an ulceroproliferative mass in the lower third thoracic esophageal lumen, reaching up to gastro-esophageal junction. A biopsy obtained during endoscopy was interpreted histopathologically as well-differentiated adenocarcinoma [Figure 1], immunohistochemically which was negative for p63 and cytokeratin 5/6. Clinically, metastasis to the left humerus head was suspected, and he was advised for whole body positron emission tomographic (PET) scan, which showed a FDG avid (maximum standardized uptake value (SUV)- 7.3) ill-defined enhancing soft tissue lesion in the right hilar region along with FDG uptake (SUV maximum-6.1) and thickening involving distal esophagus and gastro-esophageal junction. There were also three other FDG avid lesions, involving left humerus head, left adrenal gland and right superior pubic ramus. Bronchoscopy guided biopsy was taken from the right hilar mass, histopathologically which revealed poorly-differentiated squamous cell carcinoma [Figure 2], which was immunoreactive for p63, cytokeratin

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5/6 [Figure 3] and cytokeratin 19. A computed tomography (CT) guided biopsy was taken from the left humerus head, histopathologically which showed metastatic squamous cell carcinoma. The patient therefore, was diagnosed as a case of synchronous metastatic squamous cell carcinoma of lung and adenocarcinoma of esophagus associated with progressive SSc. He was planned for palliative chemotherapy with Gemcitabine (1000 mg/m^2 iv on day 1), Cisplatin (75 mg/m^2 iv on day 1) and Paclitaxel (175 mg/m^2 iv on day 1), every 3 weekly. There was no subjective improvement after receiving 2 cycles of chemotherapy. The patient died after the third chemotherapy cycle due to gross disease progression.

DISCUSSION

The association of malignancy with collagen vascular diseases is well documented in medical literature. Especially, relation between dermatomyositis and malignancy is well-recognized.[1] Systemic sclerosis (SSc) or scleroderma is a connective tissue disorder, characterized by fibrosis of the skin and visceral organs. According to the results of international studies, scleroderma is frequently accompanied by neoplastic diseases, among which the most often occurring is the neoplastic pathology of the lung and breast. Association of SSc with some other malignancies, such as cancer of the esophagus, stomach, colon, uterus, prostate, malignant lymphoproliferative disorders and functioning carcinoid tumors have also been reported.[2-7] Malignancies, mainly in lung and breast, co-exist with idiopathic SSc or with SSc-like disorders, but not with localized forms of scleroderma (morphoea). Till date, the mechanisms connecting SSc and malignancies are not well understood. The occurrence of different types of cancer with SSc suggest different underlying mechanisms, including altered immune response, organ fibrosis, as a part of paraneoplastic syndrome, common genetic and environmental links, disease-dependent factors, tumor-derived biologic substances and therapies.[5,6] The process of sclerosis itself may favour cancer in certain sites, and a reaction between T cells and neoantigens formed during irradiation may be a possible explanation of the frequent development of localized scleroderma after breast irradiation.[5,8]

Gastrointestinal disease occurs in up to 90% of patients with SSc, with the esophagus being the most commonly affected organ. Heartburn, dysphagia, and gastroesophageal reflux is well documented in scleroderma. Esophageal disease in SSc is a common and difficult-to-treat problem.[9] In a retrospective analysis of Barrett's, metaplasia and adenocarcinoma of the esophagus in scleroderma, Katzka, *et al*. have reported that, Barrett's metaplasia of the esophagus occurs in one-third of patients with scleroderma and patients with scleroderma and Barrett's metaplasia have an increased risk of complications such as, stricture or adenocarcinoma.[10] Although, periodic endoscopic or radiologic surveillance, or both, of SSc patients with gastroesophageal reflux symptoms has been recommended

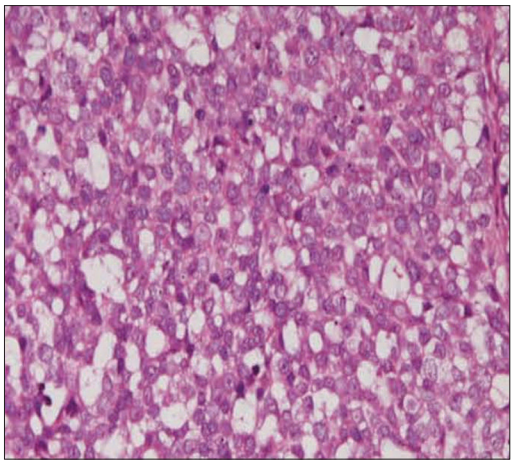

Figure 1: Histopathologic study of the esophageal biopsy showing well-differentiated adenocarcinoma with focal tubular proliferations (H and E, ×200)

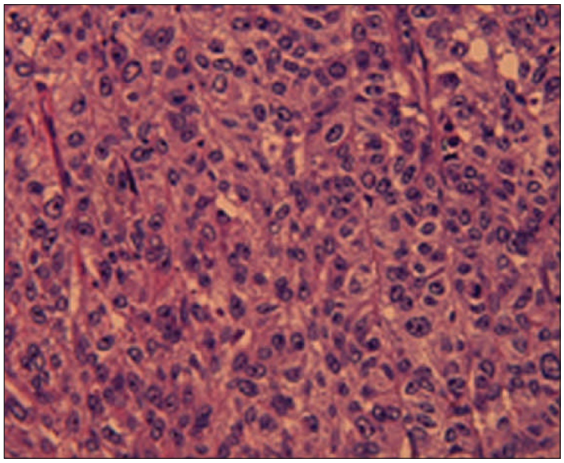

Figure 2: Histopathologic study of the bronchoscopic lung biopsy showing poorly- differentiated squamous cell carcinoma (H and E, ×200)

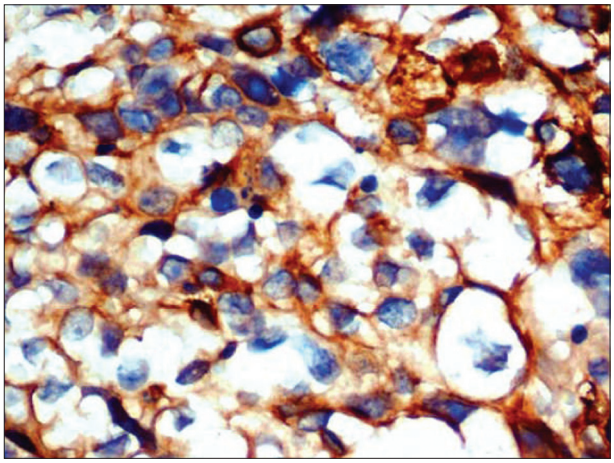

Figure 3: The focal strong cytoplasmic staining in >50% tumour cells of poorly-differentiated squamous cell carcinoma by cytokeratin 5/6. (×400)

by several authors for early detection of Barrett's mucosa and esophageal adenocarcinoma, but in their review of 680 closely followed SSc patients for esophageal carcinoma of all types, Segel MC, *et al*. did not find a significant increase in the frequency of esophageal carcinoma in SSc. Ultimately, they concluded that, regular surveillance for Barrett's esophagus and esophageal adenocarcinoma would not appear to be cost-effective because of the rarity of carcinoma, increased patient discomfort and expense, and the questionable benefit for long-term survival.[11]

Pulmonary involvement is the second most common visceral complication of SSc, after esophageal involvement. It has surpassed renal involvement as the most common cause of death. Interstitial lung disease and pulmonary vascular disease are the most commonly encountered types of lung involvement.[12] In a retrospective analysis of lung cancer in SSc, Colaci, *et al*. have reported higher frequency of lung cancer among SSc patients compared to general population, particularly within patients' subset with serum anti-Scl70 (also known as anti-topoisomerase- I) antibodies and lung involvement.[13]

The short history and rapid progression of both the malignancies and SSc in our patient suggested the possibility that SSc may represent a systemic manifestation of malignancy.

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