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Case Report

Systemic sclerosis and triple-negative breast cancer: Doubtful association

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Abstract Systemic sclerosis (SSc) is an autoimmune connective tissue disorder which is characterised by involvement of multiple systems, vasculopathy and fibrosis. In SSc, increased risk of breast and lung malignancy is observed. Studies have shown that there is 1.5 times increase in cancer risk in SSc. A 62 year old female presented with hyperpigmented lesions over forehead since few months. No other significant history. Salt and pepper pigmentation over forehead, nape of the neck was seen. Tightening of skin was present over face and distal extremities with sclerodactyly. Clinically she was diagnosed as systemic sclerosis. Her routine investigations were normal except for positive ANA, and anti scl-70 antibodies. High resolution computed tomography (HRCT) chest was done to rule out asymptomatic pulmonary involvement. HRCT revealed a mass in the right breast. Lump from breast was excised and sent for histopathological examination which revealed Infiltrating duct cell carcinoma of breast. Thorough clinical examination and investigations must be done in every elderly female who presents with late onset systemic sclerosis for underlying breast malignancy. Likewise we have to rule out asymptomatic lung and prostate cancer in elderly men who present with late onset systemic sclerosis.

Key words
Systemic sclerosis; Triple-negative breast cancer; Doubtful association.

Introduction

Systemic sclerosis (SSc) is an autoimmune connective tissue disease which is characterized by vasculopathy and fibrosis. Studies have shown a 1.5-2 fold increase in cancer risk in SSc.[1,2] Prostate, lung and colorectal were found to be predominant in men, whereas breast, colorectal and lung cancers are most common cancers in women. Patients with diffuse scleroderma had an increased breast cancer risk, while patients with limited disease had a high risk of lung cancer.[3]

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Due to better medical treatment for scleroderma-related complications, cancer became the leading cause of mortality in cases of systemic sclerosis in the present scenario. Sometimes patients with underlying cancer may develop systemic sclerosis as a part of paraneoplastic syndrome.

Case report

We report a 62-year-old female who presented with hyperpigmented lesions over the forehead for a few months. No complaint was suggestive of tightness of skin or Raynaud's phenomenon. No other significant history. On examination, salt and pepper pigmentation over the forehead and nape of the neck, upper chest **(Figure 1)** was seen. Skin thickening and tightening **(Figure 2, 3)** were present over the face, upper back. and distal upper extremities extending

Figure 1 Salt and pepper pigmentation over the upper chest.

Figure 2 Skin thickening and tightening with overlying salt and pepper pigmentation over upper back

beyond metacarpophalangeal joints (MCP) with sclerodactyly (score-9). A high-resolution computerised tomography scan (HRCT) revealed chronic interstitial lung disease (ILD) (score-2) and an incidental mass in the right breast. Her routine investigations were normal except for positive anti-nuclear antibodies and anti-Scl-70 antibodies/Anti topoisomerase 1 (score-2). Hence, according to the American College of Rheumatology, European Alliance of Associations for Rheumatology (ACR EULAR) 2013 criteria, she was diagnosed with systemic sclerosis, scoring 13.

A lump from the breast was excised and sent for histopathological examination, which revealed infiltrating duct cell carcinoma of the breast **(Figure 4)**. In our patient, breast cancer was triple negative for estrogen receptor (ER), progesterone receptor (PR) and HER 2 protein.^{9m} Technetium methyl diphosphonate

Figure 3 Skin thickening and tightening with overlying salt and pepper pigmentation over distal upper extremities.

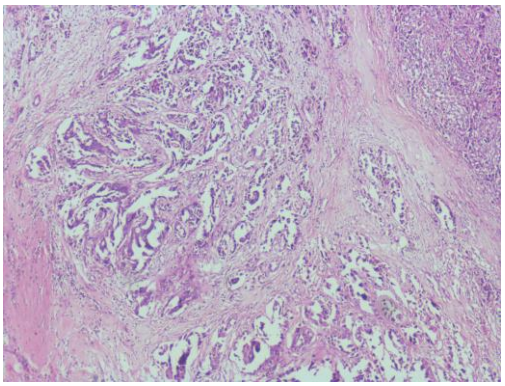

Figure 4 Histopathological image- Hematoxylin & Eosin x10- Infiltrating duct cell carcinoma of breast.

(^{99m}Tc-MDP) whole body bone scan was done, but no focal abnormalities were seen anywhere in the body to suggest active metastases. Later, a right modified radical mastectomy was done, followed by chemotherapy.

Discussion

The characteristic features of paraneoplastic scleroderma are the absence of anti-topoisomerase– 1antibodies, an increase in severity of the disease along with the progression of cancer and resolution of scleroderma with anti-neoplastic therapy. In this case, anti-topoisomerase 1 antibodies were present, and breast cancer was detected incidentally on HRCT. Hence, in this case, it is

challenging to correlate scleroderma positively with breast cancer.

In a study done by Angela Toss, the standardized incidence ratio of breast cancer in female SSc patients was 1.62 (95% CI: 0.7-3.19).[1] The female susceptibility which is seen in SSc suggests that there is role of the hormonal factors in breast cancer. While reviewing the literature, it was found that cancer was diagnosed in most of the patients within a period of 1 year before to 1 year after diagnosis of systemic sclerosis was made.[2] In a study done by Rosen has shown that anti-scl70 antibodies positive patients were associated with short cancer-scleroderma intervals. In this study, advanced age was found to be an independent risk factor for cancer.[4]

Angela Toss found in her study that early diagnosis and luminal HER-2 negativity were good prognostic features of breast cancer when associated with SSc. So proper screening of elderly SSc patients is mandatory for early detection of tumour development.[1]

Our shortcoming is we failed to examine her breasts for any masses. By divine grace, investigation (HRCT of lungs) for asymptomatic pulmonary involvement revealed underlying breast malignancy and ILD in an otherwise asymptomatic patient.

Conclusion

This case has been presented to highlight that complete physical examination and investigations of all systems, including breasts, lungs and prostate, have to be done to rule out underlying malignancy in a case of late-onset systemic sclerosis.

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