

Orlistat-Induced Bullous Leukocytoclastic Vasculitis

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Cutaneous leukocytoclastic vasculitis (LCV), also known as small-vessel vasculitis, is a process thought to be related to the presence of circulating immune complexes. Leukocytoclastic vasculitis is thought to be idiopathic in up to 50% of cases, but other common causes and associated disorders include certain medications, most frequently antibiotics; infections; collagen-vascular disease; paraproteinemias; and rarely neoplasia. We report a patient with cutaneous LCV induced by orlistat, a pancreatic lipase inhibitor that works as a weight-loss agent by decreasing the absorption of dietary fat.

Cutis. 2013;91:148-149.

Case Report

A 57-year-old woman with a history of obesity, diabetes mellitus, hypertension, hyperlipidemia, and asthma presented to the emergency department with a worsening, painful, pruritic eruption of 1 week's duration. The patient reported that the lesions first appeared on the lower extremities and then progressed within several days to include the buttocks, lower abdomen, and upper arms. Oral ibuprofen, oxycodone, diphenhydramine, and clobetasol propionate ointment 0.05%, prescribed by an outside institution 4 days prior to presentation at our emergency department, failed to control the patient's symptoms or halt progression of the eruption. She denied fever, chills, joint pain, hematuria, or abdominal pain. Three days prior to the onset of the eruption, the patient had started an orlistat regimen (60 mg daily) for weight loss. She denied taking

any other new prescription or over-the-counter agents within the last 6 months.

Physical examination revealed an afebrile obese woman in mild distress with purpuric macules, papules, plaques, and flaccid hemorrhagic vesicles and bullae, symmetrically distributed on the plantar and dorsal aspects of the feet, medial and lateral ankles, lower legs (Figure 1), thighs, buttocks, abdominal pannus, and upper inner aspects of the arms. A punch biopsy of a representative lesion revealed leukocytoclastic vasculitis (LCV) with a bullous component on hematoxylin and eosin-stained sections (Figure 2). An additional biopsy of perilesional skin for direct immunofluorescence was negative.

Routine blood and urine chemistry profiles were unremarkable. Complete blood cell count and liver function panel also were within reference range. Blood cultures were negative. Tests for hepatitis B, hepatitis C, rapid plasma reagin, and human immunodeficiency virus were negative. The serum erythrocyte sedimentation rate, protein C, protein S, rheumatoid factor, antinuclear antibody, antineutrophil cytoplasmic antibody, lupus anticoagulant, anticardiolipin antibodies, β_2 -glycoprotein antibodies, cryoglobulins, complement CH50, and antistreptolysin O titer tests all were negative or within reference range.

Following examination, the patient's orlistat regimen was discontinued and she was treated with prednisone, antihistamines, and analgesics. The lesions affecting the ankles and lower legs ultimately ulcerated; the resulting wounds, which required intermittent antibiotic therapy for bacterial superinfections, were completely healed at 1-year follow-up. The patient was able to discontinue prednisone and she did not develop any new primary lesions after discontinuing orlistat.

Comment

The close temporal relationship between the initiation of orlistat therapy and the development of LCV in our patient as well as the lack of new lesion development on discontinuation of orlistat and prednisone supports the probable pathogenic role of orlistat. Orlistat, a

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The authors report no conflict of interest.

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Figure 1. Symmetrically distributed nonblanching purpuric macules, papules, and hemorrhagic bullae on the lower legs that developed 3 days following initiation of orlistat therapy (A). Close-up of the lesions on the right leg (B).

pancreatic lipase inhibitor, is a weight-loss medication that decreases the absorption of dietary fat.¹ It is available over-the-counter and by prescription. Reported adverse reactions have been almost exclusively gastrointestinal.² One reported case of LCV associated with orlistat therapy was less severe than in our patient.³

Conclusion

Because of the obesity epidemic in the United States, agents that promote weight loss currently attract substantial media attention and are widely appealing among patients. This report provides a dramatic example of a potential cutaneous adverse effect related to orlistat.

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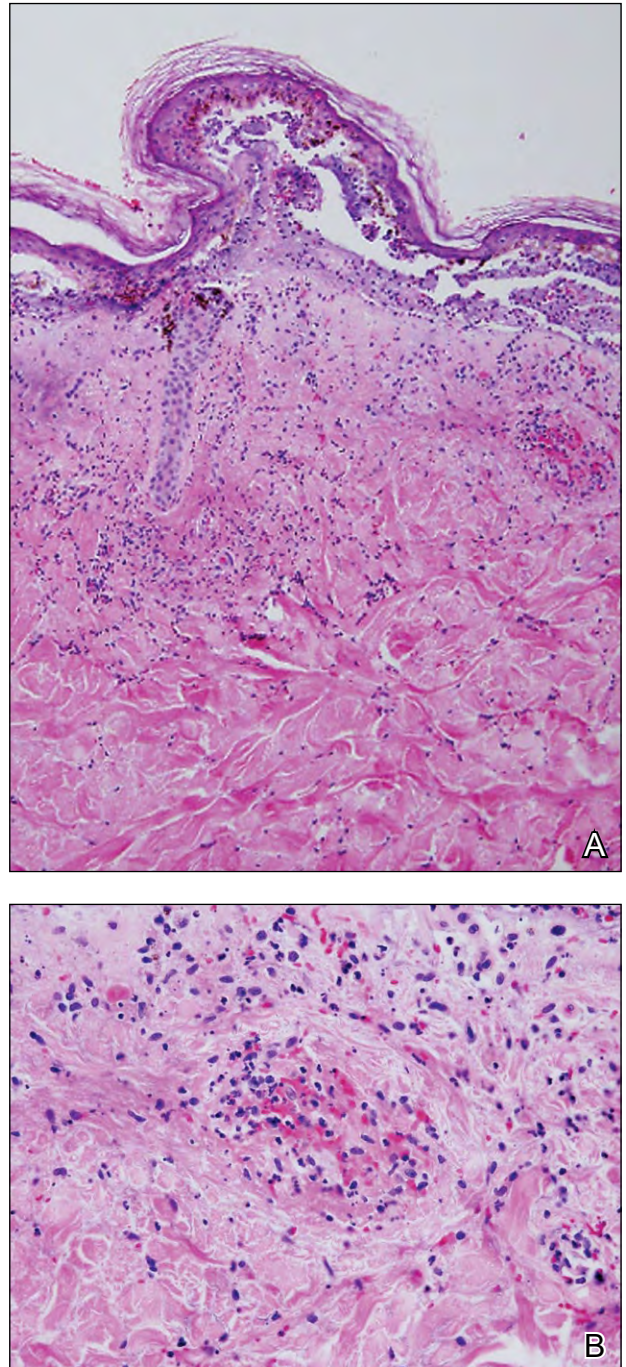


Figure 2. A biopsy specimen from the right upper arm demonstrated neutrophilic inflammation with fibrinoid necrosis of small subpapillary venules, leukocytoclasia, and extravasation of red blood cells. Sections show an overlying, neutrophil-rich subepidermal bulla (A and B) (H&E; original magnifications ×10 and ×40, respectively).

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