An emergence of adenocarcinoma in the lung following long-standing systemic sclerosis: a case report

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Abstract: Systemic sclerosis (SSc) is one of the chronic autoimmune diseases characterized by the infiltration of the excess collagen in various organs especially the skin. It is found associated with more prevalence of internal malignancies particularly the lung carcinoma. Herein we reported a case of adenocarcinoma confining within the lung in a Thai patient who had long-standing SSc. He was a 67-year-old Thai patient presenting with fever and productive cough for two weeks. He had been clinically diagnosed as having SSc based on the evidence of the sclerodactyly, the telangiectasia at the upper chest wall, multiple pitting scars at many finger tips and the interstitial lung disease and he had been treated with colchicine and azathioprine for 10 years. Besides the sclerodactyly and the telangiectasia, the lymphadenopathy and lung abnormality were not detected on the physical examination. The chest film and the computed tomography of the lung revealed a 2x2.8 cm mass at the left lower lung field. The pathology of the lung mass biopsied via the bronchoscopy was adenocarcinoma. LDH was 1,814 U/L. HIV antigen/antibody was negative. He was definitely diagnosed as having adenocarcinoma of the lung with an underlying long term SSc although he was not a smoker. He did not accept the further investigations and/or any treatment. Our case seemed to support the fact that the prevalence of cancers particularly the adenocarcinoma of the lung was significantly increased among SSc patients more than that of general population.

Key Words: Systemic sclerosis, Adenocarcinoma of lung

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Introduction

Systemic sclerosis (SSc) is a chronic autoimmune multisystem disease due to the accumulation of the excessive collagen produced by the activated fibroblasts and myofibroblasts in the various organs especially the skin\(^{(1)}\). Its diagnostic criteria consist of the skin thickening of the fingers of both hands extending proximally to the metacarpo-phalangeal joints including sclerodactyly, the fingertip ulcer or pitting scar, the telangiectasia, the pulmonary arterial hypertension or the interstitial lung disease and SSc related autoantibodies: anti-centromere, anti-topoisomerase I, anti-RNA polymerase III\(^{(2)}\). SSC usually runs chronic course so the emergence of many cancers has been recognized. In meta-analysis recruiting more than six thousand patients, the standardized incidence ratio of cancer increases among the patients with SSc more than the general population, 1.41 (95% confidence interval 1.18-1.68). And the origins of cancers are found from the lung, liver, hematologic system, urinary bladder, non-Hodgkin's lymphoma and leukemia\(^{(3)}\). For Thai patients, SSc seems to have milder clinical manifestations\(^{(4)}\) because within 25 months of follow-up, none of 116 patients with SSc died of malignancies\(^{(5)}\) but herein we report one case of adenocarcinoma confining within the lung of a Thai man.
who has been having long-standing SSc for ten years.

Case Report

A 67-year-old Thai man was admitted at the medical ward because of fever, productive cough with whitish sputum and fatigue for two weeks, no hemoptysis. He lost his body weight for 5 kg in 4 months. The physical examination revealed only multiple telangiectasia at the upper anterior chest wall and bilateral sclerodactyly without fever.

Prior this admission, he had been diagnosed as having systemic sclerosis based on the clinical combination of the sclerodactyly, telangiectasia, multiple pitting scars at the tip of many fingers and the interstitial lung disease and he had been regularly treated with colchicine as well as azathioprine for 10 years. He was not a regular smoker.

The blood tests included: Hb 6.8 g%, WBC 7,100/mm³, platelet 56,000/mm³, N 86.6 %, L12.5 %, MCV 87.1 fl, MCH 30.3 pg, LDH 1,814 U/L, normal liver function tests, creatinine 1.14 mg%, GFR 67 mL/min/1.73 m², ferritin 985.7 ng/ml, Hb A1c 5.6 %, morning cortisol 10.8 mcg/dl (normal 5-25), O₂ sat 96 %.

HIV antigen/antibody, HBsAg, anti-HCV, and VDRL were all negative, CEA 35.1 ng/ml (normal serum 0-3), CA 125 1,424.2 U/ml (normal serum 0-35), CA 19-9 1,846.9 U/ml (normal 0-37)

The fluid from bronchial washing via bronchoscopy: CEA-negative, CA-125 341.2 U/ml, CA 19-9 434.7 U/ml, the PCR for Mycobacteria: no MTB, no NTM, and no malignancy

The chest film that was later confirmed by the high-resolution computed tomography: macrocystic honeycomb reticular opacities, traction bronchiectasis, and focal ground opacities at subpleural region with apicobasal gradient distribution, consistent with usual interstitial pneumonia. An ill-defined lesion 2x2.8 cm at superior segment of left lower lung and 1x1.7 cm at lateral segment of right middle lung, lung masses could not be excluded. The multiple calcified mediastinal nodes size 0.5-1.5 cm which did not change as compared with the previous CT 6 years ago.

The bronchoscopy revealed one lung mass at the left lower lung and the microscopic pathology showed atypical cells positive for AE1/AE3, negative for CK5/6, equivocally positive for TTF-1, adenocarcinoma could not be excluded.

The bone marrow biopsy showed the moderately increased cellularity of erythroid and megakaryocytic series but markedly increased myeloid series, no hematologic malignancy.

He was clinically diagnosed as having adenocarcinoma of the lung with an underlying long standing SSc for ten years. He refused the further investigations and any modality of treatment. He was discharged home with symptomatic treatment.

Discussion

The mass in the lung of our patient was definitely diagnosed as adenocarcinoma based on the pathological findings of the tissue yielded from the bronchoscopic biopsy. The immunohistochemistry revealed positive for AE1/AE3 but negative for CK5/6 that was the important characteristic of squamous cell carcinoma(6,7) and equivocally positive for TTF-1 (thyroid transcription factor) which signified the lung as the origin of adenocarcinoma especially the terminal bronchioles(8).

In the meta-analysis including 7,000 patients
with SSc abroad, the relative risk to develop various cancers was 1.75 (95 % CI 1.41, 2.18) and the most common site of cancer was the lung\(^{9}\), RR 4.35 (95 % CI 2.08, 9.09)\(^{10}\), around one-third of all cases\(^{11}\) whereas the second common was hematological neoplasm, RR 2.24 (95 % CI 1.53, 3.29)\(^{10}\) and other less common cancers included the skin, liver, esophagus, oropharynx\(^{11}\). And the most common cell type of lung carcinoma was adenocarcinoma\(^{12}\). Our patient seemed to comply with all these facts despite being Thai people. However the increased incidence of the lung cancer in the SSc group was not found in the United States\(^{13}\).

Although the mechanism underlying the association between cancers and SSc had not yet been understood, it was found that SSc patients with positive anti-RNA polymerase I/III had the shortest interval between SSc and the onset of cancer\(^{14}\). And mechanisms of the association might be the interplay of multiple factors such as chronic immune stimulation as an autoimmune disease, the immunotherapy, and some shared genetic and/or environmental factors\(^{15}\).

The interstitial lung disease due to SSc probably aggravated by azathioprine therapy\(^{16}\) was presumed to attribute the higher incidence of lung cancer via various mechanisms such as the common pathogenesis of the 2 entities: the increased proliferation of fibroblast, increased resistance of apoptosis, unlimited cell proliferation, cellular immortality, increase of hyperplasia and metaplasia, mesenchymal cell transition, telomerase deficiency and DNA hypomethylation\(^{17}\).

**Conclusion**

The adenocarcinoma exclusively confining within the lung was diagnosed in a 67-year-old Thai man with the interstitial lung disease due to chronic systemic sclerosis under the treatment of azathioprine and colchicine for 10 years. The association between SSc and the lung cancer was discussed.

**References**

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