

Apixaban Causing Leukocytoclastic Vasculitis



Usama Bin Nasir, MD^a, Aswini Kumar, MD^b, and Arti Easwar, MD^c East Hartford, Conn

A 60-year-old white man with a medical history of hypertension, type 2 diabetes mellitus, hyperlipidemia, and nonischemic cardiomyopathy initially presented to hospital with atrial fibrillation and was started on apixaban for anticoagulation. Within 10 days of starting the apixaban, the patient presented with worsening erythematous rash on his lower extremities that quickly evolved into a burning, pruritic, petechial rash (Figure 1). The patient denied any preceding fevers, arthralgia, arthritis, or similar reactions to any other medications in the past. He was on multiple medications at home for his comorbidities including canagliflozin, aspirin, clonazepam, gabapentin, metolazone, torsemide, risperidone, and pantoprazole. He reported that he had been taking these medications for more than a year and had never had any allergic reactions or similar rash development to any of these medications. The patient denied any chemical exposure, insect bites, or allergic reaction to any food or cosmetics. The patient was restarted on all his home medications that he has been taking chronically. The doses of all these medications were unchanged. Initial blood work and chemistry were normal, including normal eosinophil count. Complete blood cell count, comprehensive metabolic panel, coagulation studies, urinalysis, and digoxin level were also within normal limits. Further studies, including antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibodies (cytoplasmic and perinuclear), complement levels (C3, C4), serum cryoglobulins, hepatitis B surface antigen, hepatitis C antibody, and HIV were all normal. Imaging studies and blood cultures remained negative throughout the hospital course. The biopsy of the lesions showed neutrophilic infiltrate surrounding and invading the vessels of the superficial vascular plexus. Focal fibrinoid necrosis of the vessel wall and nuclear debris in association with extravasated erythrocytes were also noted. Direct immunofluorescence studies revealed interstitial dermal fibrinogen and superficial perivascular IgA and C3 depositions (Figure 2). These findings were consistent with a diagnosis of immune-mediated leukocytoclastic small-vessel vasculitis. The



FIGURE 1. Left lower foot showing LCV lesions in different phase of healing.

patient's anticoagulation medicine was changed from apixaban to rivaroxaban and he was started on a course of prednisone taper for 4 weeks for treatment. The rash and associated symptoms gradually regressed toward full resolution. On follow-up visit after 3 weeks, the patient remained asymptomatic and fully compliant with rivaroxaban.

To our knowledge, this is the first reported case of apixaban causing IgA-mediated neutrophilic leukocytoclastic small-vessel vasculitis. Previously, rivaroxaban, which belongs to the same class of novel oral anticoagulants, has been reported twice to be associated with similar vasculitis.^{1,2} However, the safe introduction of rivaroxaban in this patient highlights the difference in the molecular structures of rivaroxaban and apixaban and also the lack of cross-reactivity between these medications. Our case report suggests that rivaroxaban may be safely introduced in patients who developed leukocytoclastic vasculitis (LCV) because of apixaban, but large-scale studies are warranted to fully establish the safe use of rivaroxaban in such patients. The patient was not tested with drug allergy tests; therefore, the determination that apixaban was the likely cause of LCV was a diagnosis of exclusion. Almost 30% of all LCV cases have been found to be drug induced.³ Our patient was on multiple medications that have a documented risk of LCV and other allergies, but he had been on those medicines for years. The only new medicine was apixaban and resolution of symptoms after stopping it strongly supports it as the most likely cause.

REFERENCES

1. Hasbal NB, Baştürk T, Koç Y, Sahutoğlu T, Bayrakdar Çağlayan F, Ünsal A. Leukocytoclastic vasculitis associated with a new anticoagulant: rivaroxaban. *Türk J Hematol* 2017;34:116-7.

^aInternal Medicine, University of Connecticut Health Center, East Hartford, Conn

^bDepartment of Cardiovascular Medicine, Hartford Hospital, East Hartford, Conn

^cDepartment of Pathology, Hartford Hospital, East Hartford, Conn

Conflicts of interest: The authors disclose that they have no relevant conflicts of interest.

Received for publication July 21, 2017; revised November 24, 2017; accepted for publication December 11, 2017.

Available online January 19, 2018.

Corresponding author: Usama Bin Nasir, MD, Internal Medicine, University of Connecticut, 263 Farmington Ave, Farmington, CT 06105. E-mail: unansir@uchc.edu.

J Allergy Clin Immunol Pract 2018;6:1744-5. 2213-2198

© 2017 American Academy of Allergy, Asthma & Immunology
<https://doi.org/10.1016/j.jaip.2017.12.007>

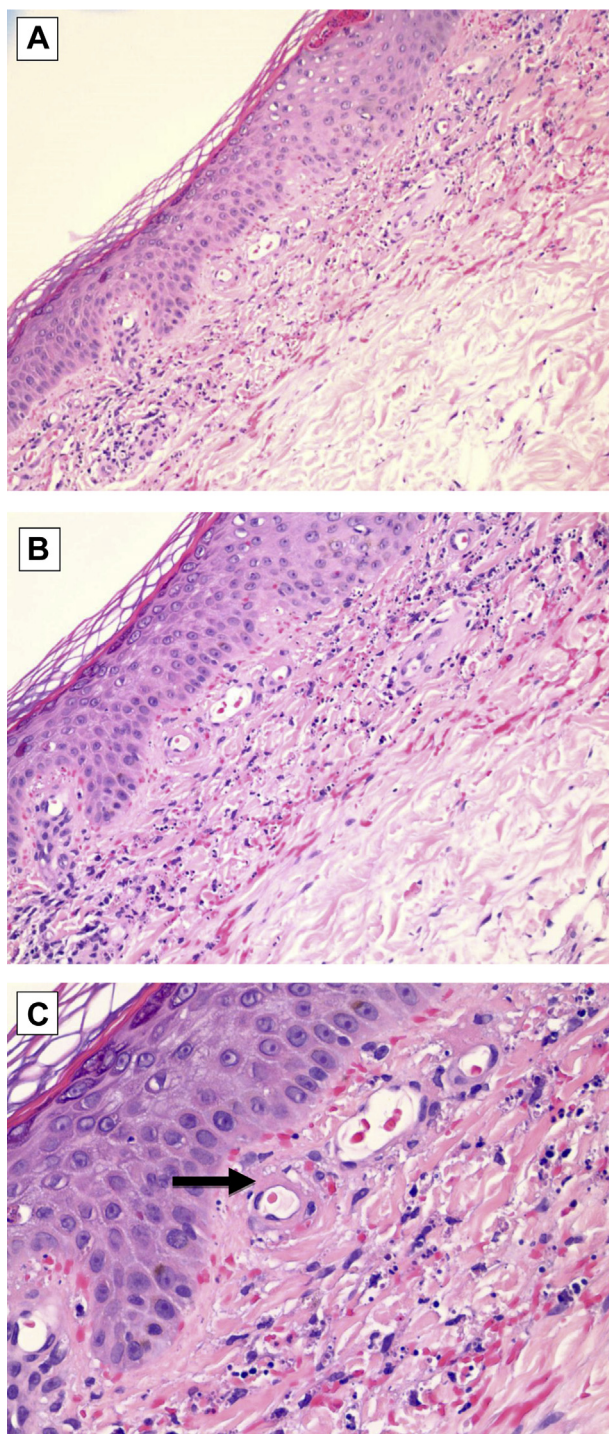


FIGURE 2. **A**, Left lower limb, punch biopsy (hematoxylin-eosin [H&E]; original magnification $\times 10$). **B**, Left lower limb, punch biopsy (H&E; original magnification $\times 20$). **C**, Left lower limb, punch biopsy (H&E; original magnification $\times 40$). The above figures show H&E sections at 10 $\times$ (Figure 2, A), 20 $\times$ (Figure 2, B), and 40 $\times$ (Figure 2, C) magnification of a punch biopsy of the left lower limb showing features of leukocytoclastic LCV. There is a perivascular neutrophilic infiltrate around the superficial vascular plexus. Fibrinoid necrosis of the vessel wall (arrow), extravasated erythrocytes, and neutrophilic nuclear debris are also evident.

2. Chaaya G, Jaller-char J, Ghaffar E, Castiglioni A. Rivaroxaban-induced leukocytoclastic vasculitis: a challenging rash. *Ann Allergy Asthma Immunol* 2016; 116:577-8.
3. Sunderkötter C, Bonsmann G, Sindrilaru A, Luger T. Management of leukocytoclastic vasculitis. *J Dermatolog Treat* 2005;16:193-206.