Apixaban-induced cutaneous leucocytoclastic vasculitis

Munim Khan,1 Mahmoud Y Madi2, Joseph Rencic3

DESCRIPTION
A 68-year-old woman with a medical history of hypertension, hyperlipidemia and atrial fibrillation presented to the outpatient clinic with bilateral lower extremity rash of 4 days duration. There was no associated pruritus or pain, she had no fevers or chills and her review of systems was otherwise negative. The patient had been started on apixaban a month prior to this presentation for a new diagnosis of atrial fibrillation, with no other recent changes to her medications. Her other medications included atorvastatin and hydrochlorothiazide. The patient did not have any new environmental exposures or dietary changes. Physical examination revealed diffuse palpable tender non-blanching violaceous coalescent macules and patches on both thighs and calves (figure 1) with purple bullae overlying a patch on the left dorsal fifth toe and the right medial calf. The rest of the body was spared, and the remainder of examination was unremarkable. Complete blood count, including eosinophil count, comprehensive metabolic panel, urinalysis, erythrocyte sedimentation rate and C-reactive protein, were within normal limits. Additional testing to rule out connective tissue diseases including components 3 and 4 levels, antinuclear antibodies, anti-Ro and anti-La antibodies, cytoplasmic antineutrophil antibodies and perinuclear antineutrophil antibodies were all negative. Infectious work-up including HIV, hepatitis C antibody, hepatitis B surface antigen, quantiFERON-tuberculosis, urinary chlamydia and gonorrhea testing was negative. The patient has also had a normal screening colonoscopy and mammogram within the last year. Punch biopsy of the left shin was performed and showed pandermal leucocytoclastic vasculitis (figure 2) with no medium vessel involvement. Direct immunofluorescence testing was performed within 4 hours of obtaining the biopsy specimen and showed strong granular deposition of IgA, IgM and complement component 3 within the dermal vessel walls consistent with leucocytoclastic vasculitis. The patient scored between 5 and 7 with the Naranjo algorithm, which suggested that the likelihood that an adverse drug had occurred was probable. Given that the patient had no other recent medication changes or allergen exposure, it is likely that this presentation was a result of apixaban initiation.1 This is bolstered by the fact that her rash resolved with cessation of the medication.2 The patient was diagnosed with apixaban-induced cutaneous leucocytoclastic vasculitis after excluding other infectious, malignant and autoimmune causes of her presentation. Apixaban was discontinued and replaced with warfarin. The patient was also treated with 20 mg of prednisone daily, which was tapered by 5 mg every 5 days until discontinuation. Outpatient follow-up 1 and 4 months later revealed near...
resolution of the rash with minimal residual hyperpigmentation. Prior case reports of direct oral anticoagulants-induced cutaneous leukocytoclastic vasculitis are summarised in table 1.2–7

### Learning points

► Cutaneous leukocytoclastic vasculitis is a histopathological term used commonly to describe small vessel vasculitis that typically presents with tender palpable purpuric lesions.

► Direct oral anticoagulants are an emerging cause of cutaneous leukocytoclastic vasculitis. This is a diagnosis of exclusion.

► In cases of drug-induced cutaneous leukocytoclastic vasculitis, discontinuation of offending agent is the mainstay of treatment. Steroids may have a role in treating cases with widespread skin involvement.

### Contributors

All authors have sufficiently participated in the conception of the idea, development of the intellectual content, design, writing and final approval of the manuscript. MK initially interviewed, examined and photographed the patient with permission. He then wrote the initial draft of this article and included the images and added the references to the article. JR re-evaluated the patient in clinic after hospital discharge in follow-up. He helped with the analysis of the case including using the Naranjo Scale and interpreting its results to validate the significance of the reported reaction.

### Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

### Competing interests

None declared.

### Patient consent for publication

Obtained.

### Provenance and peer review

Not commissioned; externally peer reviewed.

### ORCID iD

Mahmoud Y Madi
http://orcid.org/0000-0001-5759-3386

### REFERENCES


