

Widespread Scleredema Associated with Paraproteinemia and Generalized Osteoarthritis in an HLA-B39 Positive Patient

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SUMMARY Scleredema adultorum (SA) is a rare sclerotic disorder characterized by non-pitting induration of the neck with acral progression, sparing hands and feet. We report on a 57-year-old male with severe SA associated with paraproteinemia, treated with methotrexate. Such widespread skin thickening followed by severe movement restriction and inability to function on daily basis, as in our patient, has never been described. Severe osteoarthritis and finding of HLA-B39 allele in association with SA has not been previously described either. To the best of our knowledge, up to 40 patients with SA associated with paraproteinemia has been reported so far, and currently, there is no established effective treatment protocol. In our patient, low-dose methotrexate resulted in stiffness reduction, increased motility of the trunk and extremities, and ability to function on daily basis. We believe that any information about treatment outcome in SA patients should be disseminated in order to establish consensual treatment protocol for this rare disease.

KEY WORDS: scleredema, paraproteinemia, HLA-B39, osteoarthritis

INTRODUCTION

Scleredema adultorum (SA) is a rare sclerotic disorder characterized by diffuse swelling and non-pitting induration of the skin due to thickening of the dermis (1,2). Occurrence of SA has been documented in association with infections (type 1), paraproteinemia (type 2) and diabetes mellitus (type 3) (1,3). Women are diagnosed with type 1 and type 2 SA approximately twice as frequently as men (1). The SA may be self-limiting, but in patients with progressive disease, therapeutic options are poor. The presence of HLA-B39 allele may be associated with severe osteoarticular affection (4,5).

We report on a patient with SA associated with paraproteinemia, HLA-B39 allele and severe osteoarthritis. Such marked restriction of the spine, arm and leg movements due to widespread skin stiffness associated with osteoarthritis as in our patient has never been described. After 4-week therapy, low-dose methotrexate induced regression of stiffness and led to increased mobility of the trunk and extremities.

CASE REPORT

A 57-year-old male presented with 2-year history of painless, progressive, widespread skin thickening,



Figure 1. Maximal extension of the trunk and extremities due to widespread skin thickening and severe osteoarthritis.

woody induration of the skin on the neck, shoulders, trunk, arms, and legs (Fig. 1). Skin thickening and stiffness appeared gradually during two to three months. His face, hands and feet were spared; Raynaud's phenomenon and telangiectasia were absent. Widespread stiffness led to marked restriction of the spine, arm and leg movement (Fig. 2) and impaired thoracic movements with moderate restrictive ventilatory defect.

He had personal history of generalized osteoarthritis and coxarthrosis complicated with lesions of peripheral nerves, alcoholism, osteopenia, compressive fractures of L 3-4 and severe obstructive sleep apnea syndrome. During one year, he was observed at Rheumatology Department as possible eosinophilic fasciitis (EF) and was treated with low to moderate dose of prednisone. In the absence of relevant laboratory finding supporting EF diagnosis, normal finding of deep muscle biopsy and failure of corticosteroid therapy, the patient was referred to dermatologist.



Figure 2. Maximal adduction of upper and lower limbs.

At presentation, there were no abnormalities in complete blood count, serum and urine biochemical analysis except for decreased serum protein level (54g/L), with slightly reduced beta 1 (5.5%) globulin fraction. Antinuclear antibodies were negative; CH₅₀, circulating immune complexes and immunoglobulin level were normal. HLA typing revealed HLA-A3/23; HLA-B39/44 alleles.

Skin biopsy (alcian blue pH 2.5) revealed minimal epidermal changes and a markedly thickened dermis with swollen and separated collagen fibers (Fig. 3). Congo red and toluidine blue staining were negative.

The diagnosis of monoclonal gammopathy of undetermined significance (MGUS) was made based on the finding of paraprotein of the IgG lambda type in urine and serum, and absence of malignant cells in bone marrow.

Four-week methotrexate (10 mg/week) was resulted in significant regression of induration on the

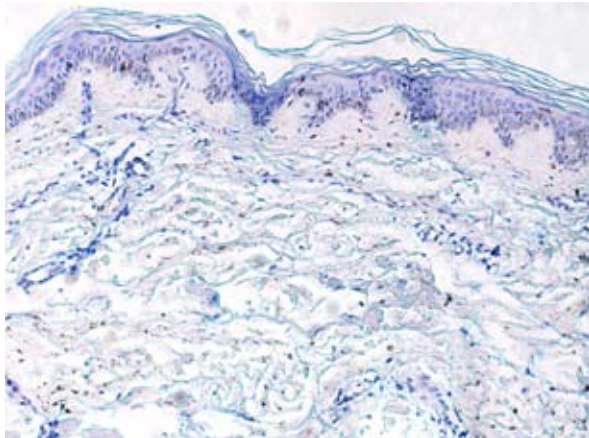


Figure 3. Alcian blue pH 2.5 staining demonstrating abundant mucin deposits between thickened and separated collagen bundles. (magnification, 25X)

neck, shoulders and upper extremities, with increased motility of the shoulder and arms. After four-month treatment, stiffness of the upper parts of lower extremities was also reduced.

DISCUSSION

Scleredema adultorum is a rare sclerotic disease characterized by non-pitting induration of the neck with acral progression, sparing hands and feet. The absence of Raynaud's phenomenon and visceral involvement permits clinical differentiation of this rare disease from systemic sclerosis (2,3).

In our patient, the diagnosis of SA was established since clinical and paraclinical findings indicated absence of systemic involvement, deep muscle biopsy demonstrated normal finding, and skin histopathology indicated mucin deposits in the dermis.

Such widespread skin thickening followed by restriction of trunk and extremity movements as in our patient has never been described. In most patients, SA tends to be localized (6), while type 2 SA tends to assume a progressive course (7).

Severe obstructive sleep apnea syndrome is reported in 25% of SA patients (6). Paraproteinemia is also found in 25% of SA patients. It has already been documented that MGUS frequently precedes multiple myeloma and that patients with SA tend to have a more aggressive and rapidly progressive multiple myeloma (7). Therefore, patients with SA associated with paraproteinemia should be carefully followed by hematologists.

According to the available data, numerous therapies for SA have been tried including pituitary extract

(1), thyroid hormone (1), colchicine (3), methotrexate (8), antibiotics (1), corticosteroids (1,3), electron beam therapy (3,9), physiotherapy (1,3), photopheresis (1,3), and phototherapy with psoralen (1,3), but none has proved consistently effective (9).

To the best of our knowledge, up to 40 patients with scleredema associated with paraproteinemia have been reported. According to literature data, only one patient with type 3 SA treated with low-dose methotrexate partially responded to therapy (8). In our patient, low-dose methotrexate led to reduced skin thickening and better mobility of the shoulder, upper and lower extremities. The finding of HLA-B39 allele has not been reported so far in SA patients and may explain development of severe osteoarticular manifestation in our patient (4).

We believe that all information about successful treatment outcome in SA patients may expand the available data pool and provide more management options to physicians.

CONCLUSION

We present a severe type 2 SA in an HLA-B39 positive male. In our patient, the association of SA and severe osteoarthritis led to reduced motility of the trunk and extremities and inability to function on a daily basis. Treatment with methotrexate resulted in increased motility and improved his quality of life.

In order to establish consensual treatment protocol for this rare disease and to improve patient quality of life, any information about treatment outcome in patients with SA should be disseminated.

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Use Nivea cream also by cloudy weather; year 1936.
(from the collection of Mr. Zlatko Puntijar)