Scleromyxedema: Successful Treatment of Cutaneous and Neurologic Symptoms

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GOAL

To understand the characteristics of scleromyxedema when it is accompanied by central nervous system dysfunction.

OBJECTIVES

1. To outline the extracutaneous manifestations of scleromyxedema.
2. To describe the clinical appearance, location, and laboratory abnormalities associated with scleromyxedema.
3. To discuss effective therapies for scleromyxedema.

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Scleromyxedema is a rare systemic disorder characterized by cutaneous sclerosis and papulosis, accompanied by deposition of mucin in the skin and other organs. We describe a case of scleromyxedema in a 62-year-old man. The cutaneous symptoms of the disorder were preceded by episodes of acute central nervous system dysfunction that included mental confusion, hemiparesis, tremor, and migraine. As the cutaneous symptoms progressed, the patient experienced persistent confusion and difficulty concentrating. Therapy with melphalan and plasmapheresis led to complete resolution of the cutaneous symptoms as well as near-resolution of the neurologic symptoms. This is the first report to describe the successful treatment of the cutaneous symptoms of scleromyxedema accompanied by reversal of chronic neurologic dysfunction.

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Scleromyxedema is a rare systemic disorder characterized by cutaneous sclerosis and papulosis, accompanied by deposition of mucin in the skin and other organs. The presentation of scleromyxedema was first described in 1906 by Dubreuilh,[1] and the disorder was later classified in 1953 by Montgomery and Underwood[2] as part of a spectrum of disorders known as lichen myxedematosus. Scleromyxedema has been associated with numerous extracutaneous manifestations, including proximal myopathy, inflammatory polyarthritis,[3,4] esophageal dysmotility, hoarseness,[5,6] and restrictive lung disease.[7]

Several reports have shown an association between scleromyxedema and disturbances of the central nervous system.[8-20] We report a patient successfully treated for both the cutaneous and neurologic manifestations of the disorder.

Case Report

A 62-year-old man presented with a 7-month history of a diffuse, eczematous, papulosquamous eruption involving the face and body. The eruption began as a pruritic area of erythema above the eyebrows bilater-

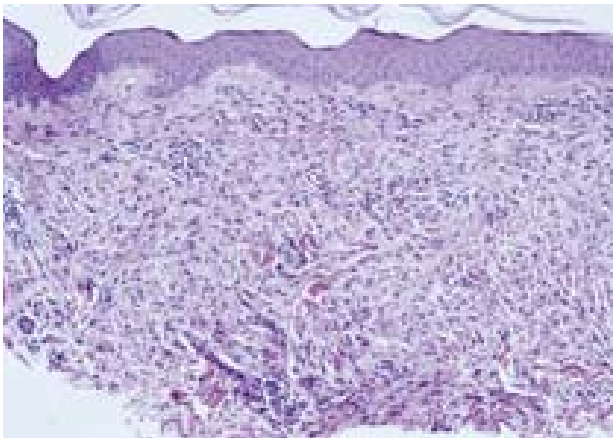

FIGURE 1. Skin biopsy taken from an indurated portion of the patient's forearm. Note the diffuse proliferation of spindled fibroblasts between and encircling collagen bundles, admixed with basophilic fibers. (H&E; original magnification, X 100).

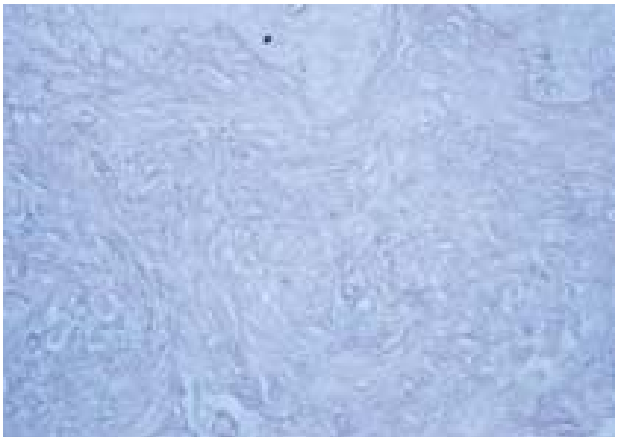

FIGURE 2. Skin biopsy from the patient's arm. The biopsy shows diffuse increased deposition of mucin, consistent with scleromyxedema (Alcian blue; original magnification, X 200).

ally, and expanded to include the entire face and upper extremities.

Over the past year, the patient had been hospitalized for several episodes of acute neurologic dysfunction. One year before presentation, he was hospitalized following an episode of confusion, right-sided throbbing headache, right-sided numbness, and visual blurring. Three similar episodes occurred over the course of the year. Over this period, the patient was studied repeatedly with magnetic resonance imaging, computed tomography, electroencephalogram, and cerebral blood flow studies, and once with magnetic resonance angiography. A computed tomographic scan performed during the first hospitalization revealed a pituitary adenoma, which was treated by transsphenoidal resection. After the third episode, evaluation for vasculitis was performed, consisting of rapid plasma reagin, lupus inhibitor, anti-cardiolipin antibodies, and erythrocyte sedimentation rate. The sedimentation rate was elevated at 75 mm/hr, but the remaining studies were within normal limits. As the year progressed, the patient developed persistent confusion and memory impairment, and became increasingly unable to concentrate. Neuropsychologic testing demonstrated impairments with language and attention.

The patient's medical history included hypertension and migraine headaches. His migraines were characterized by mild headache, flashing lights in the peripheral aspects of both visual fields, and some language disturbance, usually lasting for 1 hour. He had been free of migraines for the past 20 to 30 years, but began to experience them again 4 years before his current presentation. His recent migraines were remarkable for more pronounced confusion and language disturbance. At the time he presented to our clinic, his medical regimen included aspirin, 325 mg twice daily, verapamil, 120 mg daily, thyroxine, DDAVP®, testosterone, and hydrocortisone, 30 mg daily.

The patient's skin examination revealed patchy erythema and fine scale diffusely over the body. His face showed confluent erythema and edema with periorbital sparing. Palpation of his forearms revealed induration, and a skin biopsy was obtained from this area. At this point, a single clinical diagnosis was not apparent, and the patient was initiated on empirical therapy with topical steroids and oral minocycline, 50 mg twice daily.

The skin biopsy revealed a diffuse dermal proliferation of fibrohistiocytic cells, admixed with basophilic fibers; these findings suggested an early phase of granuloma annulare or scleromyxedema (Figure 1). An Alcian Blue stain showed a diffusely increased mucin deposition (Figure 2). No palisaded granulomatous inflammation or localized degeneration of collagen fibers was found. The histologic features were consistent with scleromyxedema.

Over the next 2 weeks, the initial topical steroid and antibiotic therapy eliminated the superficial scale, revealing marked progression of skin induration. On physical examination, a diffuse papular induration of the arms and trunk was noted. Intense erythema and edema of the face with periorbital sparing was observed (Figure 3), and progressive sclerosis of the skin over the hands now restricted the patient's manual dexterity. Over the flexural surface of the arms, the papules were arranged in a distinctive linear configuration (Figure 4). These clinical findings were recognized as supporting a diagnosis of scleromyxedema. Subsequently, serum protein elec-

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FIGURE 3. The patient's face shows intense erythema.

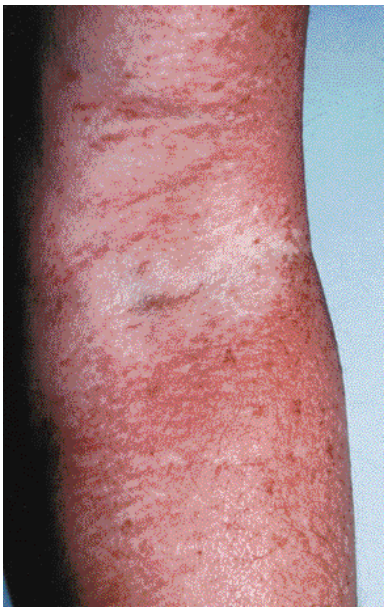

FIGURE 4. The flexural surface of the patient's arm shows erythema accompanied by an eruption of papules.

trophoresis revealed a paraproteinemia of IgG-kappa chains, measured as 0.98 gm/dl. Additional autoimmune evaluation, consisting of tests for antinuclear antibodies, rheumatoid factor, complement levels, anti-SSA, anti-SSB, and anti-centromere antibodies, was negative. Bone marrow biopsy showed no evidence of increased plasma cells, and a total body bone survey revealed no lytic lesions.

During this period, the patient's wife noted that her husband was becoming chronically and progressively confused, doing things such as putting his shoes in the refrigerator and storing orange juice in the oven. Because of the rapid progression of the neurologic symptoms, treatment with melphalan, 4 mg daily, was initiated, accompanied by six sessions of plasmapheresis.

Over the next 2 weeks, the lesions on the lower extremities grew worse. Two weeks later, the upper extremity lesions began to soften. A second round of plasmapheresis was performed. Two months after therapy was initiated, the IgG level had decreased to 0.72 gm/dl. After 5 months of therapy, the patient experienced a global, significant decrease in cutaneous infiltration.

During this period, the patient experienced angina, and cardiac catheterization revealed complete blockage of the right coronary artery. In addition, he noted several episodes of visual distortion. Ophthalmologic evaluation revealed bilateral macular edema with mild hemorrhage, which was believed to be secondary to decreased retinal arterial flow bilaterally.

Six months after initiation of therapy, the patient developed pancytopenia, requiring transfusions of platelets and packed red blood cells. Melphalan was discontinued, then resumed 1 month later on a pulse regimen that consisted of 14 mg daily for 4 days, administered every 4 to 6 weeks. The skin thickening began to recede and the patient noted that his skin was less painful and pruritic.

Nine months after therapy was begun, the patient's skin had markedly improved. In addition, he noted improvement of his short-term recall and headaches. Three months later, the lesions had completely resolved, and melphalan was discontinued. At this time, the IgG level was 0.38 gm/dl.

One year after treatment was terminated, the patient remained free of recurrence of skin lesions or episodes of headache, mental confusion, numbness, or tremor. However, he continued to experience occasional episodes of visual "stars," which lasted for less than 10 minutes and responded to aspirin. He also continued to experience chronic visual "waviness," which did not interfere with any of his regular activities.

Comments

Lichen myxedematosus is a rare disorder that presents as lichenoid papules, which may coalesce to form plaques. Scleromyxedema is a specific form of lichen myxedematosus that includes diffuse thickening of the skin, usually associated with the overlying papules.[21] The areas most frequently affected are the dorsa of the hands and fingers, axillary folds, and external surfaces of the arms and legs. Infiltration is most prominent on the forehead,[22] where it accentuates the creases of the skin, causing a leonine facies.[23] Often, scleromyxedema is accompanied by a serum paraproteinemia, usually of the IgG type. Histologically, it is characterized by deposits of acid mucopolysaccharides in the middle and deep layers of the dermis, displacing collagen fibers. Large stellate and elongated fibroblasts are found within the mucinous stroma.[21] The cause of scleromyxedema is not known.[23]

Several authors have reported an association of scleromyxedema with acute and chronic disturbances of the central nervous system. The acute presentation may include headache, confusion, hemiparesis, psychosis, seizures, and coma.[8-20] In a few patients, acute cerebral symptoms preceded the appearance of skin lesions.[10,11] In some, the acute symptoms resolved spontaneously.[10,14,16,20] In others, they resolved soon after plasmapheresis.[18,19]

Chronic neurologic impairment has been described in seven reports. Symptoms include difficulties with cognition, memory, and communication, as well as sensory and motor dysfunction.[2,10,11,13,14,18,20] One report described gradual neurologic recovery in one patient after brief therapy with cyclophosphamide and prednisone, followed by plasmapheresis. However, it did not describe similar improvement in the patient's cutaneous symptoms.[18]

This is the first report to describe treatment of scleromyxedema that led to complete resolution of cutaneous symptoms as well as recovery from chronic neurologic dysfunction. Our patient noted recovery of short-term memory and concentration and freedom from migraine headaches. Although he continued to experience unusual visual symptoms, these did not interfere with any of his regular activities.

Because of the continued deterioration of our patient's neurologic status, we elected to proceed directly to systemic chemotherapy and plasmapheresis. Although melphalan may have toxic effects, it was selected because it is the most consistently effective therapy for scleromyxedema. Other treatments, including systemic steroids, retinoids, and psoralen-ultraviolet A, are often ineffective.[20,21] Fortunately, the combination of chemotherapy and plasmapheresis proved beneficial to both his cutaneous and neurologic diseases.

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FACULTY DISCLOSURE

The Faculty Disclosure Policy of the College of Medicine requires that faculty participating in a CME activity disclose to the audience any relationship with a pharmaceutical or equipment company that might pose a potential, apparent, or real conflict of interest with regard to their contribution to the program.

Dr. Nieves reports no conflict of interest.