Bleomycin-induced Scleroderma


Abstract
Systemic sclerosis is a connective tissue disease, which can be triggered by environmental factors. We report one such case of bleomycin-induced scleroderma.

INTRODUCTION
Systemic sclerosis, may be triggered by environmental exposure to several agents like silica dust, organic solvents and drugs [appetite suppressants, carbidopa, bleomycin, pentazocin, cocaine abuse]. We report a patient with bleomycin-induced scleroderma and highlight some issues in the management.

CASE REPORT
A 50 years lady presented with complaints of irregular bleeding per vaginum. She was investigated and diagnosed as a case of carcinoma cervix stage III B. She was treated with three cycles of bleomycin (100 units), ifosfamide and cisplatin and 10 cycles of radiotherapy to pelvis and parametrium. No radiation was given to chest.

After two years of completion of therapy she complained of progressive thickening of skin over hands and face, bluish discoloration of fingers on exposure to cold, difficulty in opening mouth, difficulty in swallowing food and breathlessness on exertion of two months duration. She did not complain of retrosternal burning.

On clinical examination, blood pressure was 140/80 mm Hg, pulse 80/min and respiration of 18/min. There was sclerodactyly of both the hands up to the metacarpophalangeal joints, clubbing of fingers with peripheral cyanosis and bilateral coarse basal crepitations. Abdominal, cardiovascular, nervous system, and per vaginum examination was unremarkable. There was no evidence of muscle weakness or atrophy. Telangiectasia, pitted scars, calcinosis and digital ulcerations were absent.

Laboratory investigations showed haemoglobin of 9.7 gm/dl, total leucocyte count 3800/mm³, and ESR 62 mm in 1st hour. Peripheral blood film revealed microcytic hypochromic
anaemia. Liver and renal function tests and urine routine were normal. Chest radiograph revealed bilateral reticulonodular shadows. Pulmonary function tests showed a restrictive abnormality with decreased lung volumes but no evidence of airflow obstruction. Carbon monoxide diffusion capacity (DLCO) was 62% of the predicted normal. Contrast-enhanced computed tomography of the chest revealed diffuse interstitial pattern predominantly involving bilateral lower zones. Echocardiography was not done.

ANA was positive (speckled > 1:320). Rheumatoid factor was positive (32 IU/ml), anti-scl-70 and anti-centromere antibodies were negative. Barium swallow showed decreased peristalsis and slow emptying of barium in lower two-thirds of oesophagus with no gastro-oesophageal reflux.

The patient was diagnosed as a case of bleomycin-induced scleroderma with interstitial lung disease.

**DISCUSSION**

The pathogenesis of bleomycin-induced scleroderma is not known, although its selective concentration in the skin at lower doses explains the paucity of visceral involvement. However, at higher doses it is known to cause visceral involvement as well. Bleomycin is known to stimulate collagen production by cultured normal skin fibroblasts in vivo.1

Two points of interest in our patient were ANA positivity and development of scleroderma after only 100 units of bleomycin. Literature survey reveals ANA positivity in 50% cases of bleomycin-induced scleroderma as against 95% in idiopathic scleroderma.2 Also bleomycin-induced skin changes are seen after a cumulative dose of 165 units whereas our patient had received 100 units of bleomycin.3 Patients exposed to bleomycin develop a variety of cutaneous abnormalities including linear hyperpigmentation, indurated plaques, nodules; digital gangrene and dermal sclerosis, which is one of the most frequently recognized forms of toxicity. Our patient had no other cutaneous abnormality besides thickening.

Another point of interest in our case was the relative delay in development of scleroderma. Finch et al reported two cases of bleomycin-induced dermal sclerosis.4 All the patients sited above developed sclerosis either during treatment or within less than six months of treatment. But our patient began to develop skin thickening two years after completion of therapy.

We would like to highlight two management issues in our patient. She had pulmonary fibrosis. In patients exposed to radiotherapy, one must differentiate radiation-induced fibrosis from interstitial lung disease (ILD) due to scleroderma. Radiation pneumonitis occurs one to three months after therapy. The fibrotic or late phase follows two to four months after exposure. Bleomycin is amongst the few chemotherapeutic agents than can incenent response to irradiation. Our patient remained asymptomatic for nearly two years after therapy. Also, in this patient radiation was delivered to pelvis and parametrium alone. We, therefore, attribute the fibrosis to ILD.

The other issue of practical importance was separating radiation-induced oesophagitis from sclerodermal oesophageal dysfunction. We believe that latter is more likely in our patient since radiation was given to the pelvis and parametrium alone.

The possibility of de-novo scleroderma cannot be completely ruled out. But since the development of scleroderma in our patient is temporally related to treatment with bleomycin the possibility of bleomycin-induced scleroderma seems more likely.

**REFERENCES**