SCLEROMYXEDEMA

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Abstract — Scleromyxedema is a rare, chronic, progressive, fibromucinous disorder of unknown etiology, characterized by lichenoid waxy papules and firm induration of skin of trunk, face, forearm and hands; fibroblast proliferation and mucin deposition in the upper dermis. Cutaneous involvement is characteristic but there are several associated systemic manifestations. We observed a case of scleromyxedema with multiple systemic manifestations including endocrinopathy and hypothyroidism. Scleromyxedema is a multisystem disorder associated with multiple organ involvement including liver, muscle, kidney and could be associated with endocrinopathies including hyothyroidism.
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Key words: Scleromyxedema; endocrinopathy; hypothroidism; mucinosis.

INTRODUCTION

Scleromyxedema is a variant of papular mucinosis or lichen myxedematosus. In 1953 Montgomery and Underwood (1) classified papular mucinosis into four clinical forms:

1) A generalized lichenoid papular eruption
2) A discrete papular form
3) Localized to generalized lichenoid plaques
4) Urticarial plaques and nodular eruptions

Gottron in 1954 introduced the term "Scleromyxedema" into the literature to denote a variant of lichenoid myxedematosus that corresponds to the generalized lichenoid form of the above-mentioned classification, which characterized by a diffuse lichenoid papular eruption with underlying sclerosis of the skin and normal thyroid function. Since that time, it has become apparent that patients with sclermyxedema may have increased incidence of several systemic abnormalities (2,3,4,5). Recently we observed a 55-year-old man with a clinical picture of scleromyxedema associated with hypothyroidism and several other systemic manifestations. We believed that this would be a good opportunity to review the literature for endocrinopathic associations of scleromyxedema.

CASE REPORT

A 55-year-old man, shepherd, had no significant medical problem until four year ago, when developed pruritus and some hard papules on his upper lip followed by progressive skin tautness involving the face. The thickening of skin gradually extended from face to neck, shoulders, upper and lower limbs, so that he developed difficulty in opening his mouth and flexing fingers. He had history of hoarseness and dysphagia for solid foods since two years ago. He complained of decreased vision; loss of eyebrow and body hairs; and reaction to cold compatible with the Raynaud's phenomenon. He was admitted to the Dermatology Ward of Razi Hospital in June 1994 for further evaluations. The only significant points in his history were chronic heavy smoking and splenectomy after developing edema and ascitis without jaundice or hematemesis about 10 years ago.

Physical examination revealed tightness and diffuse infiltration of facial skin with lack of expression, deeply furrowed forehead and glabellar areas, giving him a leonine facies (Fig. 1); restricted opening of the mouth; thickening of the axillary folds and skin of hands or sclerodactyly (Fig. 2), and decreased range of motion of the fingers. There were several hard small papules over the thickened skin of the face and neck especially at the nuchal area (Fig. 3) and some few ones on the trunk and antecubital fossae. The forearm and lower limbs were less involved. The eyeborws, axillary and pubic hairs were sparse. There was generalized hyperpigmentation of skin and submandibular, axillary and inguinal lymphadenopathy. The physical examinations were otherwise normal. Significant laboratory findings in this admission included: serum alkaline phosphatases 170-240 U (N 45-150 U), normal to slightly increased serum aminotransferases (ALT, AST); hypochromia and anisocytosis in peripheral blood smear, positive anti HBS and anti HBC antibodies, trace protein in 24 - hour urine, serum calcium 7.2 - 7.6 mg/dl (N 8-10 mg/dl), serum phosphorus 2.5 - 2.6 mg/dl (N 3 - 4.5 mg/dl), serum total protein 7.4 g/dl (N 5.5 - 8 g/dl), Albumin 2.9 g/dl (N 3.2 - 5 g/dl), gammaglobulins 2.6 g/dl (N 0.9 - 1.5 g/dl). Laboratory values were within normal limits for the following determinations: complete cell blood count, urinalysis, fasting blood sugar, BUN, VDRL, HBS Ag, anti HBe antibody and 24 - hour urine for Bence Jones protein. Serum protein electrophoresis demonstrated a gammopathy of non-spiky pattern.

Bone marrow biopsy showed plasma cell proliferation (5-6%) but there was no evidence for

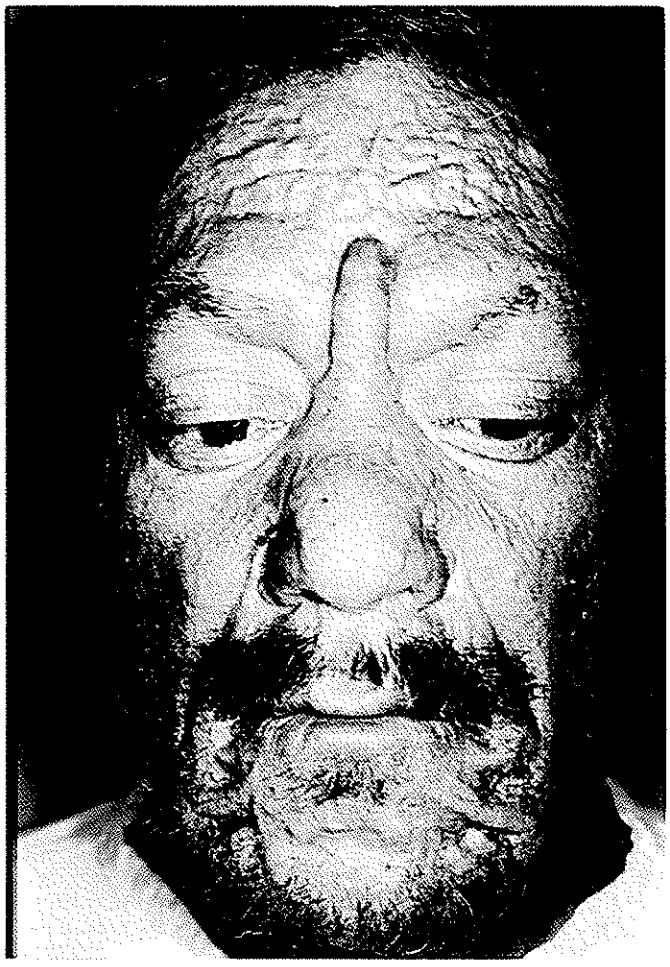

Fig. 1. Diffuse infiltration of facial skin with lack of expression.

multiple myeloma. Skull, hand and chest radiographies revealed normal findings. Esophageal barium studies revealed dilatation, decreased peristalsis, atony and localized narrowings. Full ENT examinations were not possible due to restricted opening of the mouth. The possibility of hypopharyngeal muscle involvement and decreased motility of the tongue mentioned. The patient refused direct laryngoscopy under anesthesia.

Biopsy specimen of skin showed an extensive proliferation of histiocytic cells and elongated fibroblasts (Fig. 4) in addition to diffuse deposition of a mucinous material in dermis (Fig. 5). The material was an acid mucopolysaccaride (glycosaminoglycans) that stained with alcian blue at pH 2.5 and was suceptible to hyaluronidase digestion (Fig. 6).

There was also some areas with focal sclerosis and thickened collagen bundles deep in the dermis. This combination was characteristic for the scleromyxedema.

He received two courses of melphalan (Alkeran) 8 mg/day within 2 months; the tightness of skin improved. Melphalan discontinued due to rising of liver enzymes, and etretinate (Tigason) 50 mg/day started. The patient discharged with a fair general condition. Two months later he was admitted to internal medicine ward due to generalized edema, abdominal protrusion and dyspnea. He had history of fatigue, anorexia, cough, exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, pain and swelling of extremities, scrotum and periorbital areas.

The significant physical findings were bilateral proptosis, yellowish sclera, wide spread pitting edema more prominent in lower limbs and scrotum, submandibular, axillary and inguinal adenopathy, fine diffuse (mostly basilar) rales at both lung fields, systolic

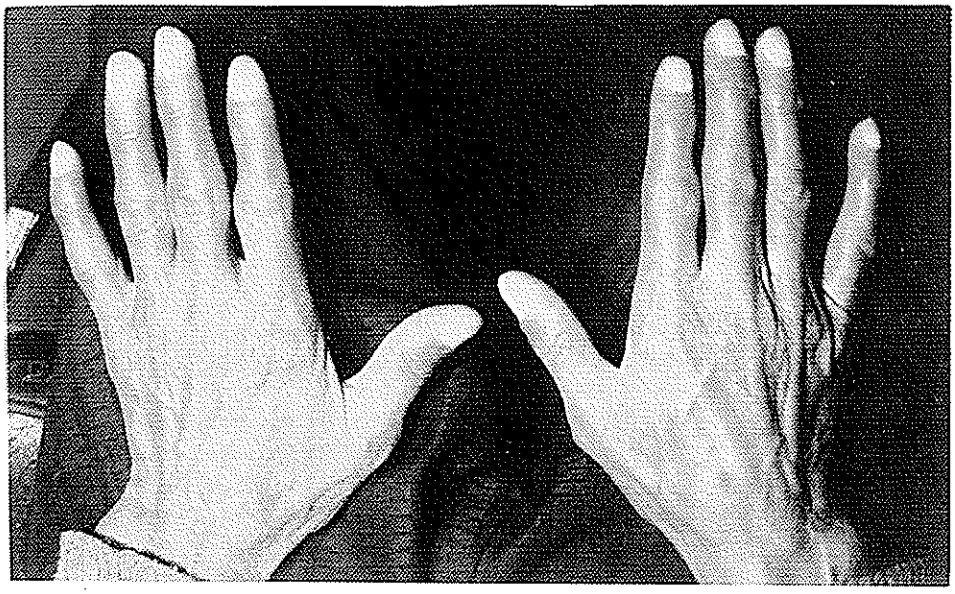

Fig. 2. Sclerodactyly, thickening of the skin of hands.

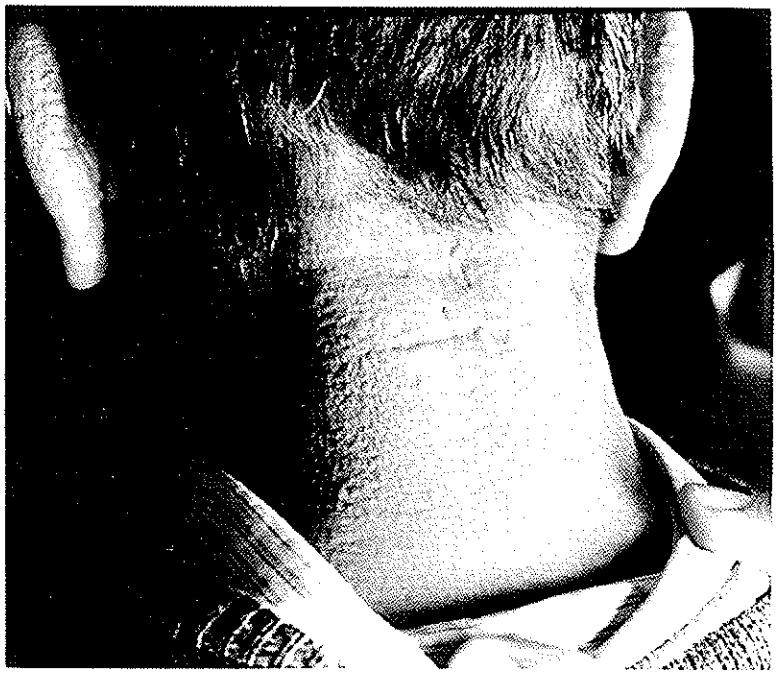

Fig. 3. Multiple small papules over the skin of the nuchal area.

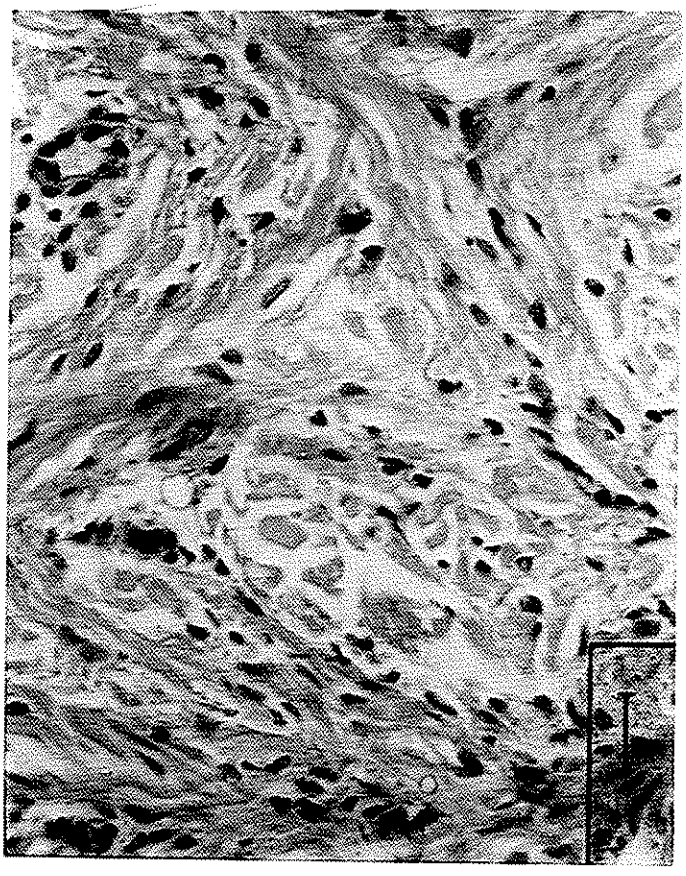

Fig. 4. Extensive diffuse proliferation of histiocytic cells and elongated fibroblasts.

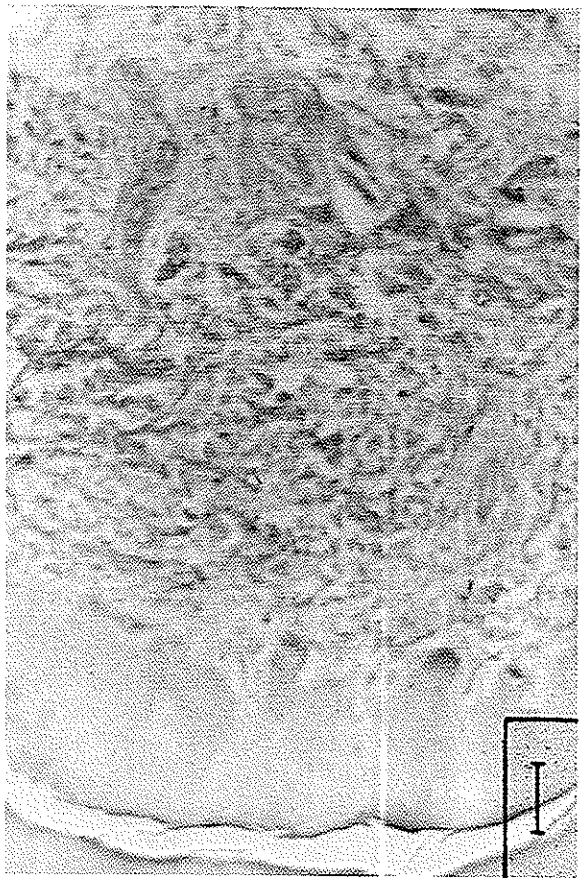

Fig. 5. Diffuse deposition of mucinous material in the dermis.

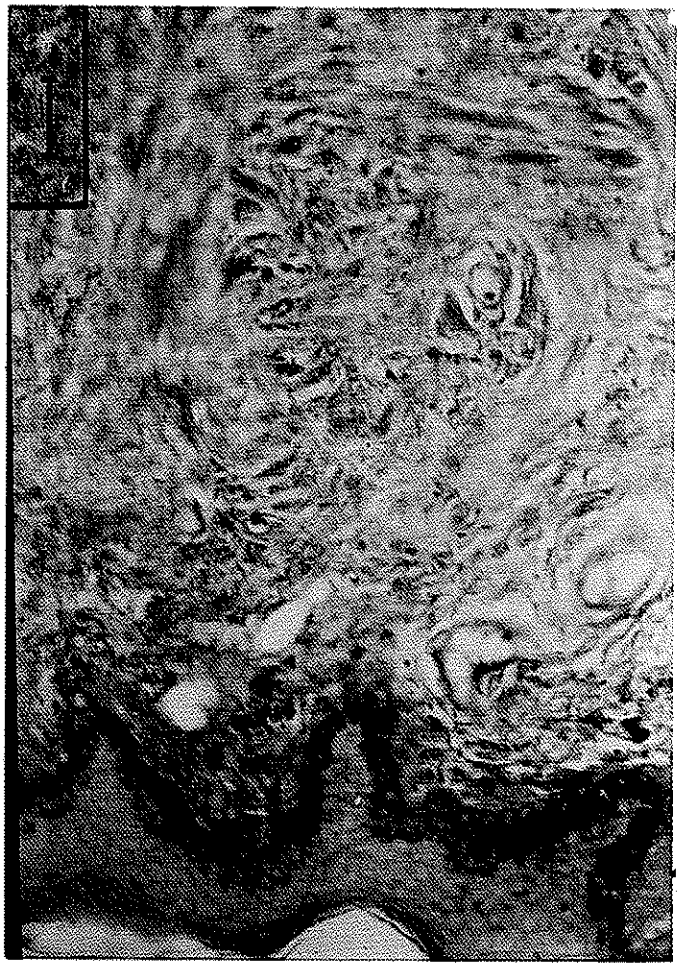

Fig. 6. Alcian blue stain shows deposition of acid mucopolysaccharides in the dermis.

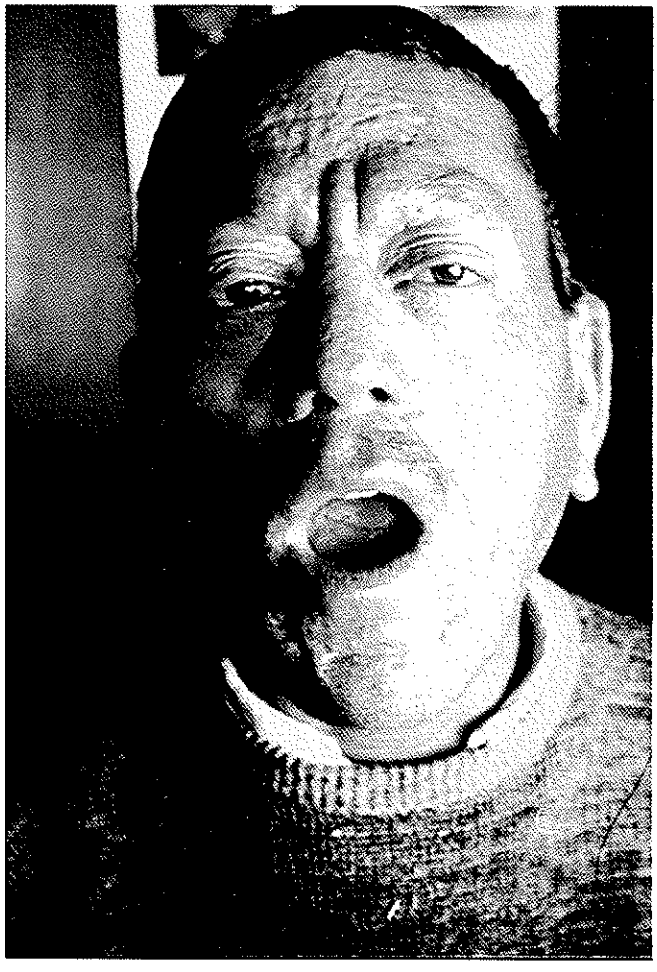

Fig. 7. Marked improvement of facial involvement after receiving etretinate and levothyroxine.

murmur grade II/VI at left sternal border and distended, tense, nontender abdomen with positive shifting dullness.

The skin findings were similar to that of the previous admission.

The abdominal sonography showed fluid in the abdominal cavity (ascitis), and hepatomegaly with normal parenchymal echogenicity. Ascitic fluid proved to be transudate by biochemical studies. Urine analysis showed hematuria. In intravenous pyelgraphy (I.V.P), kidney size and function was normal and thickening of bladder wall possibly due to chronic cystitis demonstrated. The liver function test showed: total bilirubin 3.8 mg/dl (N up to 1.5 mg/dl) direct bilirubin 1.4 mg/dl (N up to 0.5 mg/dl), SGOT 79 units (N up to 22 units), SGPT 81 units (N up to 17 units), alkaline phosphatase 488 (N 80-306).

Echocardiography revealed dilated right ventricle with moderate pulmonary hypertension and tricupsid regurgitation. The left ventricle function was normal. Thyroid studies demonstrated TSH 5.2 mU/L (N 0.3 - 3.5), T4 RIA 2.7 μg/dl (N 4.5 - 12.5), T3 RIA 41 ng/dl (N 80 - 200); were in favor of hypothyroidism. Other laboratory findings in this admission were as follows: PTH 70 mmol/L (N 40 - 100), lupus erythematosus cell (LE cell): negative, C3 75 mg/dl (N 60 - 140), C4 17 mg/dl (N 25 - 60), CH50 85/dl (N 90 - 100) antinuclear antibody titer: negative, CRP (3+), prothrombin time (PT) 21 seconds with 39% activity.

Rulling out hepatic disease as a cause of ascitis and generalized edema, performing liver biopsy was mandatory, but it was postponed due to bleeding tendency (decreased PT) and pulmonary hypertension.

The patient received levothyroxine 25 μg/day for hypothroidism, and spironolactone or furosemide for generalized edema and ascitis; and also continued etretinate, and improved partially (Fig. 7) He is followed in out-patient department of this center.

DISCUSSION

Scleromyxedema is a rare variant of papular mucinosis, characterized by diffuse sclerosis of skin and lichenoid waxy papules that vary in size from 1-4 mm. The disease typically affects adults between ages of 30 to 70 years, has no sex predilection and is usually chronic (5). The rash usually involves hands, arms, face, neck and upper trunk, but may extend to nearly all parts of the body, sparing usually the scalp and mucous membranes. The diffuse sclerotic changes of the invovled skin may result in stiffness, limitation of movement and accentuation of skin folds. The mucin deposition causes deep furrowing of the glabellar and perioral areas, giving the patient the so-called leonine facies. Facial expression may become restricted and also opening of the mouth. Sclerodactyly may be present render the patient unable to make a fist. Sparseness of hair in the eyebrow, axillary and pubic regions is repeatedly reported. The histologic picture is characteristic, reveals normal epidermis, marked mucin deposition in the paillary dermis and increased numbers of large stellate fibroblasts and collagen in the upper dermis. The mucinous substance in an acid mucopolysaccharide, stains positively with alcian blue at pH 2.5 and is digested by hyaluronidase (6).

There are numerous reports in the literature of associated systemic disorders in patients with scleromyxedema. Recently Lange and Goos reviewed 57 cases of scleromyxedema, found paraproteinemia in almost all cases, neurologic abnormalities in 24%, cardiovascular problems in 10% and myopathy in 9% of the patients (7). The association with a paraproteinemia (monoclonal gammopathy most commonly of IgG - type) in most cases of scleromyxedema is well documented in the literature, but its presence is not necessary for the diagnosis (8,9), and its role in the pathogenesis of the disease remains obscure (4). Other associated systemic abnormalities inlude neurologic symptoms (6,10) myopathy (5,11,12), cardiovascular disorders (3,5), renal insufficiency (13), carpal tunnel syndrom (5,14,15), sclerodactyly (8), Raynaud's phenomenon (16), esophageal aperistalsis (8,16), multiple myeloma (5), hepatic abnormalities including elevation of liver enzymes, and hepatomegaly (16) and psoriasis (5,17). There are few reports about coexistence of thyroid disease and scleromyxedema. Von Nagy and coworkers reported a case with association of Hashimoto's (chronic) thyroiditis, dermatomyositis and scleromyxedema (18). to the best of our knowledge, the only reported association of endocrinopathy with scleromyxedema is that of Dinnen et al (5), that reviewed 26 cases (seen at Mayo Clinic between 1966 and 1990), 3 of them had association of hypothyroidism, diabetes mellitus and hypogonadism (in one case) and diabetes mellitus or hypogonadism in the other two. We reported herein another case with associated endocrinopathy. There is controversy about multisystem character of scleromyxedema. McCuistion and Schoch (19) revealed mucin deposition in and around blood vessels in the heart, kidney, pancreas and adrenal glands in one patient; Perry et al (20) showed deposition of mucin in the renal papillae of one case, and Rothe et al (12) found mucin deposition in the muscles of a case of scleromyxedema and severe myositis; but other investigators have failed to find evidence of mucin deposition in internal orangs (1,6,10).

However, it could be suggested that there are two poles in the spectrum of clinical presentations of scleromyxedema: a disease limitted to the skin and a multiorgan disease with multiple systemic manifestations. Numerous modalities have been used in the treatment of scleromyxedema, including retinoids (11), corticosteroids (3,20), plasmapheresis (21), PUVA (22), electron beam (13) and many chemotherapeutic agents including melphalan (15), methotrexate (23) and cyclophosphamide (14). To date there is no therapeutic modality to give consistently satisfactory results. It remains to be confirmed which of the these or other new treatment options will prove succesful in this chornic multisystem disease.

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