Coexistence of Diffuse Reactive Angioendotheliotomatosis and Neutrophilic Dermatosis Heralding Primary Antiphospholipid Syndrome

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Sir,

Reactive angioendotheliotomatosis (RAE) is a rare entity characterized by a massive proliferation of endothelial cells in patients with coexistent systemic disease in which occlusive or vasculopathic processes occur leading to reactive endothelial cell proliferation, such as infectious, lymphoproliferative, autoimmune and peripheral vascular disease, cryoproteinemia and amyloidosis. RAE (1) has not been associated with primary antiphospholipid syndrome (APS). We report here the first case in which RAE and a neutrophilic dermatosis developed simultaneously and prior to clinical manifestations of primary APS.

CASE REPORT

A 51-year-old woman presented with a 6-month history of asymptomatic persistent violaceous lesions. There were no constitutional symptoms, her past medical history was unremarkable, and she was not taking any oral medications. Skin examination revealed several well-demarcated, flat-topped or dome-shaped, purple or purpuric papules and plaques over the elbows, thighs and buttocks (Fig. 1). The erythrocyte sedimentation rate was 100 mm/h (normal: < 20 mm/h), anticardiolipin antibody (aCL) of IgG isotype was persistently elevated (14–45; normal: < 10), partial thromboplastin time was 45 sec (normal: 1–40 sec) and gamma globulin polyclonal was 2.8 (normal: 0.6–1.6). The following laboratory parameters were within normal limits: complete blood cell count, antibody profile for autoimmune disease, cryoglobulin, cryofibrinogen, C and S functional proteins, lupus anticoagulant and dilute Russell viper venom time. Biopsy findings showed a dermal proliferation of closely packed, predominantly capillary-sized vessels lined by bland but plump endothelial cells, without significant atypia (Fig. 2). Variably dilated vascular spaces surrounded by pericytes were also present. There were no intravascular thrombi to suggest a pre-existing coagulopathy. Stains for endothelial markers (CD31 and factor VIII) were positive. The features were consistent with diffuse RAE.

Two months later the patient developed new erythematous or urticaria-looking asymptomatic plaques on her arms, hands and thighs, and she mentioned that she had had similar lesions in the past. There were no clinical features of Sweet’s syndrome. A skin biopsy revealed features of florid interstitial neutrophilic dermatosis indistinguishable from those of rheumatoid neutrophilic dermatosis; there were no histopathological features of vasculitis. Patient fulfilled two classification criteria for APS (small vessel thrombosis and aCL). The ulcers healed slowly with meticulous wound care and intake of aspirin 321 mg orally daily.

The RAE lesions did not respond to oral steroids, cryotherapy and treatment with alitretinoin 0.1% (Panretin) gel. Some improvement was noticed with intralesional triamcinolone acetonide 40 mg/ml. The RAE lesions were finally treated twice with purpuric doses of long-pulsed pulsed dye laser (595 nm) (Vbeam; Candela Corp., Wayland, MA, USA). The treatments were performed one month apart. After the laser treatments some lesions resolved, while others became soft, flat and grey or tan instead of purple or bright red; changes that satisfied the patient.

Fig. 1. Flat-topped or dome-shaped violaceous or purpuric papules and plaques distributed over the buttocks and thigh.

Fig. 2. Biopsy specimen from the lesions shown in Fig. 1 reveals a proliferation of closely packed, predominantly capillary-sized vessels as well as variably dilated vascular spaces lined by bland but plump endothelial cells and surrounded by pericytes; there are no intravascular thrombi to suggest a pre-existing coagulopathy (hematoxylin-eosin stain × 20).
RAE is usually self-limited, affecting mostly the middle-aged, and can be associated with constitutional symptoms. The skin lesions have a propensity to involve the limbs, and include erythematous to violaceous patches, papules or plaques that can ulcerate or blister and may mimic angiosarcoma or Kaposi’s sarcoma (1, 3). RAE has been classified into several histopathological types (4), including diffuse dermal, intravascular, tufted angioma-like and glomeruloid types – the case described in this report is a diffuse RAE. No specific treatment is available, since RAE may respond to treatment of the underlying disorder. Antibiotics for occult infections and systemic steroids have been used with variable results.

Some authors have suggested that RAE may be a stage in the revascularization process of the thrombotic vessel (4). Potential etiologic factors include immune complexes, bacterial antigens, cryoproteins, venous stasis and local hypoxia. RAE in our case is secondary to aCL, which fits with the proposed mechanism of vascular reactions such as rheumatoid neutrophilic dermatitis. It is also supported by the fact that several lesions in our patient showed histopathological features of both RAE and neutrophilic dermatitis. We believe that the associations among RAE, neutrophilic dermatosis and APS in our patient are caused by aCL through the mechanisms outlined above.

REFERENCES