Scleredema-associated IgA myeloma with myelofibrosis in a young adult: a case report

Genç bir yetişkinde miyelofibroz ile sklerema ilişkili IgA miyelom: Bir vaka raporu

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Abstract

Scleredema of Buschke is a rare fibromucinous connective tissue disorder of unknown etiology. It is often associated with a benign monoclonal gammopathy and rarely with myelomatosis. We report a case of scleredema-associated IgA myeloma with myelofibrosis in a 24-year-old male patient. Scleredema generally affects young adults and onset of associated monoclonal gammopathy is at a younger age than when not associated with scleredema. However, presentation at a much younger age (24 years in our case) is very unusual. Although mucin deposition in the bone marrow has been reported in scleredema, to the best of our knowledge, myelofibrosis has not been reported. *(Turk J Hematol 2008; 25: 195-7)*
Key words: Scleredema, myeloma, myelofibrosis, Ig A-kappa.

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Özet

Buschke sklereması nedeni bilinmeyen az görülen bir fibromüsinöz bağ dokusu hastalığıdır. Genellikle iyi huylu bir monoklonal gamopati ile; nadiren de miyelomatoz ile birlikte olur. Biz 24 yaşında bir erkek hastada görülen miyelofibroz ve siklerama ile birlikte olan immun globulin A miyeloma olgusunu sunuyoruz. Sklerama genellikle genç erişkenlerde görülmekte olup monoklonal gamapati ile birlikte olanlarda hastalığın başlangıç yaşı skleredama ile olmayanlara göre daha erkendir. Ancak hastamızda olduğu gibi 24 yaşında ortaya çıkması olağan dışıdır. Kemik iliğindeki musin birikimli skleredama bildirilmesine rağmen bildiğimiz kadarı ile miyelofibrozis henüz bildirilmemiştir. *(Turk J Hematol 2008; 25: 195-7)*
Anahtar kelimeler: Sklerema, miyelom, miyelofibroz, Ig A-kappa.

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Introduction

Scleredema of Buschke or scleredema adultorum is a rare primary cutaneous fibromucinosis of unknown etiology that is characterized by extensive woody, non-pitting induration of skin throughout the body, with systemic involvement being rather uncommon. There is a known association with benign monoclonal gammopathy and less commonly with frank myelomas [1,2]. The disease runs a variable course and is usually self-limiting; however, a few fatal cases have been reported [3].

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Case Report

A 24-year-old male presented with an eight-year history of progressive diffuse cutaneous thickening, which initially started from the face and slowly progressed over time to involve the trunk, arms and thighs. Hands and feet were relatively spared. He had difficulty in swallowing and walking. There was no preceding history of diabetes, infection or trauma. There was no history of Raynaud's phenomenon. On examination, he had diffuse induration of skin on face, trunk, arms and legs, and consistent pressure demonstrated a brawny edema. The face was woody and expressionless (Figure 1) and diffuse thickening of the tongue was noticed. There was limitation of neck, arms and feet movements. The spine showed kyphotic deformity.

On investigation, the patient had anemia (Hb 105 g/L) with normal total leukocyte and platelet counts, and erythrocyte sedimentation rate (ESR) of 55 mm in the first hour. Peripheral smear showed rouleaux formation. However, no leukoerythroblastic picture or tear-drop poikilocytes were seen. Blood urea, electrolytes, blood glucose level, liver function test, thyroid function test, rheumatoid factor and antinuclear antibody tests were normal. Serum protein electrophoresis showed an abnormal M band (25.5%, 1.8 g/dl) in the β-γ interzone, which on immunofixation was identified as a monoclonal IgA-kappa protein. Total serum protein levels were 7.9 g/dl. Serum β2 microglobulin level was 5500 µg/L (normal: 700-3400 µg/L). Polyclonal γ globulins were reduced. Urine was negative for Bence Jones protein, and urine protein electrophoresis did not reveal any M band. Twenty-four hour urine albumin was 0.02 g/day. Chest X-ray and skeletal survey revealed diffuse osteoporosis of the spine and bilateral phalanges.

Pathological findings

A skin biopsy from the left shoulder showed normal epidermis and increased broad fibrous bands in the deep dermis. However, Alcian blue stain for any mucin deposition in the skin was negative. Congo red staining for amyloidosis was negative. A bone marrow aspirate from the iliac crest showed 55% plasma cells including immature forms (Figure 2). The bone marrow biopsy showed loose, edematous stroma with interstitial as well as focal increase in plasma cells. There were areas of increased fibrosis with presence of coarse reticulin fibers (reticulin grade 3) (Figure 3). The Alcian blue stain for any mucin deposition was negative. Focally, the bony trabeculae showed areas of new bone formation (Figure 4). Hence, the patient was diagnosed as scleredema-associated IgA multiple myeloma with myelofibrosis and started on thalidomide, dexamethasone and zoledronic acid.

Discussion

Scleredema was first described by Buschke in 1902 as a systemic disease with woody, non-pitting induration of the skin starting at the nape of the neck and gradually spreading throughout the body, sparing the palms and soles [4]. It usually affects young adults with slight female predominance. The disease has been divided into two main types. The first is a self-limiting form often occurring after an acute febrile episode and resolving spontaneously within a few months [4]. The second

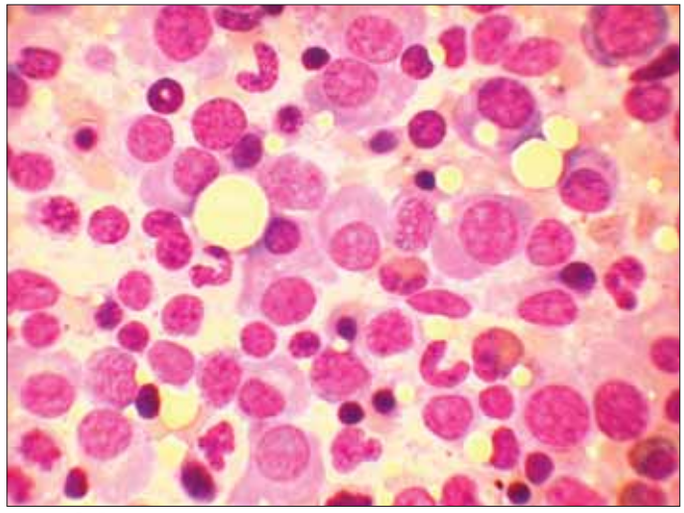

Figure 2. Bone marrow aspirate showing plasma cells including immature forms (hematoxylin and eosin, x1000)

Figure 1. Expressionless face with limited mouth opening and diffuse skin involvement

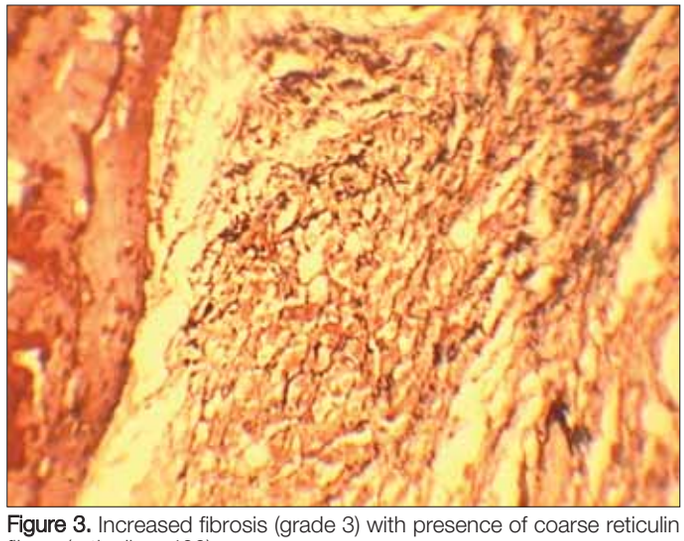

Figure 3. Increased fibrosis (grade 3) with presence of coarse reticulin fibers (reticulin, x400)

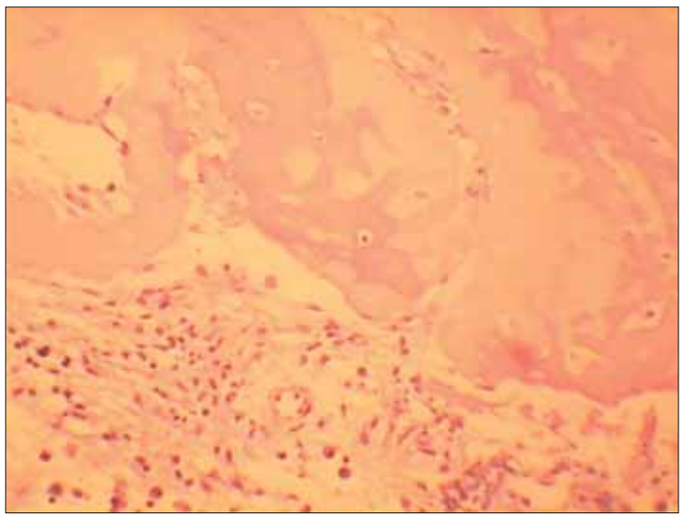

Figure 4. Focal areas of new bone formation (hematoxylin and eosin, x400)

type is associated with diabetes mellitus and runs a prolonged course [5]. There have been many reports of an association with a monoclonal gammopathy [6,7]. Rarely, there have been cases of scleredema associated with multiple myeloma [1,2]. In such cases, the scleredema presents several years before the monoclonal gammopathy [7].

Various hypotheses have been proposed to explain the association of scleredema with monoclonal gammopathy. According to Kovary et al. [8], the presence of immunoglobulins reflects a state of chronic immunostimulation due to antigenic substances present in the connective tissue. Another possibility is that the scleredema is caused by the monoclonal gammopathy, as the serum from the affected patient has been shown to stimulate collagen synthesis in normal skin fibroblast cultures [6]; however, any clear evidence is lacking. It is also possible that the gammopathy and scleredema are caused by the same etiological factor, which is hitherto unknown.

Mild marrow fibrosis may be observed in at least 27% of cases of myeloma but extensive fibrosis is rare [9,10]. Although mucin deposition [11] in the bone marrow has been reported in scleredema, to the best of our knowledge, myelofibrosis has not been reported. Whether the myelofibrosis was part of the primary disease process itself, reflecting extracutaneous systemic involvement, or whether it was secondary to myeloma is difficult to discriminate, since mucin can be absent in late lesions of scleredema, which show only fibrosis.

A variety of treatment approaches have been tried with variable success rates, including corticosteroids, immunosuppressants, thyroid hormones, antifibrotic therapy, hyaluronidase and electron beam therapy. The myeloma chemotherapy usually results in pronounced improvement of the associated scleredema [1,2,6]. Our patient also showed an improvement in the texture of the skin and generalized well-being after receiving chemotherapy, but he has not yet been evaluated with follow-up serum immunoglobulin levels or a repeat bone marrow biopsy. He was discharged after the first cycle of chemotherapy and is on regular follow-up.

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