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Case presentation

Scleromyxedema secondary to hepatitis c virus and successfully treated with antiviral therapy

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Abstract

Scleromyxedema (SM) is a chronic and progressive fibromucinous disease with no known etiology. We report a patient with scleromyxedema associated with hepatitis C virus, successfully treated with interferon and ribavirin therapy.

Introduction

Scleromyxedema (SM) is a chronic and progressive fibromucinous disease with no known etiology. It is characterized by generalized papular and sclerodermoid eruptions, dermal mucin deposition, fibroblast proliferation, and dermal sclerosis and thickening [1-3]. Even though the etiology of SM remains unknown, most theories suggest that paraproteinemia (primarily IgG-lambda type) plays a major role in pathogenesis [3]. Current treatment options are limited and disease evolution is often unpredictable with most cases progressing to involve multiple organ systems resulting in significant morbidity and mortality [4]. Scleromyxedema has been associated with a wide variety of diseases including diabetes mellitus, hypothyroidism, pulmonary fibrosis, Parkinson disease, hyperlipidemia, multiple sclerosis, multiple malignancies, and rarely with hepatitis C virus (HCV) [1]. We report the first case of scleromyxoedema secondary to hepatitis C virus successfully treated with interferon and ribavarin therapy.

Case synopsis

A 57-year-old woman presented to our dermatology clinic with a 5-month history of pruritic, indurated, subcutaneous papules involving the scalp, face, neck, upper trunk, dorsal hands, and palms. The patient reported that the lesions first arose on the hands and from there spread to the face, primarily involving her eyelids and jawline, followed by her trunk. She also reported a history of generalized fatigue, malaise, and arthralgias involving the proximal interphalangeal (PIP) joints as well as the elbows and shoulders. She denied any history of diabetes mellitus, blood dyscrasias, or autoimmune diseases.

Prior to her presentation to our clinic, the patient had been treated with hydroxychloroquine and topical corticosteroids, but complained that her lesions were progressing despite treatment. She had also undergone autoimmune serological testing, which revealed normal antinuclear, anti-SSA, and anti-SSB antibodies.

Physical Examination: On initial presentation to our clinic, physical examination demonstrated indurated erythematous subcutaneous plaques with peau d'orange changes involving the upper back and chest (Figure 1 A-B). Her face, primarily the eyelids and jaw line, scalp, palms, and dorsal hands showed multiple erythematous indurated subcutaneous papules and plaques without any epidermal changes (Figure 2). She was also found to have extensive papular lesions along the lateral aspects of her digits, resulting in limited range of motion. No mucosal lesions were identified.

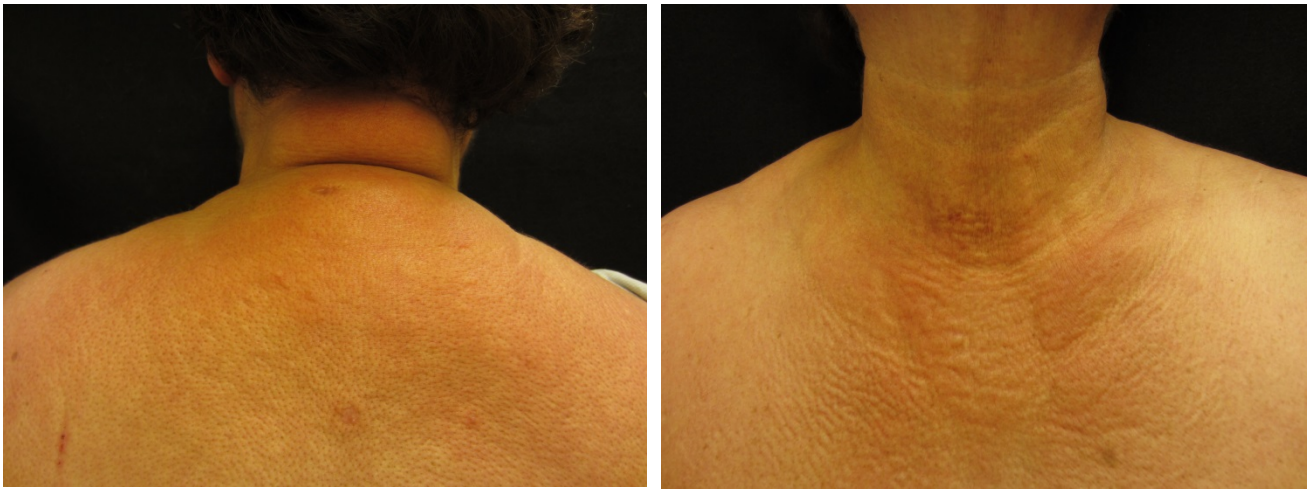


Figure 1. A). Indurated erythematous subcutaneous plaques with peau d'orange changes involving the upper back. B). Indurated erythematous subcutaneous plaques with peau d'orange changes involving the neck and chest.

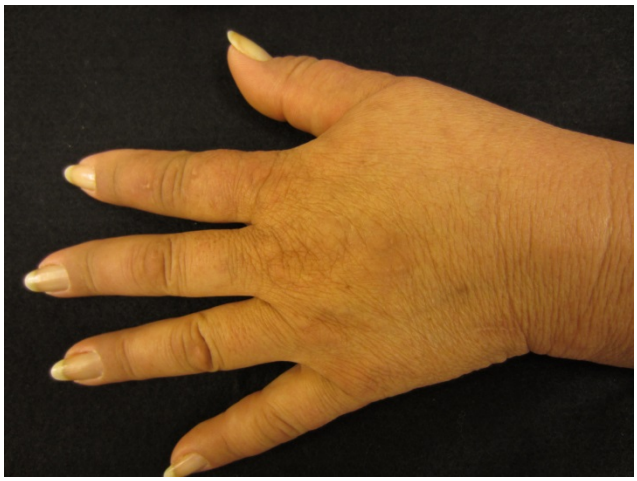
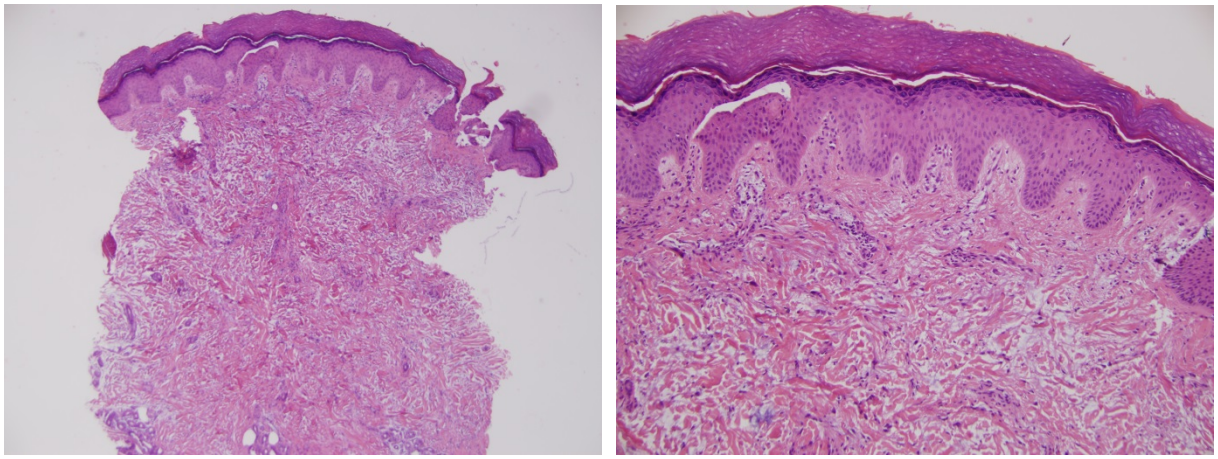


Figure 2. Multiple erythematous indurated subcutaneous papules and plaques without any epidermal changes involving the dorsal hands

Histopathological Findings: Multiple biopsies were obtained and histopathological analysis demonstrated increased reticular dermal mucin with a mild proliferation of fibroblasts and deep dermal sclerosis, consistent with a diagnosis of scleromyxedema (Figure 3 A-D). Direct immunoflouresence (DIF) was non-specific with focal positivity for C1q, IgA, and IgM as well as strong linear staining for C5b-9.



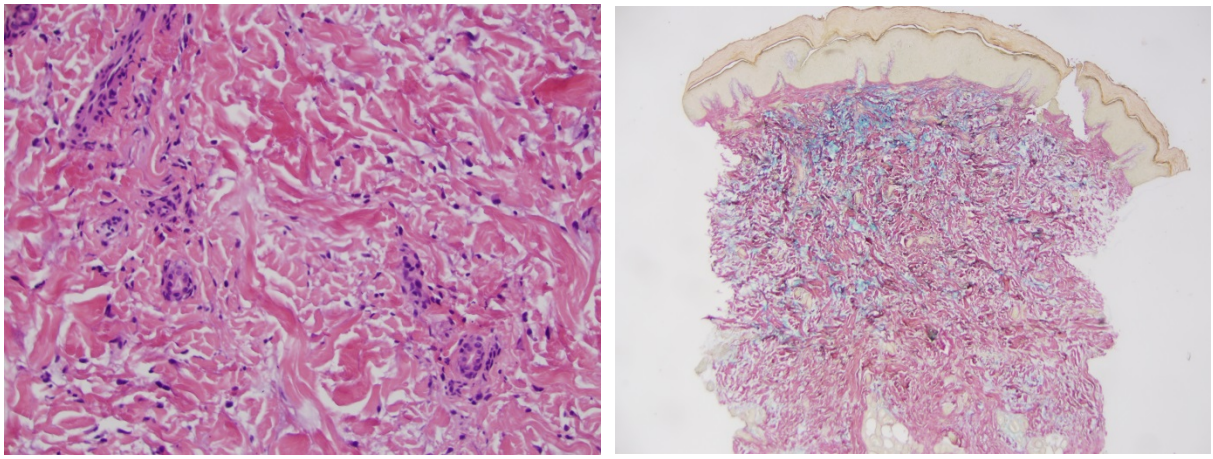


Figure 3. A-C).Increased reticular dermal mucin with a mild proliferation of fibroblasts and deep dermal sclerosis, consistent with a diagnosis of scleromyxedema (A: 4x, B:10x, C: 20x). D). Colloidal iron stain highlights increased mucin in the superficial and mid-dermis.

Laboratory findings: Laboratory investigations revealed mildly elevated liver function tests, with an ALT of 68 and an AST of 48. Thyrotropin (TSH), T3, T4, hemoglobin A1C, anti-double stranded DNA, anti-SSA, anti-SSB, anti-RNP, anti-Jo, Anti-Scl70, c-ANCA, p-ANCA, and ACE levels were all within normal limits. Serum protein electrophoresis was also performed and did not reveal any monoclonal bands.

Clinical course and patient outcome: Upon discovery of her elevated liver function tests, the patient underwent further testing, including hepatitis serologies. Hepatitis C RNA by PCR was found to be positive with a value of 3, 200,000 IU/mL (Reference range: 43,000 – 69,000 IU/mL). Hepatitis A serology and hepatitis B core antibody were negative.

She denied any IV drug use or needle sharing but did report receiving a blood transfusion thirty eight years prior for cesarean section complications. The patient was then referred to the gastroenterology department, and started treatment with a 24-week course of ribavarin and pegylated interferon-alpha-a2. Shortly after initiation of therapy, she noted significant improvement in her skin sclerosis and induration. Her photosensitivity and pruritus gradually resolved.

At her 6-month post-treatment follow up, the patient's upper chest and back showed significant improvement with only slight sclerosis and induration and interval resolution of peau d'orange changes (Figure 4A). The previously noted indurated plaques and nodules involving the face, neck, and dorsal hands had markedly improved and she had regained function and full range of motion of her PIP joints (Figure 4B).

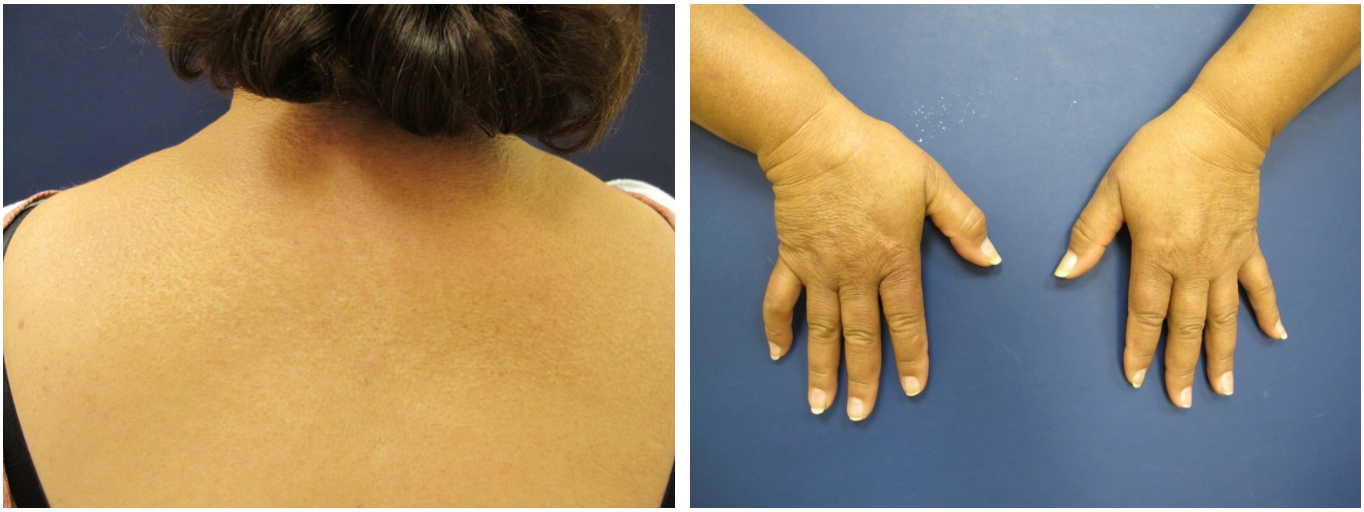


Figure 4. A/B: Post treatment involving the upper back and dorsal aspect of hands

Discussion

Scleromyxedema (SM), also known as Arndt-Gottron (S-AG) syndrome, is a rare disorder characterized by diffuse waxy papules with extensive thickening, dermal mucinosis and sclerosis, and a wide variety of systemic manifestations including proximal myopathy, arthritis, eosinophilia, dysphagia, hoarseness, cerebral symptoms, and arteriosclerotic changes [5,10-11]. Clinically,

SM is characterized by generalized papular eruptions, often linearly arranged, that often coalesce into diffuse scleroderma-like indurated plaques [10]. These lesions tend to involve large surface areas including the trunk and upper extremities. Involvement of the face can ultimately result in a leonine facies appearance [10]. SM is most often diagnosed in middle-aged patients, 30-80 years of age, and equally affects men and women [1-3, 7]. Histopathological findings consist of hyperproliferation of atypical dermal fibroblasts, inflammatory cells, and diffuse mucin deposition, confirmed with alcian blue at pH 2.5, in the papillary and mid-rectiular dermis [5,9].

The etiology is not well understood but IgG-lambda monoclonal gammopathy is found in more than 80% of patients with SM and is thought to play a role in pathogenesis [3,7]. The relationship between the cutaneous findings in SM and the paraproteinemia is not well understood. The clinical course of SM tends to be a chronic and progressive disease and spontaneous remission is rare [3,7]. Treatment options are limited, often ineffective, and associated with serious life-threatening side effects including bone marrow suppression, irreversible peripheral neuropathy, Cushing's syndrome, and osteoporosis [9]. Current therapies consist of chemotherapy agents such as mephalan and cylcophosphamide, plasmaphoresis, retinoids, intravenous immunoglobulins (IVIG), psoralen plus ultraviolet A (PUVA), thalidomide, autologous stem cell transplant, and corticosteroids [7].

SM has been associated with many systemic disorders: autoimmune processes including diabetes mellitus and multiple sclerosis, malignancies, lymphoproliferative disorders, and a variety of metabolic abnormalities, but it has rarely been reported with hepatitis C virus [7]. Hirooka et al, document eight cases of lichen myxedematosus (LM) in association with hepatitis C virus and liver dysfunction published in Japan from 1994-1998 [13-17]. Treatment with antiviral therapy was not reported. Jahangir et al, report a case of a 42-year-old HCV positive male with negative protein electrophoresis scleromyxedema [10]. Treatment was not discussed, however, they recommend hepatitis screening in all cases of SM.

Hiroyuki and colleagues also reported a case of a 55-year-old Japanese female with scleromyxedema and anti-HCV antibodies [13]. Rebora et al, reports a case of SM secondary to chronic hepatitis C infection treated with interferon-alpha therapy [12]. However, unlike our patient, the reported patient had exacerbated cutaneous symptoms thought to be related to interferon's enhancement of fibroblastic growth factor (FGF) resulting in increased mucin production by fibroblasts [12]. Finally, SM has also been described in a patient with underlying hepatocellular carcinoma secondary to HCV successfully treated with tumor resection [11].

Our patient presented with both physical exam findings and histopathological characteristics consistent with scleromyxedema. Her initial work up yielded no evidence of an underlying disease or possible cause. However, after being diagnosed with hepatitis C virus and initiated on therapy she started to have significant improvement in her symptoms. At her 6-month follow up, after completing ribavirin and interferon therapy, she had only minimal residual sclerosis and complete resolution of her arthritis. The patient's drastic response and improvement secondary to antiviral therapy highly suggest hepatitis C as the underlying cause of her cutaneous symptoms. This case demonstrates the first reported case of SM successfully treated with antiviral therapy.

In conclusion, this case demonstrates the first reported case of scleromyxedema secondary to hepatitis C successfully treated with antiviral therapy. We recommend considering hepatitis C virus when working up the possible etiology of SM, especially in the cases with an otherwise unknown etiology and negative workup.

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