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A RARE CUTANEOUS MANIFESTATION OF SYSTEMIC SCLEROSIS

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ABSTRACT

A 43-year-old male with a history of intravenous drug use and alcohol consumption presented to the emergency department with three-month history of failure to thrive. The patient exhibited a constellation of constitutional symptoms including cough, weight loss, fatigue, decreased appetite, nausea and vomiting. The skin examination revealed multiple subcutaneous hyperpigmented, indurated plaques and nodules on the trunk and arms. Laboratory evaluation revealed abnormal autoimmune tests, anaemia, elevated inflammatory markers and radiological evidence of interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH). An excisional biopsy from a skin lesion demonstrated dermal sclerosis consistent with scleroderma. The patient was diagnosed with diffuse systemic scleroderma with cutaneous findings consistent with nodular or keloidal scleroderma variant. This case highlights a rare cutaneous variant of systemic scleroderma called nodular or keloidal scleroderma.

KEYWORDS

Systemic sclerosis, scleroderma, cutaneous manifestations, nodular scleroderma

LEARNING POINTS

- Nodular scleroderma can be a diagnostic challenge due to its rarity and wide clinical presentation, which can mimic other medical conditions such as keloid or hypertrophic scar, storiform collagenoma, sclerotic dermatofibroma or sclerosing perineuroma.
- Clinicians should have a high degree of suspicion for nodular scleroderma when a patient presents with firm nodular or keloidal skin lesions, to diagnose and treat it appropriately.
- It is important to recognise nodular scleroderma early because timely and accurate diagnosis is crucial for appropriate management to prevent severe debilitation and scleroderma-related complications, and to improve patient outcomes.

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INTRODUCTION

Scleroderma is an uncommon connective tissue disorder characterised by skin sclerosis and multisystemic manifestations. It manifests in two primary forms: localised scleroderma and systemic sclerosis[1]. Systemic sclerosis is characterised by sclerosis of the skin and internal organs[2]. It can be classified into different subtypes, based on the extent of skin involvement and the type of internal organ involvement. Limited systemic sclerosis presents with skin induration distal to the elbows and knees and – to a lesser extent, the face and neck – while the trunk and proximal extremities are spared. These patients generally have prominent vascular manifestations, including severe Raynaud's phenomenon and mucocutaneous telangiectasias, sometimes followed by later onset of pulmonary arterial hypertension (PAH). Many patients with limited systemic sclerosis have manifestations of CREST syndrome (calcinosis cutis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasias). Diffuse systemic sclerosis presents with skin induration that extends proximally to the upper arms, thighs and/or trunk. Patients with the diffuse type are more likely to have a rapid progression of skin thickening with early development of lung fibrosis and an increased risk of renal crisis and cardiac involvement[3]. The localised scleroderma, or morphoea, is limited to thickening and hardening of the skin, with no involvement of other organs. Nodular scleroderma, also known as keloidal scleroderma, is a sub-type of localised scleroderma. It manifests as raised, firm plaques or nodules with extensive dermal fibrosis and hyalinised collagen bundles. The lesions are typically located on the posterior aspect of upper back and arms and can look like a keloid, sparing face and hands[4]. The pathogenesis of nodular scleroderma lesions is not clear and is still under investigation. We report a unique case of a patient presenting with features of diffuse systemic scleroderma with cutaneous findings of nodular scleroderma.

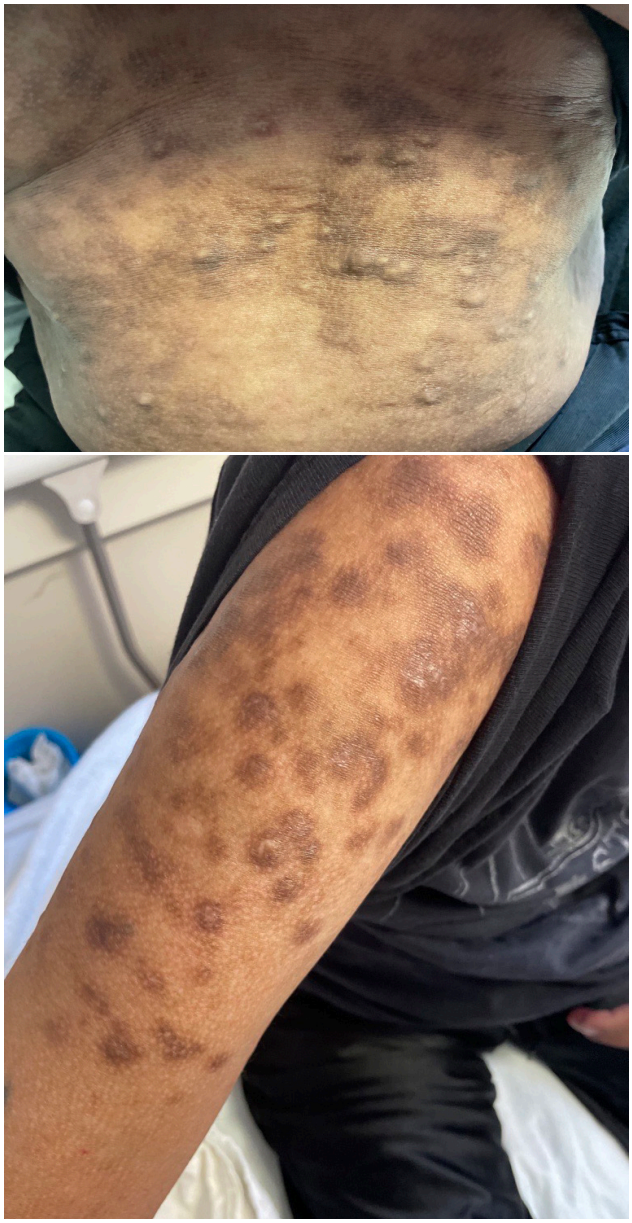

Figure 1. Diffused subcutaneous hyperpigmented plaques and nodules over the torso and the upper extremity.

CASE DESCRIPTION

A 43-year-old male with a history of intravenous drug use and alcohol consumption presented to the emergency room with a three-month history of failure to thrive. The patient reported a productive cough with white sputum, generalised weakness, fatigue, weight loss, anorexia, nausea and intermittent vomiting. Additionally, he had diffused subcutaneous hyperpigmented, indurated plaques and nodules over the torso, back and upper extremities, along with shiny hands and fingertip ulcers. The skin lesions were non-pruritic and non-tender *(Fig. 1)*. The patient had normal blood pressure and was afebrile, but tachypnoeic with 93% oxygen saturation on room air. Our case has been diagnosed based on a combination of clinical, laboratory and pathological reports. In the blood work, the erythrocyte sedimentation rate was 3 0 mm/hr (normal range: 0–10 mm/hr), and the C-reactive protein level was 15 mg/l (normal range: <5 mg/l). Antinuclear antibodies (ANA) tested positive at a titre of 1:640 (reference range: 1:80) with a speckled pattern. RNA polymerase III antibodies were also positive at 137 U/ml (reference range: <19 units), with specific autoantigen reactivities as follows: RP11 at 111 U/ml (reference range: <11 SI), RP155 at 110 U/ml (reference range: <11 SI), and SS-A 52 at 183 U/ml (reference range: <20 units). Anti-centromere and Scl-70 antibodies were negative. Fibrillarin (U3 RNP), anti-U1 RNP antibody, anti-Smith antibody and anti-ribonuclear protein were all negative.

Based on the imaging and procedures conducted, a chest X-ray revealed diffuse bilateral opacification, and a computed tomography scan of the chest showed diffuse ground glass opacities with bronchiectasis, predominantly at the lung bases. The computed tomography (CT) scan of the chest revealed an enlarged right atrium, a small pericardial effusion and chronic reflux of contrast into the inferior vena cava, which may indicate right heart dysfunction. There was

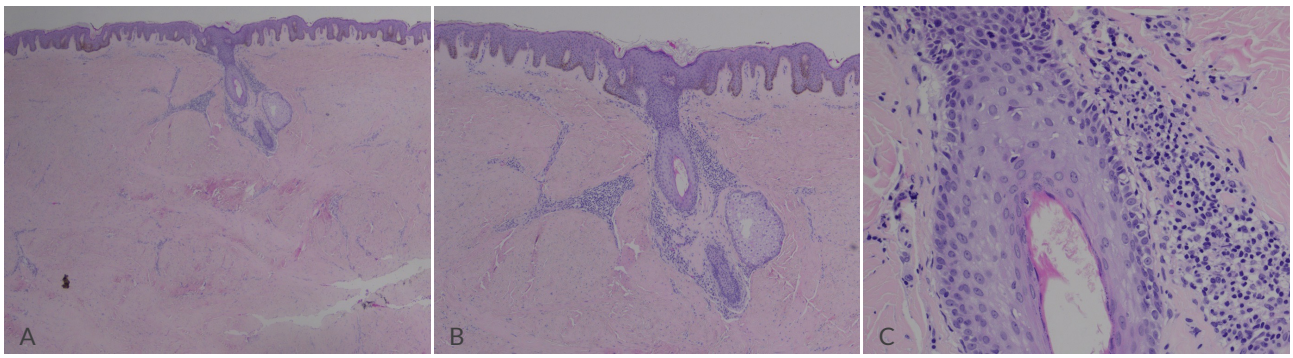

Figure 2. Histological findings. A) Entrapment of adnexal structures with an increase in sclerotic dermal collagen (haematoxylin-eosin, 20X); B) Dense diffuse sclerosis involving the entire dermis (haematoxylin-eosin, 40×); C) Mild perivascular and perifollicular lymphoplasmacytic inflammation (haematoxylin-eosin, 200×).

also a dilated main pulmonary artery measuring 3.5 cm in diameter, a finding often associated with PAH. A CT scan of the abdomen suggested that the oesophagus was fluid-filled and somewhat dilated throughout its course, with perihepatic ascites along the diaphragmatic surface of the liver. Echocardiography revealed a moderately enlarged right ventricle with moderately reduced systolic function. The right atrium was also moderately enlarged, and there was moderate tricuspid regurgitation. The estimated pulmonary artery systolic pressure was 83.6 mmHg, assuming a right atrial pressure of 15 mmHg, indicative of severe pulmonary hypertension. Right heart catheterisation revealed precapillary pulmonary hypertension, with a pulmonary artery pressure of 60/30/40 mmHg, a pulmonary artery wedge pressure of 4 mmHg and cardiac output/cardiac index values of 2.75/1.61. Using the Fick method, the cardiac output/cardiac index was 3.6/2.1. The pulmonary vascular resistance was 13 Wood units using thermodilution cardiac output and 10 Wood units using Fick. There was no change in pulmonary pressure after administering inhaled nitric oxide at 40 ppm for 5 minutes. Following the administration of 900 ml of normal saline, the pulmonary artery wedge pressure increased from 4 mmHg to 12 mmHg.

An excisional biopsy of the skin lesions was also performed for an accurate diagnosis. Histopathological examination of the biopsy showed an increase in sclerotic dermal collagen and a mild perivascular and periadnexal lymphoplasmacytic infiltrate, consistent with scleroderma *(Fig. 2)*.

The patient was diagnosed with diffuse systemic sclerosis with ILD and PAH, with a skin presentation of nodular scleroderma. After a multidisciplinary meeting, the patient was discharged with prescriptions for amlodipine, mycophenolic acid, furosemide, macitentan, and sildenafil. No topical treatment was prescribed for skin lesions. Systemic symptoms showed improvement during follow-up visits with the rheumatology and heart failure teams. However, skin manifestations remained stable, showing neither improvement nor worsening.

DISCUSSION

Systemic sclerosis is a complex autoimmune disorder characterised by skin and multisystemic involvement[2]. In diffuse cutaneous systemic sclerosis, cutaneous manifestations consist typically of indurated plaques on the trunk and extremities. Nodular scleroderma is characterised by hyperpigmented nodules and is an infrequent skin manifestation of systemic sclerosis[5,6]. Anti-RNA polymerase III antibodies were elevated in our patient. These antibodies are a specific marker for systemic scleroderma and may be associated with severe multisystemic disease and diffuse cutaneous involvement, as observed in our patient. This case underscores the significance of considering a range of clinical and laboratory findings to precisely diagnose and treat patients with overlapping features of different scleroderma subtypes. It presents a rare and atypical presentation of scleroderma, which can pose a diagnostic challenge for dermatologists, rheumatologists and primary care physicians. Although this presentation is rare, it is important for healthcare professionals to recognise this variant. Le et al. reported two cases of nodular scleroderma in patients with diffuse and limited systemic scleroderma[7]. Another case presented by Srisuttiyakorn et al. also reported nodular scleroderma as a presenting skin manifestation in patient diagnosed with systemic sclerosis[8]. A review presented by Richarz et al. also highlights that the presentation of nodular scleroderma is more commonly associated with systemic sclerosis scleroderma[9]. Treating nodular scleroderma poses significant challenges. It can be managed using both topical and systemic immunosuppressant medications. The most common treatments include topical or intralesional steroids, systemic steroids, topical calcipotriene, psoralen photochemotherapy, cyclosporine, D-penicillamine, methotrexate, mycophenolate, extracorporeal photochemotherapy and a trial of UVA1 phototherapy[10,11].

CONCLUSION

We present a rare case of a 43-year-old male with diffuse systemic scleroderma with nodular scleroderma variant, complicated by ILD and PAH. This case underscores the importance of recognising the diversity in the presentations of scleroderma and the diagnostic complexity that arises when distinct subtypes overlap. Timely and accurate diagnosis is crucial for appropriate management and improved patient outcomes.

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