A case of leukocytoclastic vasculitis caused by novel anticoagulant rivaroxaban.

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Abstract

Cutaneous leukocytoclastic vasculitis (LCV) is type of small vessel vasculitis that commonly presents as palpable purpura involving the lower extremities and buttocks. Approximately half of cases are idiopathic, but the disease may be triggered by infection, drug reaction, inflammatory disease, or other causes. We report a case of leukocytoclastic vasculitis secondary to the novel anticoagulant rivaroxaban (Xarelto®).

Keywords: leukocytoclastic vasculitis, rash, novel anticoagulant, rivaroxaban, Xarelto

Introduction

Leukocytoclastic vasculitis (LCV) is type of small vessel vasculitis characterized histologically by neutrophilic infiltration through small-sized vessels with hyalinization of the vessels and fibrinoid necrosis [1]. The type of endothelium targeted in LCV is usually the postcapillary venule within the dermis. The disorder frequently presents as palpable purpura involving dependent areas including lower legs and buttocks, but can also involve skin at the trunk and upper extremity [2]. Less common skin manifestations include urticarial plaques, bullae, nodules, or ulceration [2, 3]. Approximately half of LCV cases are idiopathic, but the disease can be triggered by infections (e.g., hepatitis B or C, HIV, Streptococcus), reactions to certain medications (e.g., NSAIDs, beta-lactams, sulfa drugs), connective tissue disease, or malignancy [1, 3]. In cases of medication-induced LCV, symptoms typically present between 7-10 days after initial medication exposure, but can occur sooner [4, 5]. Definitive diagnosis of LCV requires biopsy of affected skin, though classic histological findings may be lacking in specimens obtained after 48 hours [2]. In the absence of systemic organ involvement, LCV is a self-limited disease with an excellent prognosis and low recurrence rate [2]. The mainstay of therapy for acute LCV is treatment or removal of the etiologic trigger, if one can be found. Systemic corticosteroids are reserved for more severe cases or those with internal organ involvement [2, 3].

Case Synopsis: A 38-year-old woman with a history of chronic right lower extremity lymphedema from a thermal injury sustained in childhood presented to the emergency department for right lower extremity pain and swelling after a prolonged automobile trip. Laboratory and imaging findings revealed a deep venous thrombosis of the right lower extremity and type II diabetes mellitus, for which she was prescribed rivaroxaban, 15mg twice daily, and metformin, 500mg once daily. Twelve days later, the patient returned to the emergency department with a diffuse purpuric skin eruption that started four days after initiating the new medication regimen. Per examining physician, the skin lesions appeared sterile and were not accompanied by systemic symptoms of infection or internal organ dysfunction. The patient was instructed to discontinue rivaroxaban therapy and was discharged home.

The patient was admitted to the hospital one week later, after arriving to the hospital with complaints of foul-smelling discharge, erythema, and edema consistent with a secondary infection of the existing skin lesions on her right lower extremity. Otherwise,
the patient stated that her rash had started to improve in all other affected areas. She confirmed that her only current home medication was metformin and denied any known allergies to medications or foods, recent fever, chills, cough, hematuria, or sick contacts. Physical exam findings noted the presence of purpuric papules (Figure 1A) distributed primarily from the patient’s waist downward, somewhat mirroring the distribution of her prior thermal injuries (Figure 1B). Over the patient’s chronically lymphedematous right lower extremity were multiple large coalescent hemorrhagic papules and plaques with foul-smelling purulent drainage (Figure 2A). Examination of the patient’s upper extremities revealed multiple pink urticarial-appearing plaques (Figure 2B). There was no mucous membrane involvement and the

Figure 1. A) Hemorrhagic crusted papules and petechial with the erythematous papules representing newer lesions as compared to the darker crusted papules. B) Purpuric papules scattered along abdomen with background ecchymoses secondary to low-molecular weight heparin injections.

Figure 2. A) Right lower extremity with chronic lymphedema and multiple hemorrhagic plaques with foul-smelling purulent drainage. B) Right forearm with indurated papules and plaques, some with early wheal.
remainder of the physical exam was otherwise unremarkable. Complete blood cell count, comprehensive metabolic panel, and urinalysis were within normal limits. ESR and CRP were elevated (60 mm/hr and 3.91 mg/dL, respectively). HIV, Hepatitis Panel, ANA, ANCAs, cryoglobulins, urine drug screen, and serum complements were all negative or within normal limits.

Punch biopsies performed at the right upper arm (Figure 3A) and left lateral upper thigh (Figure 3B) showed a diffuse predominantly neutrophilic inflammatory infiltrate in the papillary and upper reticular dermis with extravasated erythrocytes and scattered increased eosinophils. The small-caliber vessels showed transmural migration of neutrophils with destruction of the vessel wall as evidenced by the fibrinoid degeneration consistent with leukocytoclastic vasculitis. Direct immunofluorescence was not performed. Over the course of the patient’s hospital stay, the palpable purpura of the lower extremities and urticarial lesions of the forearms continued to show improvement. Right lower extremity pain, edema, and purulent drainage quickly resolved with empiric antibiotics as well as heparin therapy with bridging to warfarin in place of rivaroxaban. Upon discharge, she restarted metformin without recurrence of skin lesions and continued warfarin therapy for the deep venous thrombosis. At her follow-up appointment 12 weeks post-discharge, she reported compliance with her medications and had not displayed signs or symptoms of recurrent LCV.

Case Discussion

The temporal relationship between rivaroxaban administration in our patient and initial symptomatic onset, lack of other known etiologic triggers, and resolution of symptoms following discontinuation of the medication implicates rivaroxaban as the trigger for her LCV. Although the patient presented with a cutaneous infection, another potential cause of LCV, before a final dermatopathologic diagnosis was made, the symptomatic timeline indicates that her infection was the consequence of LCV rather than the cause.

Drug-induced LCV can be a challenging diagnosis to make as the differential diagnosis for LCV is broad and timing or quality of symptoms can vary by case [4]. Careful history-taking to establish a precise timeline of symptoms and to eliminate other possible etiologic triggers is paramount. Rivaroxaban (Xarelto®) is a novel anticoagulation drug, which acts by direct inhibition of factor Xa of the coagulation cascade [6]. It is part of a drug class becoming increasingly prescribed over traditional forms of anticoagulation such as warfarin or low-molecular weight heparins owing to its oral bioavailability, lack of requirement for INR monitoring, and efficacy for patients with contraindications to other anticoagulant classes [7]. The upturn in popularity of rivaroxaban and other
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Table 1 Summary of anticoagulant-induced leukocytoclastic vasculitis.

To our knowledge, the reported case represents only the third rivaroxaban-induced LCV described. This rare but serious side effect may be more common than the current body of literature suggests because of underreporting. Publication of similar findings is encouraged to assess true prevalence and identify possible risk factors of patients susceptible to this adverse drug reaction.

References
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