Case Report

A Case of Nephrogenic Fibrosing Dermopathy

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Abstract

Introduction: Nephrogenic fibrosing dermopathy is a recently recognised fibrosing disorder originally identified as a scleromyxoedema-like cutaneous disease in patients with renal disease. Clinical Picture: A 45-year-old lady with systemic lupus erythematosus presented with well-defined erythematous, non-tender, indurated plaques on both legs 4 months after haemodialysis for rapidly progressive glomerulonephritis and acute renal failure. Skin biopsy showed dermal fibrosis with increased proliferation of dermal fibroblasts and collagen bundles separated by clefts. There were increased dermal deposits of mucin and an increase in elastic fibres. Treatment and Outcome: Haemodialysis was instituted for 2 weeks followed by monthly intravenous cyclophosphamide. Skin lesions remained unchanged 8 months later despite normalisation of renal function. Conclusion: Nephrogenic fibrosing dermopathy appears to be a definite new entity in patients with underlying renal insufficiency. Further multi-centre collaborative study is necessary to identify the prevalence, cause, treatment and prognosis of this disorder.

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Key words: Fibrosis, Haemodialysis, Renal disease

Introduction

Nephrogenic fibrosing dermopathy (NFD) is a recently described and recognised fibrosing disorder occurring in patients with renal disease. The condition resembles scleromyxoedema clinically and histologically, and was originally termed "scleromyxoedema-like illness of haemodialysis". The cause and prevalence remain unknown.

Case Report

A 45-year-old Indian woman with systemic lupus erythematosus (SLE) and secondary antiphospholipid syndrome (APS) presented with a 1-month history of erythematous painless plaques on both shins.

Five months prior to onset of the leg lesions, she had been admitted for active SLE with rapidly progressive glomerulonephritis, oliguria and acute renal failure. Serum creatinine rose from 135 μmol/L to 658 μmol/L, despite intravenous methylprednisolone for 3 consecutive days. Haemodialysis was administered for 2 weeks, with gradual improvement of renal function. She was commenced on pulse intravenous cyclophosphamide monthly. Four months later, she presented with lesions on both legs. There were well-defined erythematous, non-tender, indurated plaques confined to both legs, associated with pitting oedema (Fig. 1). There were no joint deformities. The palms and sclera were not involved.

The clinical diagnosis included tumid lupus erythematosus, pretibial myxoedema and the recently described entity of NFD. The patient was clinically euthyroid. The serum creatinine was 77 μmol/L, erythrocyte sedimentation rate was 7 mm/hour and thyroid function tests and full blood count were normal. There was no peripheral eosinophilia. Serum protein electrophoresis was not performed, but serum globulins were not elevated. Hepatitis B surface antigen was negative. A punch biopsy of the plaque on the leg revealed dermal fibrosis with extension along the fat septae into the subcutis (Fig. 2). There was increased proliferation of dermal fibroblasts and collagen bundles were separated by clefts (Fig. 3). Immunohistochemical stains revealed diffuse positivity of dermal spindle cells for CD34. In addition, there were increased dermal deposits of mucin and an increase in elastic fibres.

Topical treatment was not attempted. The skin lesions remain unchanged at 8 months. Serum creatinine remains within the normal range.

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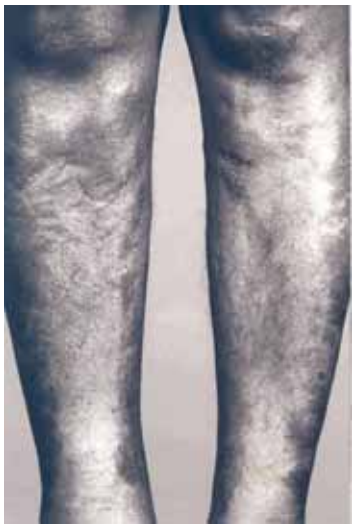

Fig. 1. Indurated plaques on both legs of a 45-year-old patient with nephrogenic fibrosing dermopathy.

Fig. 2. Dermal proliferation of spindle cells with septal extension into the subcutis. (Haematoxylin and eosin stain, original magnification x40)

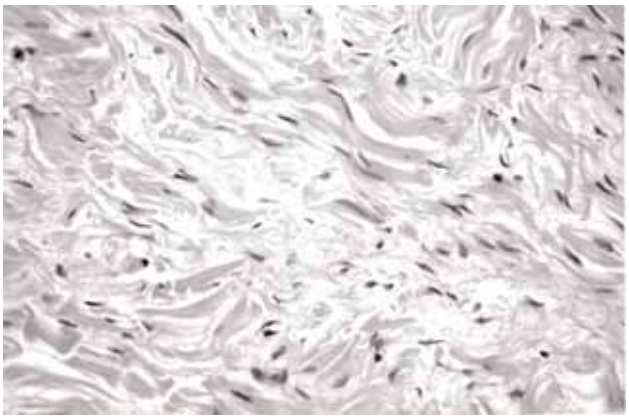

Fig. 3. Dermal fibroblasts and thickened collagen bundles separated by clefts. (Haematoxylin and eosin stain, original magnification x400)

Discussion

The clinical and immunohistological features of this patient are consistent with a diagnosis of NFD.[1] The disease was originally identified as a scleromyxoedema-like cutaneous disease in renal-dialysis patients.[2] This cohort of 14 patients had renal disease of various causes prior to the onset of skin lesions, with 9 having undergone renal transplantation several days to >2 years earlier. These patients had acquired an erythematous to brawny thickening and hardening of the skin of the limbs and torso, with papules, nodules and joint contractures in some. In lesional skin within 20 weeks of clinical onset, there were numerous epithelioid, stellate dermal spindle cells in the reticular dermis, with thickened collagen bundles separated by prominent clefts. CD34-positive dermal dendrocytes were found to entwine and encrust thick, glassy elastic fibres. There were foci containing epithelioid to stellate factor XIIIa-positive cells with abundant mucin.

Three patients have been diagnosed with NFD at 1, 2 and 120 months following liver transplantation.[3] All patients had renal dysfunction and required haemodialysis before and after liver transplantation. The kidney function of 2 patients was improving at the time of diagnosis of NFD, possibly indicating that improvement in renal function does not influence the clinical course of NFD.

In another series of 13 patients with NFD, it was noted that many of these patients also had other underlying serious comorbid diseases, such as severe acute or chronic hepatobiliary disease, pulmonary fibrosis and cardiomyopathy.[4] NFD did not, however, appear to predispose to new systemic manifestations until the report of a patient with end-stage renal failure (ESRF) who developed NFD 6 days after rejection of a cadaveric kidney transplant.[5] He died 11 months after the onset of NFD and, at autopsy, was found to have extensive fibrosis and calcification of the diaphragm, psoas muscle, renal tubules and rete testes.

Anticardiolipin or antiphospholipid antibodies may feature in the pathogenesis of the disorder.[6] Our patient had significant lower limb oedema, a history of APS and longstanding immunosuppression. It has been postulated that oedema, coupled with immunosuppression, in patients with antiphospholipid antibodies results in the proliferation of fibroblast-like cells and mucin deposition in the dermis.[6] There is a suggestion that myofibroblasts and cytokines, such as transforming growth factor-β (TGF-β), may be involved in disease pathogenesis.[4]

The differential diagnoses of NFD include fibrosing disorders such as scleromyxoedema and systemic sclerosis. In scleromyxoedema, waxy papules arranged in a linear fashion are typically found on the face, neck and hands. There is associated paraproteinaemia and systemic manifestations, such as arthritis, myopathy and cerebral symptoms.[7] Facial lesions are uncommon in NFD. In morphoea and systemic sclerosis, there is decrease in fibroblasts, more hyalinisation of the collagen and no

increase in dermal mucin, in contrast to NFD. Systemic involvement in systemic sclerosis includes pulmonary fibrosis, dysphagia and cardiac abnormalities.

There is no definite treatment for NFD. Photophoresis and thalidomide are currently being attempted.[6,8] A patient with ESRF of unknown aetiology and NFD treated with oral prednisone 1 mg/kg body weight showed no improvement.[9] Three patients who developed NFD after liver transplantation were treated with 1 to 3 five-day courses of plasmapheresis exchange at intervals of 2 to 4 weeks, and demonstrated complete or partial disappearance of the skin lesions and associated contractures.[3] It has also been suggested that decreasing the dose of erythropoietin in patients with renal disease may improve NFD in some patients, as recombinant erythropoietin has potential fibrogenic properties.[10] The skin lesions of our patient remain unchanged after 8 months, despite normalisation of renal function.

NFD appears to be a definite new entity. A toxin, drug or infectious agent are various postulates in the pathogenesis of NFD, in view of its recent recognition and clustering of reported cases.[5] Previous reports have not highlighted any association of the disease with respect to age, sex or race. Further multi-centre collaborative study is necessary to identify the prevalence, cause, treatment and prognosis of this disorder.

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