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BRIEF COMMUNICATION

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Successful Treatment of Painful Cutaneous Vasculopathy With Rivaroxaban in a Patient With Systemic Lupus Erythematosus

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ABSTRACT

Novel oral anticoagulant (NOAC) medications have revolutionized hematology and cardiology. Recently, NOACs have demonstrated additional promise in dermatology. Specifically, rivaroxaban, a direct factor Xa inhibitor NOAC, has been shown to be successful in the treatment of livedoid vasculopathy. Herein, we describe a patient with systemic lupus erythematosus who presented with painful cutaneous vasculopathy, demonstrated on biopsy with occlusive microvascular fibrin thrombi without evidence of concurrent vasculitis. Interestingly, imaging and laboratory studies did not show evidence of hypercoagulability, arterial disease, or embolic disease. The patient's vasculopathy and pain progressed despite antiplatelet therapy, often considered first-line in cases of microvascular occlusive disease. However, with rivaroxaban therapy, the patient experienced complete regression of her painful lesions, thereby supporting a further role for NOACs in cutaneous vasculopathy treatment.

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INTRODUCTION

Cutaneous vasculopathies are disorders in which blood vessel occlusion, in the absence of vasculitis, is observed on skin biopsy. Cutaneous vasculopathy has a broad histopathologic differential including embolization, platelet plugging, cold-related gelling or agglutination, vessel-invasive microorganisms, systemic coagulopathies, vascular coagulopathies, and miscellaneous syndromes such as cocaine levamisole toxicity.[1] In patients with biopsy-proven nonvasculitic cutaneous vasculopathy, a systemic laboratory and imaging work-up is warranted given the potential for visceral involvement in these diseases and their numerous associations with systemic vascular and autoimmune conditions.[1] In the case of a negative systemic work-up, dermatologic treatment historically involved antiplatelet therapies. We present a case of a patient with systemic lupus erythematosus and cutaneous vasculopathy who, after failing to respond to antiplatelet therapy, rapidly improved with rivaroxaban anticoagulation.

CASE

A 59-year-old woman with a history of systemic lupus erythematosus (SLE), breast cancer, and cerebrovascular disease (transient ischemic attack and right carotid thrombosis) presented to dermatology for evaluation of an increasingly painful violaceous rash of her left lateral foot and 5th toe of two months' duration. She complained of constant 8/10 stabbing foot pain which had worsened in spite of aspirin 325mg daily therapy prescribed by her primary care physician for the past two months. Ibuprofen, acetaminophen, and hot/cold packs could not relieve her severe pain. As a result, she was prescribed short-term narcotic pain medication. Of note, she had not previously required or requested narcotics. She denied recent cardiac catheterizations, trauma, fever or chills, chest pain, limb pain, shortness of breath, or neurologic symptoms. She denied previous discoloration of her extremities or association of symptoms with cold temperature or stress. She denied recent treatment with anticoagulants or a family history of blood clots. She did not have a history of illicit drug use.

The patient was referred by her rheumatologist, with whom she followed for a history of SLE manifested by inflammatory arthritis, photosensitive cutaneous lupus and tumid lupus (confirmed with skin biopsy prior to presentation), and antinuclear antibody titer 1:40. Her SLE was well controlled with hydroxychloroquine 300mg once daily. One month after the onset of her foot lesions, she had a flare of biopsy-proven tumid lupus lesions on her shoulders and upper arms that was treated by her PCP with an intramuscular injection of methylprednisolone 125 mg. She noted no change in the foot lesions following this treatment. She had a history of right common carotid thrombosis which was managed surgically with carotid endarterectomy,

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FIGURE 1. Retiform violaceous patch on the lateral left foot.

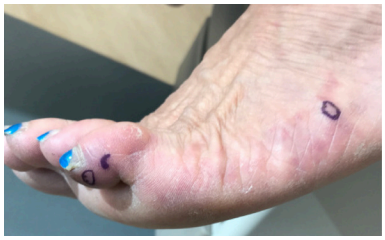


FIGURE 2. Dusky violaceous macules with surrounding violaceous patch on the plantar aspect of left 5th toe.

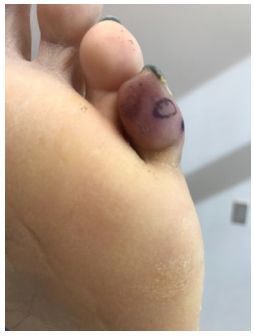
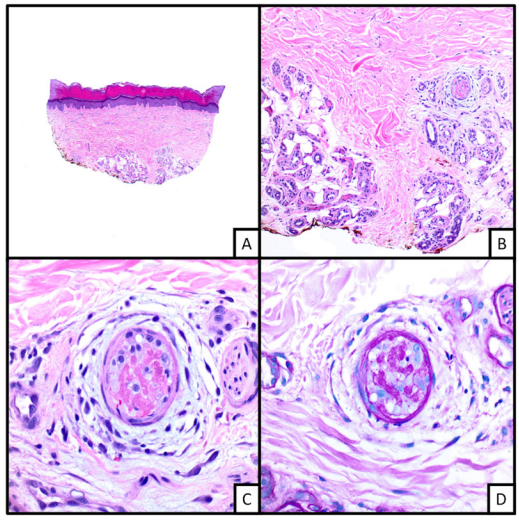


FIGURE 3. Histologic examination of a punch biopsy from the left lateral foot shows acral skin with no significant changes in the epidermis and minimal perivascular lymphocytic infiltrate in the dermis (A, H&E 2X), in the deep dermis fibrin thrombi are identified within the blood vessels (B, H&E 10X). Higher magnification of fibrin thrombi (C, H&E 40X), Periodic acid-Schiff special stain highlighting the fibrin within the vessel (D, PAS 40X).



and for which she took aspirin 81 mg daily and atorvastatin 20mg daily. Her breast cancer was in remission without complication after treatment 8 years prior with bilateral mastectomy, dose-dense Adriamycin (doxorubicin) and cyclophosphamide, trastuzumab, and radiation.

Upon presentation to dermatology, physical examination revealed a tender, erythematous and retiform violaceous patch extending up the lateral aspect of her left foot (Figure 1). The plantar aspect of her left 5th toe was remarkable for dusky, violaceous, ill-defined, blanchable macules (Figure 2).

At this time, the clinical differential diagnosis included etiologies of cutaneous vasculopathy such as acquired or inherited causes of hypercoagulability with particular concern for antiphospholipid syndrome, embolic disease, and cold-related precipitation syndromes. Additional considerations included vasculitis, chilblain lupus erythematosus, and peripheral arterial disease. To help elucidate the diagnosis, a biopsy was recommended.

4mm punch biopsies were obtained of both the toe and lateral foot lesions. Biopsy of the 5th toe revealed numerous telangiectasias but was otherwise unremarkable. Biopsy of the left lateral foot, however, revealed focal periodic acid-Schiff-highlighted fibrin thrombi in deep dermal vessels without evidence of cholesterol emboli, vasculitis or other inflammation, interface dermatitis, or dermal mucin (Figure 3).

Laboratory work-up, including extensive hypercoagulability studies, was unremarkable. Complete blood count, white blood cell differential, protein C, S, and antithrombin activity, prothrombin and factor V Leiden mutation testing, anti-cardiolipin and anti-beta 2 glycoprotein antibodies, dilute Russel viper venom screen, homocysteine level, cryoglobulin screen, C3/4 complements, C-reactive protein, and serum creatinine were normal. Erythrocyte sedimentation rate was slightly elevated at 22mm/hr. Transthoracic echocardiogram and blood cultures were normal. A duplex ultrasonography of the left lower extremity showed stable small, homogenous plaques in the left common femoral artery, left superficial femoral artery, and left popliteal artery without evidence of occlusion and with normal ankle/brachial index.

Given histopathologic evidence of cutaneous vasculopathy and lack of response to aspirin, the patient was started on rivaroxaban 20mg once daily. Fortunately, she achieved rapid resolution of her foot pain and discoloration within two months of therapy and no longer required narcotic pain management.

DISCUSSION

Rivaroxaban is a direct factor Xa inhibitor NOAC used for stroke prevention in atrial fibrillation as well as venous thromboembolism treatment and prophylaxis.[2] Rivaroxaban anticoagulation is advantageous for its fixed dosing without the need for laboratory monitoring. Rivaroxaban is excreted renally, with dose reductions recommended for patients with creatinine clearance

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30-50ml/min, while use is contraindicated in patients with creatinine clearance <30ml/min.[3] Rivaroxaban is metabolized by cytochrome P450 3A4 and is a substrate for the p-glycoprotein transporter, which are both inhibited by systemic azole antifungals.[2] Dermatologists should be aware of rivaroxaban in terms of its drug interactions, but also as a potential dermatologic therapy.

In dermatology, rivaroxaban has recently been shown to be effective in the treatment of livedoid vasculopathy (LV), with its success suggesting a role for NOACs in the treatment of nonvasculitic cutaneous vasculopathy in general. Prior to the advent of NOACs, a 2012 review of LV treatment amongst dermatologists indicated that most case series utilized antiplatelet agents as first-line therapy.[4] However, recently, multiple case reports have demonstrated successful treatment of LV with rivaroxaban, dosed at 10mg or 20mg once daily or 10mg bid.[5-10] In many cases, these patients had failed initial treatment with alternative immunosuppressive, antiplatelet, or anticoagulant therapies.[5-7,10]

In the case presented herein, an unremarkable laboratory and imaging work-up coupled with a biopsy demonstrating dermal fibrin thrombi without evidence of vasculitis was concerning for cutaneous vasculopathy. It is unknown if over time her lesions would have progressed to become more chronic and ulcerative, as is commonly seen in the "atrophie blanche" lesions of LV. Regardless, we observed a rapid, complete response to rivaroxaban, demonstrating its potential utility in patients with idiopathic cutaneous vasculopathy. Furthermore, this case indicates that rivaroxaban therapy remains useful in cutaneous vasculopathy even in the absence of laboratory evidence of hypercoagulability. Most importantly, this case suggests that early intervention with a NOAC in cutaneous vasculopathy can eliminate the need for significant pain medication as well as prevent progression to ulceration and atrophy. Dermatologists should be aware of the potential therapeutic use of NOACs in patients with cutaneous vasculopathy.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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