

CASE REPORT

Coexistence of scleroderma with multiple myeloma: a rare association

Smeeta Gajendra,¹ Richa Gupta,¹ Ritu Gupta,¹ Lalit Kumar²¹Laboratory Oncology Unit, DR BR A IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, India²Department of Medical Oncology, DR BR A IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, India**Correspondence to**Dr Ritu Gupta, drritugupta@gmail.com**SUMMARY**

Coexistence of scleroderma with multiple myeloma (MM) is an unusual finding with unclear significance. Only 13 cases of MM with scleroderma have been reported until now. We report a case of a 24-year-old man with 8-year history of progressive thickening of skin all over the body. Histopathology of skin lesion was consistent with scleroderma. Bone marrow biopsy showed interstitial and focal increase in plasma cells and increased bone marrow fibrosis. Skeletal survey showed osteopenia, but no osteolytic lesion or fracture. The patient was diagnosed as scleroderma with coexistence of immunoglobulin A, κ MM. The patient recovered with improvement of skin lesions after 9 months of therapy with thalidomide and dexamethasone.

BACKGROUND

Scleroderma is a rare connective tissue disorder of unknown aetiology characterised by wooden, non-pitting induration of the skin. It first affects the face and neck and then spread symmetrically to the shoulders, trunk, arms and legs. The disease usually affects people of 30–50 years age group. Scleroderma is reported to be associated with Sjogren syndrome, rheumatoid arthritis and systemic lupus erythematosus.¹ 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. Inflammation and deregulation of immune system in this autoimmune disorder may cause clonal expansions of plasma cells but such aberrations still remain under investigation. We report a case of a 24-year-old man who presented with scleroderma and MM.

CASE PRESENTATION

A 24-year-old man presented with progressive thickening of skin all over the body for 8 years with rapid progression over the past 3–4 months, dysphagia and bleeding per rectum since 2 months. The patient had not taken any treatment for the skin lesions. There was no history of Raynaud's phenomenon. On physical examination patient had thickened tight skin all over the body with restricting range of movements and contracture of many joints.

INVESTIGATIONS

Haemoglobin 96 gm/L, total leucocyte count 5×10^9 /L and platelet count 208×10^9 /L was noted. Blood glucose, serum creatinine and serum

immunoglobulin levels were within the normal range. Serology for rheumatoid factor and antinuclear antibodies was negative. 25-Hydroxy vitamin D was low (<5 ng/mL; normal 9–37.6 ng/mL). Parathyroid hormone level was normal (21.15 pg/mL; normal 15–65 pg/mL). On serum protein electrophoresis, a dense monoclonal band of 1.6 gm/dL (24.2%) of immunoglobulin IgA κ subtype was present in $\beta\gamma$ interzone. No monoclonal protein was detected in urine. Histopathology of the skin lesions showed diffuse dermal fibrosis. Bone marrow aspirate showed infiltration by 55% plasma cells including many abnormal forms. A bone marrow biopsy showed interstitial and focal increase in plasma cells and increased bone marrow fibrosis (grade 2). On flow cytometric evaluation, plasma cells were positive for CD38, CD138, CD56, CD52; negative for CD19, CD45 and monoclonal for κ light chains. On skeletal survey, there was diffuse osteopenia with osteolysis of phalanges on both sides and osteoporotic changes in all the vertebrae. The patient was diagnosed to have scleroderma coexisting with MM.

TREATMENT

Treatment with thalidomide (100 mg/day) and dexamethasone (40 mg/day weekly) was started.

OUTCOME AND FOLLOW-UP

The patient recovered with improvement in skin thickening and increased range of movements after 9 months of therapy.

DISCUSSION

Scleroderma is a chronic autoimmune connective tissue disease involving changes in the skin, blood vessels, muscles and internal organs such as heart, lungs and kidneys. It is a condition that occurs when the immune system mistakenly attacks and destroys healthy body tissue. Patients with scleroderma can have specific antibodies (antinuclear antibody, anticentromere or antitopoisomerase) in their blood which suggest autoimmunity. It is characterised by formation of scar tissue (fibrosis) in the skin and organs of the body leading to thickness and firmness of involved areas. There may be a history of a preceding infection in 65–90% of cases; however, associations have also been reported with diabetes, monoclonal gammopathy (usually IgG- κ), MM, primary hyperparathyroidism, rheumatoid arthritis, Sjogren syndrome and systemic lupus erythematosus.¹ There is possibility that inflammation and molecular deregulation events in autoimmune disorders precedes clonal proliferation of plasma cells and lead to the emergence of MM. In literature

To cite: Gajendra S, Gupta R, Gupta R, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200639

Table 1 Cases of systemic sclerosis with multiple myeloma

Cases	Age/sex	Monoclonal protein	Duration (years)	Therapy
Korting <i>et al</i> ²	37/F	IgG κ	2	Improvement after myeloma therapy
Doyle <i>et al</i> ³	58/F	NA	4	NA
	62/F		40	
Ohta <i>et al</i> ⁴	64/M	IgG κ	11	Improvement after myeloma therapy
Hodak <i>et al</i> ⁵	74/F	IgG κ	4	Improved after 1.5 years of melphalan
Rimon <i>et al</i> ⁶	62/F	IgG λ	22	NA
Salisbury <i>et al</i> ⁷	76/F	IgA κ	0.1	Improvement after 9 months of cyclophosphamide and prednisolone
Nakanishi <i>et al</i> ⁸	50/M	IgG κ	3	NA
Schmidt <i>et al</i> ⁹	46/M	IgG λ	22	NA
Pujol <i>et al</i> ¹⁰	74/M	IgA κ	15	Improvement after myeloma therapy
Valente <i>et al</i> ¹¹	56/F	IgA κ	6	Improvement after melphalan and prednisolone
Bachleitner-Hoffman <i>et al</i> ¹²	73/F	IgG	24	Improvement after vincristine, melphalan, cyclophosphamide and prednisolone
Colovic <i>et al</i> ¹³	55/F	IgG λ	20	Improvement after 6 cycles of endoxan, thalidomide and dexamethasone
Present case	24/M	IgA κ	8	Improvement after 9 months of thalidomide and dexamethasone

cases of scleroderma associated with monoclonal gammopathy of undetermined significance have been reported but association of scleroderma with MM is rare (table 1).^{2–13} As enumerated in table 1, the age of the patients ranged from 37 to 76 years, in contrast to the relatively young age of the patient in our case. The duration of development of MM from appearance of skin lesions of scleroderma is variable and ranges from 1 month to 40 years. In our case, the patient was diagnosed as MM after a period of 8 years from the onset of the skin lesion. The association of the two diseases may be due to a number of circulating factors inducing immunostimulation of B cells. The second possibility of developing MM may be related to the use of immunosuppressive drugs. In our case, diffuse osteopenia with osteolysis of phalanges on both sides and osteoporotic change in vertebrae was observed but no osteolytic lesions were seen in axial skeleton, unlike MM, which is characterised by osteolytic lesions of the axial skeleton. Colovic *et al*¹³ postulated that plasma cells express osteoprotegerin (OPG) which blocks the interaction between RANKL and RANK receptor on osteoclast surface leading to impaired osteoclast resorption and preservation of bone structure. Unfortunately, OPG levels could not be investigated in our patient.

Treatment of scleroderma is directed towards the individual feature affecting different areas of the body. Because scleroderma is an autoimmune disease, one of the major pillars of treatment is the use of immunosuppressants such as methotrexate, cyclophosphamide, azathioprine and mycophenolate. Corticosteroids and non-steroidal anti-inflammatory drugs are also used. In scleroderma, T-helper type 2 (Th2) cells stimulate the production of antibodies and interleukin-4, a protein with profibrotic properties. The T-helper type 1 (Th1) cells produce interferon- γ (IFN- γ), a protein that prevents fibroblast production of collagen and it is possible that shifting the disease's target from the Th2 cells to the Th1 cells may decrease collagen production, and thereby reduce fibrosis. Thalidomide is an immune modulatory drug that has been shown to stimulate production of Th1 cells. Thalidomide is used for the treatment of MM and it acts as an antiproliferative, antiangiogenic and apoptotic agent and inhibits myeloma tumour growth.¹⁴ Thalidomide is effective in treating chronic graft-versus-host sclerodermatous skin change, and a small dose-escalating trial demonstrated improvement of skin fibrosis on histopathology.¹⁵ Most of the previously reported cases and the present case showed that treatment used for MM effectively manage systemic sclerosis.

In view of the possible coexistence of scleroderma with MM, it is suggested that all patients with scleroderma should be screened for monoclonal gammopathy irrespective of the age of presentation and patients with raised monoclonal protein should be followed up carefully to check for progression to MM.

Learning points

- ▶ Coexistence of scleroderma with multiple myeloma (MM) is an unusual finding with unclear significance.
- ▶ In view of coexistence of scleroderma with MM, it is suggested that all patients with scleroderma should be screened for monoclonal gammopathy irrespective of the age of presentation and those with a monoclonal protein should be followed up carefully to check for progression to MM.

Contributors SG and RG prepared and wrote the manuscript with the help of clinical information from LK. The final draft was reviewed and edited by RG.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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