Case Report

Mixed Connective Tissue Disease Associated with Skin Defects of Livedoid Vasculitis


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Abstract: A 21-year-old woman who had a 2-year history of mixed connective tissue disease (MCTD) developed rapidly evolving ulcers consistent with livedoid vasculitis (LV) in all distal extremities. She presented clinically with Raynaud’s phenomenon, polyarthritis and swollen hands; serologically with high titres of ANA and anti-nRNP; and immunogenetically with HLA-DR4 and HLA-DR53. Although there was initial success in treatment except for the skin defects over the ankles, the patient died from disseminated intravascular coagulation. We suggest that LV may be a poor prognostic manifestation in MCTD.

Keywords: Livedoid vasculitis; Mixed connective tissue disease

Introduction

Mixed connective tissue disease (MCTD) as an overlap syndrome combining features of systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and polymyositis/dermatomyositis (PM/DM), together with the presence of antibodies to U₁ small nuclear ribonucleoprotein (snRNP), shows various skin manifestations [1]. Livedoid vasculitis (LV) is a cutaneous occlusive vasculopathy characterised by chronic recurrent bizarrely shaped painful ulcerations of the feet, ankles, and legs, which heal to leave hyperpigmentation and white atrophy [2]. LV has been described with systemic inflammatory disorders, including SLE, rheumatoid arthritis (RA), DM, polyarteritis nodosa, SSc, antiphospholipid syndrome (APS) and cryoglobulinemia [2–7]. In this paper we report a case of a patient with MCTD who had a rare skin lesion of LV.

Case Report

On 17 January 1999 a 21-year-old Korean woman was hospitalised because of multiple painful non-healing ulcers on the hands and lower legs. The ulcers began as multiple petechial lesions and over the following 2 months formed variously sized ulcers and crusted lesions (Fig. 1A,B).

In February 1997, Raynaud’s phenomenon (RP) and swelling had begun on the distal third finger of her left hand. In January 1998 generalised myalgia, arthralgia, and arthritis developed in both wrists and ankles. Treatment with steroids and NSAIDs at a private clinic did not prove effective. Three months later the patient complained of non-pitting oedema on both hands and face. In the winter of that year, despite self-administration of various oriental herbal medications, the RP and oedema spread throughout both hands. She had no familial history of any rheumatic diseases and no history of smoking. She had been healthy until 2 years previously.

The results of routine laboratory tests revealed no abnormal findings. Creatine kinase was 81 units (normal 30–180). The bleeding time, prothrombin time (PT) and
activated partial thromboplastin time (aPTT) were in the normal range. The serum levels of proteins C and S, fibrinogen and antithrombin III were all normal. Rheumatoid factor was 53.1 IU/ml (normal <20.0). Antinuclear antibodies (ANA) were positive at a titre of 1:10240 and showed a speckled pattern. The extractable nuclear antigens tested by the double immunodiffusion method were negative for anti-Sm, anti-SS-A/Ro, anti-SS-B/La, anti-Scl-70, and anti-Jo-1. However, anti-U1RNP was positive up to a serum dilution of 1:64. Antineutrophilic cytoplasmic antibodies were positive at a titre of 1:80, and showed a perinuclear pattern. Antidouble-stranded DNA (dsDNA) using the *Crithidia luciliae* indirect immunofluorescence assay was negative. Complement C3 and C4 were within the normal range. Cryoglobulin, VDRL, antestreptolysin O, anticardiolipin antibody and lupus anticoagulant were also negative. Viral markers of hepatitis B and C were negative. Serum protein electrophoresis showed no abnormal monoclonal spikes. In pulmonary function testing the diffusion capacity of the lung (DLco) was moderately decreased to 53.3%. Radiologically, the PA chest view was normal and no abnormal bone changes were shown. The biopsy taken from the lower leg showed necrosis of the epidermis. The small blood vessels in the superficial and deep dermis showed hyalised blood vessel walls with fibrinoid necrosis, fibrin thrombi and plump endothelial cells. Characteristically, inflammatory cells were sparse, unlike in other forms of vasculitis (Fig. 2).

The patient showed high anti-nRNP titres, swollen hands, synovitis and Raynaud’s phenomenon, which was compatible with a diagnosis of MCTD according to Alarcon-Segovia [8]. The histological features on biopsy confirmed a diagnosis of LV. During hospitalisation the patient was treated with prednisolone (PD, 30 mg/day, 0.5 mg/kg), hydroxychloroquine (400 mg/day), low-dose aspirin (100 mg/day), nifedipine (90 mg/day), pentoxifylline (1200 mg/day), limprost (prostaglandin E1 (PGE1), 30 μg/day) and warfarin (2 mg/day, international normalised ratio (INR) 2–3). One month later the pain at the tips of the fingers and toes had disappeared. The ulcers had improved markedly without any newly developed skin lesions. However, the skin defects on the lateral surface of both ankles remained persistent. Afterwards, PD was tapered but the other medications were maintained.

On 28 April 1999 she was readmitted because of a low-grade fever, dry cough and newly developed pus-like discharges on both lower legs and a gangrenous second finger of the right hand. Wound cultures of the hand and legs showed infection with *Staphylococcus aureus* and *Enterobacter cloacae*, respectively. A pneumonic infiltration was observed in the left lower lobe and lingular segment. We tried a more aggressive means of wound dressing with intravenous antibiotics according to the sensitivity test results. In 3 weeks the chest infiltration had decreased and the culture on the skin lesions also revealed no growth. However, the patient complained of nausea and recurrent ischaemic pain in both extremities, evident by the purple colour changes. Laboratory studies revealed the leukocyte count to be 3500/μl, haemoglobin (Hb) 13.4 g/dl, platelet count 85000/μl, and INR 1.77, with a warfarin

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**Fig. 1.** The skin with a livedoid background shows multiple whitish healed scars on the hands (A) and crusted ulcers over the feet (B).

**Fig. 2.** Photomicrograph of a biopsy specimen from the lower leg showing luminal fibrin thrombi and fibrinoid necrosis in small dermal vessels, with rarely any deposition of inflammatory cells and necrosis of the overlying epidermis (haematoxylin and eosin; ×100).