

Co-Existence Of Systemic Sclerosis And Adenocarcinoma Of The Lung With Cutaneous Metastasis In Young Female Patient

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ABSTRACT

Systemic sclerosis is a connective tissue disorder in which lung can be involved. There are various pulmonary manifestations like interstitial lung disease (UIP, NSIP), pulmonary arterial hypertension; recurrent aspiration etc. Lung malignancy is the well recognized manifestation, although rare. We are reporting a case of systemic sclerosis with adenocarcinoma of lung with cutaneous metastasis, which was diagnosed simultaneously. Diagnosis of systemic sclerosis was based on clinical appearance as well as on serological testes and lung carcinoma with cutaneous metastasis was diagnosed on cytological specimen from lung and skin swelling.

Key-words: Systemic sclerosis (SSc), FNAC, Adenocarcinoma.

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INTRODUCTION

Systemic sclerosis (SSc) is a heterogenous disorder characterized by endothelial dysregulation of fibroblasts resulting in excessive production of collagen and profound abnormalities of the immune system. These changes cause progressive fibrosis of the skin and internal organs, system failure and death.¹ Development of this diseases is associated with complex interactions between the endothelial cells, lymphocytes, macrophages, fibroblasts as well as with the action of a number of mediators, including cytokines, chemokines and growth factors-excreted by inflammatory and mesenchymal cells, which play an

important part in the development of fibrosis.²

The immunological reactions involved in the pathogenesis of systemic sclerosis are claimed to promote also the development of malignancy.³ The most common malignancies associated with SSc include lung and breast cancer and subsequently neoplasm of the hematopoietic and lymphatic system. Many studies have reported an increased frequency of neoplasm in patients with SSc, with lung carcinoma, bronchoalveolar carcinoma, being the most common.⁴ Metastasis is not uncommon in pulmonary neoplasm. The usual sites for metastasis of lung cancer

include hilar and mediastinal lymph nodes, adrenal glands, liver, brain, bone and skin.⁵ The incidence of skin metastasis from lung cancer varies from 1-12% of cases.⁶ All histological types of lung cancer may develop metastasis in the skin.⁷ As lung malignancy in systemic sclerosis is not common and skin metastasis in lung cancer is also not common, that is the reason we are reporting this case.

CASE REPORT

A 40 year non smoker female was admitted in respiratory and TB department with complaints of loss of appetite since 5 month, non-productive cough and low grade fever since 2 month, progressive dyspnea since one and half month, left sided back pain and change of voice since one month. Further exploration revealed decrease mouth opening and slowly progressive resorption of all the finger of both hand since one year, and slowly progressive increasing of swelling over right elbow since two month. She also gave history of numbness of extremities during cold season.

On examination, hands, feet and facial appearance were typical of SSc. There was large swelling of about 10 x 8 cm size over right elbow. Swelling was firm, non tender, immobile and its temperature was not raised. (Fig-1) Chest examination was consistent with moderate pleural effusion on left side. Except feeble peripheral pulse on left side, other systems examination were normal. On laboratory examination, hemogram was normal, blood sugar was 83

gm/dl, creatinine was 0.7 mg per dl, liver function test was within normal limit, electrolytes were normal and serum for HIV was nonreactive. Serum for dsDNA was positive (46.90 IU/ml), ANA was positive (4.60IU/ml) and anti-centromere antibody was also positive whereas, RA factor was negative and LE cell was not detected. Two sputum samples for microscopic examination were negative for AFB.



Figure-1: Elbow joint showing about 10 X 8 cm sized swelling, which was hard in consistency, immobile and non-tender. Skin overlies the swelling was normal and temperature of the swelling was also normal.



Figure 2: Chest x-ray PA view showing left sided pleural effusion with homogenous shadow along the left heart border.

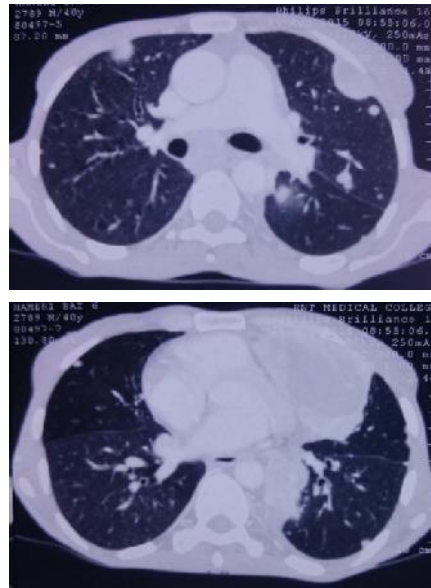


Figure-3: Multiple heterogeneously enhancing soft tissue density masses with internal necrotic areas of varying sizes in bilateral lung field; most of them being pleural based with largest in antero-inferior segment of left upper lobe.

Skiagram of the chest showed left sided pleural effusion with homogenous opacities along the left heart border. (Fig-2) Ultrasonography of abdomen and pelvis was normal except contracted gall bladder. CECT of the thorax showed multiple heterogenous enhancing soft tissue mass in both lung fields. There was no feature of interstitial lung disease. (Fig-3) MRI of right elbow joint with contrast showed heterogenous enhancing mass with necrotic / cystic area near elbow joint suggestive of malignant lesion. (Fig-4) X ray AP view of both hand showed acrolisis of the terminal phalanges of both hand. (Fig-5)



Figure-4: A well defined avid heterogenous enhancing mass lesion with necrotic cystic areas in the inter & intra muscular compartment of the lower arm near the elbow.



Figure-5: X-ray AP view showed acrolisis of terminal phalanges of all fingers of both hands.

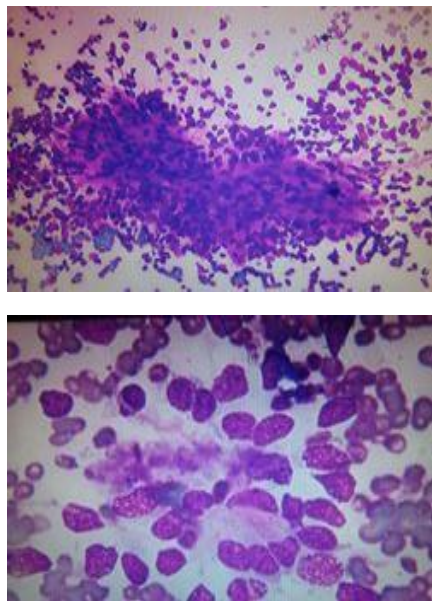


Figure-6 A & B: Photomicrograph of FNAC of lung (A low power, B high power) showing groups and clusters of malignant cells with glandular arrangement at places.

USG guided pleural aspiration was done which was exudative in nature with lymphocytic predominance cells but, pleural fluid ADA was 20U/ L. USG guided FNAC (fine needle aspiration cytology) of left lung mass was done and the cytology was suggestive of moderately differentiated adenocarcinoma. (Fig-6)

FNAC of the swelling over right elbow was also suggestive of moderately differentiated adenocarcinoma. The cytological picture of FNAC of the swelling over right elbow joint was identical to as that of FNAC of lung. On the basis of examination, dermatologist consultation along with blood investigations SSc was diagnosed and on FNAC adenocarcinoma of the lung was diagnosed and on FNAC of swelling, cutaneous metastasis was confirmed. During hospitalization we

manage conservatively then after confirmation of diagnosis patient was referred to radiotherapy department for further management.

DISCUSSION

Pulmonary involvement in systemic sclerosis is second in frequency only to esophagus involvement and has surpassed renal involvement as the most common cause of death.⁸ Pulmonary involvement is common in all SSc subsets, including diffuse cutaneous systemic sclerosis, limited cutaneous systemic sclerosis, and SSc sine scleroderma.⁹ Interstitial lung disease and pulmonary vascular disease, particularly pulmonary arterial hypertension are the commonly encountered types of lung involvement.¹⁰ Other manifestations are pleural effusion, pneumothorax, alveolar haemorrhage, aspiration pneumonia, etc. Apart from that, lung malignancy is the well recognized complication of SSc. The association between the neoplasm and SSc complicated with lung fibrosis was described for the first time in 1953 by Zatuchni et al.¹¹ The risk factors for development of malignancy in patients with systemic sclerosis are female gender, increased age and diffuse systemic sclerosis.¹² The relationship between the duration of scleroderma and the type of carcinoma has been described.¹³ The standardized incidence ratio for lung cancer is 7.4-16.5 times higher than in the general population.¹⁴

A variety of mechanism have been postulated in systemic sclerosis patients that

predispose them to malignancy: defect in immune surveillance, impaired clearance of cardiogens, increased susceptibility to malignant transformation due to epithelial hyperplasia, inflammatory secretion of reactive oxygen radicals and familial susceptibility.⁸ Occurrence of SSc and malignancy together has been noted in three modes: 1) when PSS is present many years before the appearance of tumor; 2) both appear at the same time and 3) tumor appears one or more years before SSc.¹⁵ In this index case lung malignancy and systemic sclerosis diagnosed simultaneously.

Bielfeld¹⁶ described 21 cases of neoplastic lesions in patients with SSc - in 8 patients the malignancy preceded SSc by 3 to 24 year, in five cases both of the diseases were diagnosed in the same year and in 8 patients SSc manifested 5-20 years before the neoplasm. Role of antibodies in causation of malignancy in patients with SSc is controversial. A study conducted in Australia demonstrated that there was no association between the incidence of cancer and the presence of anti-centromere antibodies (ACA) or anti-topoisomerase antibodies.¹⁷ The results of the study by Higuchi¹⁸ demonstrated that the presence of ACA significantly increased the risk of cancer in SSc patients. On the other hand French investigators¹⁹ contradicted this observation because they found no association between the frequency of neoplastic changes and antinuclear antibodies and anti-Scl-70-antibodies. It has been suggested that anti-Scl-70 antibodies present in 10-15% of patients with SSc, directed against

topoisomerase I, which is involved in DNA repair, may disturb the reparation of damaged genome, whereas anticentromere antibodies (ACA) found in 80% of patients with SSc may lead to chromosome damage. In both cases the risk of neoplastic transformation increases. On the other hand, E-selectin over-expression observed in SSc¹⁶, which influence the endothelial cells, may facilitate cancer invasion by stimulation of the angiogenesis. Moreover, the neoplastic cells may express E-selectin ligand and adhere to endothelial cells facilitating tumor metastasis; therefore SSc may promote the spreading of neoplasm.²

CONCLUSION:

Although rare, lung malignancy is well recognized manifestation of SSc. Lung malignancy in SSc may present as mass or mass with pleural effusion. Lung malignancy can occurred even in the area of interstitial lung disease. Symptoms are non-specific, so high index of suspicion is required while treating patient of systemic sclerosis with lung involvement. Metastasis in the skin may be the first sign of lung cancer, so physician should suspect metastases in case of any atypical and asymptomatic lesions in the skin in smokers as well as in non smokers and investigate accordingly.

REFERENCES

1. Hassoun M P. Lung involvement in systemic sclerosis. *Presse Med*, 2011; 40: e 3-e 17.
2. Tamby MC. New insight into the pathogenesis of systemic sclerosis.

- Autoimmune Rev. 2003;2:152-57.
3. Lee P, Alderich C, Wilkinson S, et al. Malignancy in progressive systemic sclerosis- association with breast carcinoma. *J Rheumatol.* 1983;10: 665-66.
 4. Talbott JH, Barrocas M. Carcinoma of the lung in progressive systemic sclerosis: a tabular review of the literature and a detailed report of the roentgenographic changes in two cases. *Semin Arthritis Rheum.* 1980;9: 191-217.
 5. Golijan EF. Rapid review pathology. 2nd ed. St. Louis: Mosby; 2006:321-4.
 6. Hidaka T, Ishli Y, Kitamura S. Clinical features of skin metastasis from lung cancer. *Intern Med.* 1996;35:459-62.
 7. Laura Pajaziti, Syzana Rexhepi Hapciu, Shkendije Dobruna, Naim Hoxha, Fisnik Kurshumliu and Artina Pajaziti. Skin metastases from lung cancer: a case report. *BMC Research Notes.* 2015; 8:139.
 8. Maria do Scocorro, Teixeira Moreira Almeida. Scleroderma Lung Disease- Other Lung Complication in systemic Sclerosis. *Almeida Rheumatology.* 2012;S:1-5.
 9. Le Roy E C, Black C, Fleischmajer R, et al. scleroderma (systemic sclerosis): classification, subsets and pathogenesis. *J Rheumatol.* 1988;15:202-05.
 10. Le Pavec J, Launay D, Mathai S C, Hassoun P M, Humbert M et al. Scleroderma lung disease. *Clin Rev Allergy Immunol.* 2011;40:104-16.
 11. Zatuchni J, Campbell WJ, Zarafonitis CJD. Pulmonary fibrosis and terminal bronchiolar carcinoma in scleroderma. *Cancer.* 1953;6:1147-58.
 12. Wooten M. Systemic sclerosis and malignancy: a review of literature. *South Med J.* 2008;101:59-62.
 13. Benedek T G. Neoplastic associations of rheumatic disease and rheumatic manifestations of cancer. *Clin Rheiatr Med.* 1988;4:333-55.
 14. Rosenthal A, McLaughlin JK, Gridley G, Nyren O. Incidence of cancer among patients with systemic sclerosis. *Cancer.* 1995;76:910-14.
 15. Janmcja A. K., Tandon, Sanjeev Gupta, K.B. et al. lung malignancy in progressive systemic sclerosis. *Indian Journal of Tuberculosis;* 1998,45,161-63.
 16. Bielefeld P. Sclerodermie systemique et cancers: 21 observation et revue de la literature. *Rev Med Interne.* 1996; 17:810-13.
 17. Koch AE, Halloran MM, Haskell CJ, et al. angiogenesis mediated by soluble forms of e-selectin and vascular cell adhesion molecule-1. *Nature.* 1995;376: 517-19.
 18. Higuchi M. Anticentromere antibody as a risk factor for cancer in patients with systemic sclerosis. *Clin Rheumatol.* 2000;19:123-26.
 19. Kyndt X, Hebbard M, Queyrel V, et al. Sclerodermie systemique et cancer. Recherche de facteur predictifs de cancer chez 123 patients sclerodermiques. *Rev Med Interne* 1997; 18: 528-30.