A case of concurrent systemic sclerosis and scleredema

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INTRODUCTION

Scleroderma and scleroderma mimics belong to a heterogenous group of sclerosing skin diseases that share the clinical features of skin hardening and thickening with or without adherence to underlying fascia.[1] These diseases are distinguished by the activation of dermal fibroblasts (or mesenchymal cells) with subsequent distortions in the quantity and organization of the extracellular matrix. Although the triggering events are various, they typically stimulate an immune response, resulting in cytokine release and mesenchymal cell/fibroblast recruitment and activation. Variations in cell recruitment and differentiation account for the separate histologic and clinical manifestations. Although sclerosing skin diseases share common features, multiple such disorders are rarely found together in the same patient. We describe a case of concurrent systemic sclerosis (SSc) and scleredema (scleredema adultorum of Buschke [SAB]).

Abbreviations used:

AI: antibody index
SAB: scleredema adultorum of Buschke
SSc: systemic sclerosis

CASE REPORT

A 57-year-old white man presented to the rheumatology division after referral for sclerodermatous connective tissue disease. Past medical history was significant for gastroesophageal reflux disease, dysphagia status after esophageal dilation, hypertension, sleep apnea, anxiety, and fibromyalgia. The patient developed Raynaud phenomenon and arthralgias of the hands and feet 1 to 2 years before without evidence of ischemic lesions. The arthralgias progressed from his shoulders and knees to generalized pain with increasing weakness (ie, difficulty rising from a chair) and trouble completing daily tasks. Review of systems was positive for mild dyspnea on exertion, heartburn, fatigue, xerostomia, joint pain, dysphagia, and muscle weakness. Physical examination findings included facial telangiectasias, synovitis, 4+/5 strength in the bilateral hip flexors/extensors, and abnormal nailfold capillaries (dilated capillaries, hemorrhages, and scattered avascular areas). Modified Rodnan Skin Score was 14 with an unusual pattern—most prominent thickening involved the abdomen and upper back, with relative sparing of the face, hands, and feet. Laboratory and immunologic studies showed a positive antinuclear antibody (1:1280), anti-centromere B antibody of greater than 8.0 antibody index (normal range 0.0-0.9 AI), and anti-Smith/ribonucleoprotein weakly positive at 2.8 AI (normal range 0.0-0.9 AI). Test results for anti-Scl-70, anti-RNA polymerase III, anti-Ro, anti-La, anticardiolipin IgA and IgG, anti-double-stranded DNA, anti-Jo-1, anti-cyclic citrullinated peptide antibodies, lupus anticoagulant, rheumatoid factor, and renal and liver function were normal. Hemoglobin A1c was 6.7% (4.0%-6.0 %). Methotrexate, prescribed before referral for "mixed connective tissue disease," provided some relief of his joint pain; however, over the

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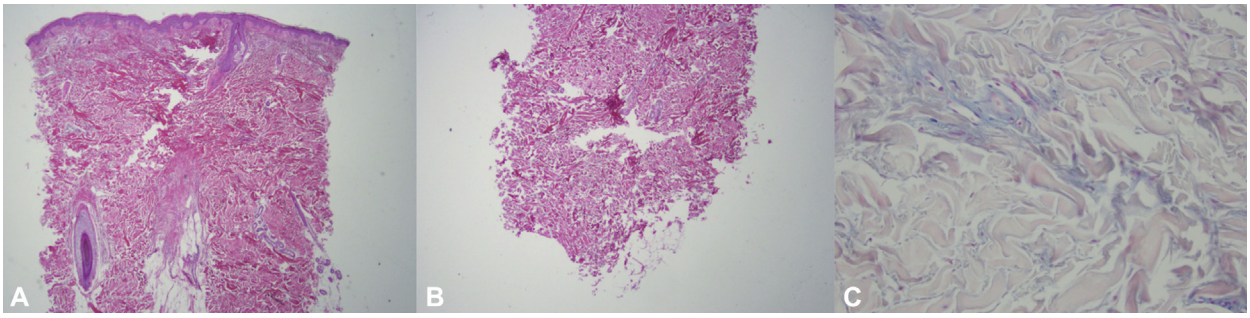

Fig 1. Samples from biopsy of the upper portion of the back (original magnification ×20) show (**A**) thickened dermal collagen without inflammation and (**B**) subcutis displacement without destruction or fibrosis. (**C**) Alcian blue stain highlights increased dermal mucin. Original magnification, ×200.

next 6 months, he developed worsening skin thickening, primarily over his trunk, with minimal involvement distally.

Although the overall clinical presentation was consistent with SSc, given the atypical distribution of skin thickening, he was referred to a dermatology specialist. The patient's dermatologic examination was significant for induration of the calves, upper back, and trunk; normal range of motion of the fingers; absence of cutaneous calcinosis; and 1+bilateral lower extremity pitting edema. Distal symmetric sclerosis, sclerodactyly, digital scars, and loss of substance from the finger pulp were absent. Biopsy samples from the upper portion of the back and abdomen showed skin with increased dermal mucin without inflammation, dermal sclerosis, or increased fibroblasts (Fig 1). Histology and clinical examination findings were consistent with scleredema.

DISCUSSION

SSc is a chronic, autoimmune connective tissue disease of unknown etiology leading to skin and internal organ fibrosis.[1,2] Fibrosis is thought to arise from widespread microvascular damage, mononuclear immune cell dissemination, release of proinflammatory and fibrogenic cytokines, and excessive mesenchymal/fibroblast production and deposition of collagen in the extracellular matrix.[1,3]

SAB is a rare, symmetric, and progressive nonpitting swelling and induration of unknown etiology.[1,4] Classically, it affects the back of the neck, upper portion of the back, and shoulders and spares the hands and feet.[1,4,5] Diagnosis requires characteristic pathologic findings, including thickened dermal collagen bundles with interfibrillar spaces filled with amorphous mucin, which consists of hyaluronic acid, glucosamine, and fibronectin.[1,3-5]

Although these conditions share the common physical finding of dermal sclerosis, they have different anatomic distributions, clinical associations, and pathophysiology.[1,2,4,5] By comparison, the fibrosis seen in SAB is thought to be due to accumulation of mucopolysaccharides and exhibits little evidence of inflammatory pathology, whereas in SSc, vascular alterations and inflammatory infiltrates are typical.[1,3-5] Furthermore, the deep dermal fibrosis, adnexal atrophy, and eccrine entrapment in SSc are contrasted by the mild upper dermal fibrosis with mucin-induced subcutis displacement in SAB.[1,3] It is therefore striking that 1 individual would present with both of these syndromes concurrently.

The patient presented with characteristic features and American College of Rheumatology/European League Against Rheumatism criteria for SSc[6]: telangiectasias, Raynaud phenomenon, abnormal nailfold capillaries, and anti-centromere antibody. However, skin involvement in SSc almost universally involves the distal fingertips/extremities, and it involves the trunk only in severe forms of diffuse cutaneous disease; the back and shoulders are generally spared.[1,2] Furthermore, although methotrexate monotherapy was helpful for the patient's SSc-associated inflammatory arthritis, it was ineffective for his skin induration, suggesting a noninflammatory skin pathology. Overall, his presentation is most consistent with systemic sclerosis sine scleroderma with concomitant scleredema. Unfortunately, there are no standard treatment protocols for SAB, and treatment is usually directed at the underlying cause.[1,4] In our case, we maximized methotrexate therapy and encouraged weight loss and improved diet.

Although this patient has a mildly elevated hemoglobin A1c level, suggestive of type 3 SAB, the absence of poorly controlled insulin-dependent diabetes suggests that this case is more consistent with the fourth type of SAB, described in association with miscellaneous conditions (ie, HIV, Sjögren syndrome, IgA deficiency, etc).[1,4] Previous case

studies have shown the coexistence of SAB with other rheumatologic diseases, including Sjögren syndrome, rheumatoid arthritis, ankylosing spondylitis, and dermatomyositis.[4,7,8] To the best of our knowledge, there no report in the literature that describes the simultaneous appearance of SSc and SAB. This case to highlight multiple disease associations of SAB—autoimmune, rheumatologic, oncologic, and sclerodermatous—and the importance of high clinical suspicion in atypical disease presentations.

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