CLINICAL VIGNETTE

Efficacy of Intravenous Immunoglobulins in Difficult-to-Treat Livedoid Vasculopathy

Ralph Yachoui, MD

Livedoid vasculopathy (LV) is a non-inflammatory thrombotic vasculopathy characterized by recurrent painful lower limb ulcerations. These resolve leaving ivory-white atrophic scars with surrounding telangiectasias known as atrophie blanche.[1] LV is thought to be the result of several coagulation disorders; therefore, most treatments are based on anticoagulation. We report a case of refractory LV in a woman successfully treated with pulsed intravenous immunoglobulins (IVIG).

Case Report

A 49-year-old woman was referred to our rheumatology department due to refractory painful ulcers on her lower legs. She had a 20-year history of lower extremity lesions which periodically ulcerated and became painful. She was diagnosed as having LV at another institution and was treated with chronic anticoagulation with enoxaparin. Her flares were initially mild occurring once a year. They worsened in severity and duration after she moved to a warm climate 3 years ago, occurring on average four times a year. Numerous therapies were initiated including antiplatelet agents, pentoxifylline, oral steroids, Rivaroxaban, warfarin, and more recently Rituximab (for 1 year), with no relief.

She had a history of seizure and heterozygous prothrombin G20210A mutation. Her sister had the same genetic mutation. There was no family history of blood clots. She had 20 pack-year smoking history and drank alcohol occasionally. She was allergic to penicillin. Examination at our center revealed reticulated erythematous non-blanchable patches on arms, thighs, legs, and feet. On the distal part of her lower legs, well-demarcated tender ulcers with hemorrhagic crusts were present (Figure 1). There was no sensory or motor deficit in the legs.

Complete blood count and comprehensive metabolic panel were normal, as were blood levels for antinuclear antibodies, antiphospholipid antibodies, cryoglobulin, cryofibrinogen, antineutrophil cytoplasmic antibodies, and protein electrophoresis. Except for prothrombin G20210A mutation heterozygosity, all remaining thrombophilia factors were negative or within normal limits. A review of an old biopsy specimen showed dermal blood vessels occluded by thrombi without frank leucocytoclastic vasculitis.

IVIG at the dose of 1 g/kg monthly was initiated with complete resolution of the lesions after 3 infusions. It was well tolerated and was continued for 1 year without any recurrence.

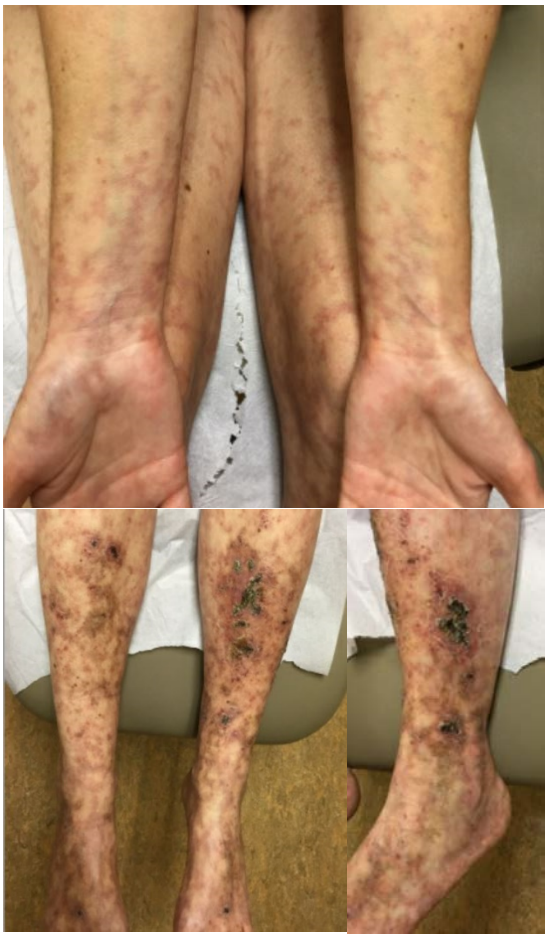

Figure 1

Discussion

LV, also known as atrophie blanche, is a rare and under-diagnosed clinical entity. The estimated incidence of LV is 1:100,000 individuals, predominantly affecting young to middle-aged females, with a sex ratio of 3:1.[2] It may mimic cutaneous vasculitis or stasis dermatitis clinically, therefore, biopsy is helpful in confirming the diagnosis.

Typical histological include thrombotic occlusion of small dermal vessels with intraluminal fibrin deposits, segmental hyalinization of the vessel wall, and sometimes endothelial proliferation or red blood cell extravasation. Neutrophilic infiltrate of the blood vessel walls and fibrinoid necrosis, the hallmark of true vasculitis, are typically absent.[3] The disease is manifested by multiple skin flares always accompanied by

severe pain. Flares consist of purpura and necrotic ulcers and persistent livedo reticularis.[1,3] In our patient, the flares may have been triggered by warm temperature.

The pathophysiology of LV is not clearly understood but an underlying hypercoagulable state is the cornerstone of the disease.[4] Our thrombophilia screen revealed prothrombin G20210A mutation heterozygosity. LV is considered the end result of hypercoagulation disorders, including Factor V Leiden mutation, protein C and protein S deficiency, prothrombin gene mutation, antithrombin deficiency, activated protein C resistance, hyperhomocysteinemia and the antiphospholipid syndrome.[4] Of note, our patient was a chronic smoker, which might have exacerbated her skin flares.

Finding effective treatment is a challenge for clinicians and consensus is lacking due to the paucity of available data.[5] Therapy usually includes smoking cessation and prevention of trauma, in addition to addressing any underlying coagulation disorder. Various anticoagulant and antiplatelet agents have been reported to be effective in individual cases or case series.[6] A recent review of LV treatment[7] confirmed the most prescribed treatment was anticoagulation in 98% of cases. Another study reported low molecular weight heparin and antiplatelet agents were the most often used first-line therapy and that anticoagulation with heparin was the most successful treatment.[8]

Difficult-to-treat or refractory patients such as ours pose a real problem. In the recent French cohort,[8] eight patients (32%) had severe disease with healing taking over 3 months, with no response to conventional anticoagulant or antiplatelet agents. Our patient had also failed oral glucocorticoids and Rituximab therapy, which supports the non-inflammatory nature of LV. Previous small case series have used IVIG in severe disease with favorable response.[9-12] A complete remission occurred in our patient only after 3 infusions and persisted after 1 year of treatment. Similar positive results were reported in another recent study of 8 patients with severe disease refractory to anticoagulation.[8] These patients were successfully treated with IVIG with 94% having > 50% improvement and 63% achieving complete remission. IVIG can be an interesting alternative treatment for the most severe cases.

Figure Legend

Figure 1. Livedo reticularis involving the upper and lower limbs. Well-demarcated erythematous ulcers on the distal lower extremities.

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