Scleroderma-like Initial Presentation of Multiple Myeloma

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Abstract
Systemic sclerosis (SSc) is a multisystem connective tissue disease affecting skin and internal organs. Certain drugs, environmental toxins and some viruses have been implicated in SSc-like illnesses. Scleroderma may be associated with some connective tissue disorders or autoimmune diseases but coexistence of scleroderma with multiple myeloma (MM) is an unusual finding. We here report a case of a 59 years old female patient with 5 months history of progressive thickening of skin all over the body. Multiple myeloma was diagnosed by osteolytic lesion in skull X-ray, increase in clonal plasma cells by bone marrow biopsy, very high Kappa light chain in serum light chain assay and detection of M band by serum protein electrophoresis.

Introduction
Systemic sclerosis (SSc) is a chronic multisystem complex connective tissue disease of unknown etiology affecting the skin and internal organs, occurs more commonly in women. Hallmark of SSc is induration and thickening of the skin (scleroderma).¹ Scleroderma is reported to be associated with Sjogren syndrome, rheumatoid arthritis and systemic lupus erythematosus. It is also associated with solid tumours such as lung, breast, stomach and rectum but association with multiple myeloma (MM) has seldom been reported. To the best of our knowledge, only 13 cases of scleroderma associated with MM have been reported in the literature.² Inflammation and deregulation of immune system in SSc may cause clonal expansions of plasma cells but such aberrations still remain under investigation. Most scleroderma patients present with positive ANA and anti Scl 70/antitopoisomerase (diffuse) and/or antictromer (localized variety) and follow a chronic course.³ Some paraneoplastic syndromes like MM or solid organ tumours may mimic clinical features of scleroderma but with rapid progressive course and negative autoantibody.

Case Report
59 years female patient, known cased diabetes and hypertension presented with features of generalized thickening and tightening of skin (Figure 1) for 5 months and mild difficulty in deglutition for last 3 months. Oral ulcer, photosensitivity, fever, alopecia or joint pain were absent. Patient gave history of dry eye and dry mouth for last 3 months. She also gave history of digital colour changes on exposure to cold water or cold environment (Raynaud’s phenomenon). On examination, pallor and bilateral pitting type of pedal oedema were found. On musculoskeletal examination, fixed flexion deformity of both wrist, elbow, small joints of hand (Figure 2) and proximal muscle weakness were found. Investigation showed, Hb-9.8 gm/dL, total leucocyte count-8700/μL, Platelet count- 286000/μL, ESR-122 mm/1st hr. Liver function test, urea, creatinine and uric acid were within normal limit. Anti Nuclear Antibody (ANA) with ANA profile were negative. HBsAg, Anti-HCV and HIV were non reactive. Chest X-ray, ultrasonography of abdomen did not reveal any abnormality.

Initially we thought it was a case of systemic sclerosis. But due to very rapid progression (within 5 months) of this disease and negative ANA with ANA profile, we considered a paraneoplastic syndrome to be the etiology of this scleroderma like clinical scenario (ie Pseudoscleroderma). For this we searched for multiple myeloma and other solid organ tumours. We found serum calcium level was 12.1 mg/dL, Serum IgG 2240 mg/dL (reference range: 700-1700), IgM 77 mg/dL(50-300), IgA 199 mg/dL (70-350). Serum light chain assay showed: Kappa light chain-766 mg/L(3.3-19.4) and Lambda light chain-2.59 mg/L(5.71-26.3). Kappa Lambda ratio was 295.8(0.26-1.65) and serum ß2 microglobulin was 3781 ng/ml (609-2366). Xray of skull showed multiple osteolytic lesions (Figures 3 and 4). M band were detected by serum protein electrophoresis (Figure 5) but Bence Jonce protein was not detected by urine analysis. Bone marrow aspiration and biopsy showed 12% plama cell (Figure 6). Even after extensive search

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we did not find any solid organ tumour. Then she was started on injection Bortezomib 1.3 mg/m² subcutaneous once daily on Day 1,4,8,11 followed by a 10 day rest period (days 12-21) for six cycles and tablet Cyclophosphamide 300 mg/m²/day on day 1, 8, 15 and 22 for 4 cycles. We also gave tablet dexamethasone 40 mg once daily from day 1 to 4 and day 9 to 12. Tablet Acyclovir was given as anti-viral prophylaxis. Patient is doing well with improvement in skin lesions after one year of post treatment follow up.

**Discussion**

SSc is a chronic autoimmune connective tissue disease that occurs when the immune system damages normal body tissue. It involves the skin, blood vessels, muscles and internal organs such as gastro intestinal tract, heart, lungs and kidneys.\(^2\)

Patients with scleroderma can have specific serum auto antibodies like antinuclear antibody, anticientromere or antitopoisomerase (anti Scl 70) antibody. It is characterised by formation of scar tissue (fibrosis) in the skin and organs of the body leading to thickening of involved areas.\(^2\)

Scleroderma may be associated with diabetes, monoclonal gammopathy of undetermined significance, MM, primary hyperparathyroidism, rheumatoid arthritis, Sjogren syndrome and systemic lupus erythematosus.\(^3\)

In world literature association of scleroderma with monoclonal gammopathy of undetermined significance had been reported but scleroderma like initial presentation of MM is very rare.\(^4,5\) Scleroderma like intial presentation of MM may be due to inflammation and molecular deregulation that precedes clonal proliferation of plasma cells. The duration of development of multiple myeloma from appearance of skin lesions of scleroderma is variable.\(^3,6\) In our case, the patient was diagnosed as MM after a period of 5 months from the onset of the skin lesion.

Multiple myeloma is a plasma cell dyscrasia. MM can be diagnosed by bone marrow clonal plasma cell>10%, M protein in serum and/ or urine and myeloma related organ or tissue impairment (end organ damage including bone lesion).\(^7\)

In our case, bone marrow plasma cell was 12% with high monoclonal Kappa light chain in serum light chain assay, M band was found in serum protein electrophoresis and multiple osteolytic lesions were found in x-ray of skull. Serum calcium and serum ß2 microglobulin levels were also high. MM is ideally treated by combination of lenalidomide, bortezomib, and dexamethasone which achieves close to a 100% response. Other similar three-drug combinations (bortezomib, thalidomide, and dexamethasone or bortezomib, cyclophosphamide, and dexamethasone) also achieve >90% response rate.\(^7\) We used bortezomib, cyclophosphamide, and dexamethasone as these drugs are freely available in our hospital. Patient is doing well after one year of follow up.

**Conclusion**

The main purpose of this case report is to raise awareness among the medical students and clinicians that MM can present initially like SSc. So whenever we get a patient with SSc like clinical presentation but with negative autoantibody profile specific for SSc, we must exclude other paraneoplastic syndromes, specifically MM. Early detection of MM with this type of unusual initial presentation would help us to initiate early treatment and modify disease course.
References


