Livedoid vasculopathy – a challenging disease

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To the Editor,

Livedoid Vasculopathy (LV) is a chronic recurrent thrombo-occlusive vasculopathy of unknown pathogenesis that has been associated with hypercoagulable states and several connective tissue diseases[1]. It particularly affects middle-aged women and presents as painful purpuric papules, mainly distributed over the lower legs that subsequently ulcerate and slowly heal with residual white atrophic stellate scars[2]. Neurological involvement is rare and probably secondary to the ischemia of the vasa nervorum[3]. Treatment is often challenging and usually based on case series. We present a refractory LV case associated with peripheral neuropathy, successfully treated with rituximab.

A 58-year-old woman presented with a 3-year history of pain, paresthesiae and multiple leg ulcers. She had an irrelevant medical history and her physical examination was normal except for the presence of multiple reticulate and ulcerated lesions in both the anterior surface of her legs and around the ankles, with areas of intense red/violaceous macules, very painful to touch. Neurological examination revealed hypoesthesia in the dorsum of both feet.

Blood counts, hepatic and renal function, erythrocyte sedimentation rate and C reactive protein were normal; homocysteine, protein C and S activity, activated protein C resistance and antithrombin III showed normal levels; cryoglobulins, cryoagglutinins, lupus anticoagulant and anti-phospholipids antibodies were absent; G2021A prothrombin and C677T methylenetetrahydrofolate reductase mutations were negative. Antinuclear antibodies, anti-dsDNA, antineutrophil cytoplasmatic antibodies, rheumatoid factor, circulating immune complexes and anti-ENA (jo-1, RNP, SCL-70, Sm, SSa and SSb) were also negative. Immunoglobulins, C3c and C4c were within normal ranges and serum proteins electrophoresis had no alterations. HIV and HCV serologies were negative. Ag HBs was negative but AcHBc and AcHBs were positive (5.08 and 714 respectively UI/L), although HBV DNA was undetectable. Electromyography showed lower limbs sensitive polyneuropathy but skin and sural nerve biopsies were inconclusive.

For suspected vasculitis, a 3-month course of 1mg/Kg/day prednisolone was tried, unsuccessfully. A symptom control strategy based on gabapentin was implemented but 2 years later, recrudescent pain justified a new skin biopsy that revealed the presence of eosinophilic, PAS positive material within dermal vessels with minimal inflammatory infiltrate and, on immunofluorescence, perivascular immunorreactivity to fibrinogen and dermal vessels deposits of IgM and C3c, consistent with LV. The patient was medicated with warfarin and immunoglobulins (IvIg) (2 gr/Kg over five days, every 4 weeks). With treatment maintenance, the patient experienced improvement of pain and dysesthesiae, and cicatrization of leg ulcers. However, 8 years later, aggravation of pain and cutaneous ulcers was again noticed. Warfarin and IvIg were stopped and the patient was started on rituximab 1.0 g, 2 infusions, 14 days apart, associated with entecavir for HBV reactivation pro-

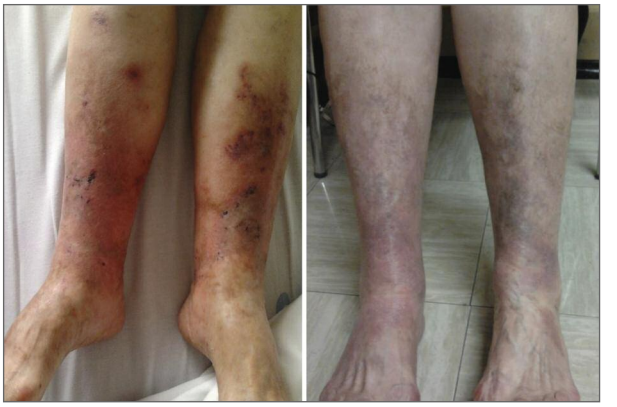

FIGURE 1. Cutaneous lesions (left) before and (right) one year after treatment with Rituximab

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phylaxis. Since then, the patient presented gradual improvement and currently, 1 year later, she has full cicatrization of her leg ulcers (Figure 1) and no need of analgesia, referring only mild dorsal feet hypoesthesia.

A previous case report[4] describes improvement of both pain and ulcers related to cutaneous LV after treatment with rituximab.

The case presented emphasizes that even after prolonged involvement, peripheral neuropathy may improve with rituximab treatment. Despite the typical absence of neutrophil infiltration on the blood vessels, accumulating clinical experience suggests that B cells may be key players in LV pathogenesis.

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