Successful treatment of livedoid vasculopathy with rivaroxaban

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INTRODUCTION

Livedoid vasculopathy is a disorder which is thought to be caused by systemic dysregulation of coagulation, resulting in the formation of fibrin thrombi in the superficial dermal plexus. Chronic disease often results in painful, punched out ulcerations and atrophie blanche on the lower extremities, predisposing affected patients toward infection and high morbidity. Treatment of livedoid vasculopathy is controversial and often ineffective. Owing to the postulated pathophysiology, rivaroxaban recently was suggested as a treatment modality and seems to induce significant improvement in some patients. Herein, we report the successful treatment of recalcitrant livedoid vasculopathy in one patient with no identifiable coagulopathy and propose that a therapeutic trial of rivaroxaban may be helpful in patients with no detectable underlying coagulability disorders. Further evidence of clinical efficacy is needed to confirm the benefit of rivaroxaban in patients with livedoid vasculopathy.

CASE REPORT

A 57-year-old woman presented to our clinic shortly after a receiving a diagnosis of livedoid vasculopathy. She had a 2.5-year history of painful, violaceous, retiform macules and papules on the bilateral lower extremities with ulcerations and scarring (Fig 1). The diagnosis of livedoid vasculopathy was made based on the appearance of the lesions, clinical history, and biopsy of a lesion from the left ankle showing dilated vascular structures with fibrin in the vessel wall, epidermal ulceration, and hemorrhagic serum crust. The patient gave no history of venous thrombosis, recurrent miscarriages, strokes, or venous insufficiency. She also had no known family history of lupus, clotting disorders, or miscarriages. Numerous hypercoagulability studies (Table I), cancer screenings, and autoimmune tests found no abnormalities. Various treatments reported to improve livedoid vasculopathy were tried with no improvement in pain or physical findings. Cellulitis developed, which was treated and resolved with intravenous and oral antibiotics. She finally experienced mild improvement on a regimen of nifedipine, 30 mg daily, aspirin, 325 mg daily, and pentoxifylline, 400 mg 3 times daily. However, she acutely worsened after the pentoxifylline was tapered to once daily, prompting us to resume 3-times-daily dosing. Despite this treatment regimen, she continued to have numerous ulcerations with infections on her lower extremity, including by *Staphylococcus aureus*, and had to be hospitalized for treatment. Psoralen plus ultraviolet light therapy was tried in between infectious episodes with no improvement.

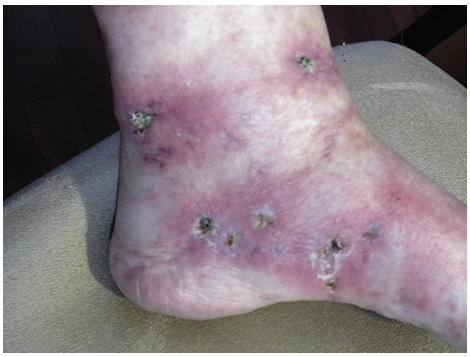

Fig 1. Livedoid vasculopathy presenting with ulcerations on the left lower extremity (pre-treatment).

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Table I. Laboratory studies performed

Tests	Results
Homocysteine level	Normal
Protein C level	Normal
Protein S level	Normal
Anticardiolipin antibodies	Negative
Lupus anticoagulant	Negative
Beta-2 glycoprotein 1 antibodies	Negative
Cryoglobulins	Negative
Factor V Leiden mutation	Negative
Prothrombin gene mutation (G20210A)	Negative

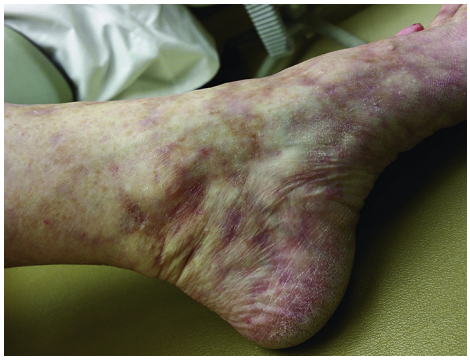

Fig 2. Well-healed ulcers after 8 months of rivaroxaban.

One and a half years after we began seeing the patient, we decided to initiate a trial of rivaroxaban at 20 mg daily. At her 2-month follow-up, the patient's pain had greatly improved, and many of her ulcerations had resolved. No sign of infection was present, and only residual scarring was noted on physical examination. The improvement seen on rivaroxaban was markedly better than that of any previous treatment the patient had received and has continued to be efficacious after 8 months of treatment with complete healing of all previous ulcers and no new ulcers (Fig 2).

DISCUSSION

Livedoid vasculopathy is a disease that generally affects the lower extremities. Classically described in young to middle-age women, livedoid vasculopathy often presents as livedoid purpura with punched-out ulcerations, often resulting in atrophie blanche.[1] At one time, atrophie blanche was considered synonymous for livedoid vasculopathy. However, by its current usage, atrophie blanche–like lesions are not specific to livedoid vasculopathy. For this reason and because of a lack of consistent diagnostic criteria, the literature on livedoid vasculopathy is often not clear. Clinical differential diagnoses include other vascular diseases such as antiphospholipid antibody syndrome or venous stasis disease. Therefore, a biopsy may aid in arriving at the correct diagnosis. Histopathology may show a mild perivascular lymphocytic infiltrate, hyalinization of small dermal vessels, and intraluminal thromboses.[2]

Livedoid vasculopathy is seen in patients with and without identifiable coagulation abnormalities.[3] Accordingly, anticoagulation therapy is believed to be helpful in at least some cases of livedoid vasculopathy. Our patient had longstanding, intractable livedoid vasculopathy complicated by recurrent skin infections. Despite a thorough coagulation workup, she did not have any identifiable coagulation abnormalities. Her favorable response to rivaroxaban, however, may suggest an occult coagulation abnormality that portended a tendency toward livedoid vasculopathy and remained undetected by laboratory testing. Rivaroxaban has been described in the treatment of livedoid vasculopathy.[4] However, there has been only one reported case of a patient who was treated successfully with no known coagulopathy.[5] Our case also shows the potential utility of rivaroxaban in the treatment of livedoid vasculopathy with no identifiable coagulation disorder. Unfortunately, it is not possible to determine the role of rivaroxaban in the treatment algorithm of livedoid vasculopathy without a multicenter therapeutic trial. An ongoing phase II multicenter trial is currently assessing the efficacy of rivaroxaban in treating pain in livedoid vasculopathy.[6] Results from this trial are not yet available. In our experience, we believe that the current anecdotal evidence is sufficient to warrant a trial of rivaroxaban for patients with recalcitrant livedoid vasculopathy, even in the absence of known coagulopathy.

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