

Cutaneous thrombotic vasculopathy related to poorly controlled ulcerative colitis



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Cutaneous gangrene caused by thrombotic vasculopathy is a rarely described extr-intestinal complication of ulcerative colitis.¹⁻⁵ We report a case of cutaneous thrombotic vasculopathy associated with poorly controlled ulcerative colitis, possibly caused by enteric losses of antithrombin III.

CASE REPORT

A 33-year-old white woman presented to the hospital with a 1-day history of a rapidly progressing, painful, racemose purpuric eruption involving her chest, shoulders, arms, back, buttocks, and thighs. Smaller purpuric macules and patches had also formed on the bilateral ears, neck, and dorsal surfaces of her feet (Figs 1 and 2).

She was discharged from the hospital 3 days earlier after being admitted for evaluation of a 4-month history of bloody diarrhea. Colonoscopy during that hospital admission revealed superficial mucosal ulceration with a loss of a vascular pattern, extending 35 cm to the sigmoid colon from the anal verge. Colorectal biopsy specimens revealed findings consistent with chronic active colitis and proctitis. A diagnosis of ulcerative colitis was made. She was started on high-dose methylprednisolone and discharged on prednisone 60 mg/day. However, after discharge, she continued to have 8 to 9 episodes of bloody diarrhea per day, sometimes passing blood clots.

Serologic studies obtained during the present hospitalization revealed a leukocytosis with left shift ($18.6 \times 10^3/\text{mCL}$; normal range, $4.0\text{--}10.0 \times 10^3/\text{mCL}$), hemoglobin 13.4 gm/dL (normal range, 11.4–14.4 gm/dL), and normal platelet count ($163 \times 10^3/\text{mCL}$; normal range, $150\text{--}400 \times 10^3/\text{mCL}$). Coagulation

studies showed a prolonged prothrombin time of 18.2 seconds (normal range, 9.4–12.5 seconds), normal partial thromboplastin time of 30.5 seconds (normal range, 25.1–36.5 seconds), an international normalized ratio of 1.57, fibrinogen level of 345 mg/dL (normal range, 200–393 mg/dL), low antithrombin III activity assay of 80% (normal range, 83–128%), and elevated d-dimer of 51,523 mg/mL (normal range, <574 mg/mL).

The silica clotting time and dilute Russell viper venom time screen ratios were within the normal reference range. Enzyme-linked immunosorbent assay for anticardiolipin, anti- β 2-glycoprotein 1, antiphosphatidylserine immunoglobulin M and immunoglobulin G, and antiprothrombin immunoglobulin G antibodies were all normal.

Additional tests for activated protein C resistance, factor V Leiden, prothrombin gene mutation, and paroxysmal nocturnal hemoglobinuria were negative or normal. Antinuclear antibodies and extractable nuclear antigen antibodies, complement components 3 and 4, rheumatoid factor, and cryoglobulins were all negative or normal. A urine drug screen for cocaine was also negative.

Skin biopsy specimens of her back showed thrombotic vasculopathy but no vasculitis (Fig 3).

Computed tomography scans of the chest, abdomen, and pelvis with and without intravenous contrast did not demonstrate any evidence of thromboembolism. Venous Doppler ultrasonography of the bilateral lower extremities was normal. A magnetic resonance imaging scan of the brain showed no evidence of ischemic or embolic phenomena. Transesophageal echocardiography showed normal biventricular function and did not reveal endocardial clot or masses.

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Fig 1. Thrombotic vasculopathy. Racemose purpura on the superior back and posterior shoulders on day 2 of admission.



Fig 2. Thrombotic vasculopathy. Macular purpura on the pinna, lateral face, and neck on day 2 of admission.

The patient was diagnosed with cutaneous thrombotic vasculopathy related to poorly controlled ulcerative colitis. She was treated with a high-intensity heparin drip with rapid improvement in cutaneous pain, followed by recession of the existing racemose purpuric patches and macules (Fig 4). However, while receiving high-intensity heparin, the patient required antithrombin boluses to achieve goal anti-

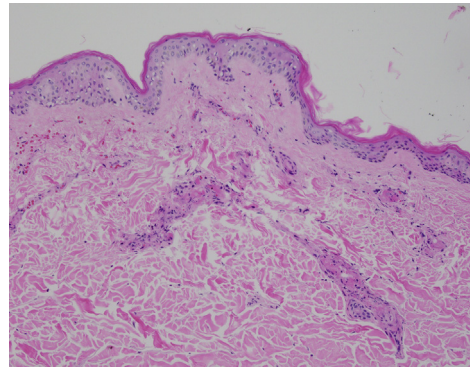


Fig 3. Thrombotic vasculopathy. Vascular thromboses within the reticular dermis without associated vasculitis. (Hematoxylin–eosin stain; original magnification: $\times 200$.)



Fig 4. Thrombotic vasculopathy. Recession of racemose purpura on the posterior shoulder and upper back 6 days into high-intensity unfractionated heparin infusion.

Xa levels and therapeutic antithrombin III activity. Although on anticoagulation, the patient did not experience worsening hematochezia.

Infliximab infusions were administered with eventual diminution in stool frequency. The patient was transitioned from a heparin drip to subcutaneous enoxaparin 1.5 mg/kg/day. She was discharged after 13 days of hospitalization, still receiving enoxaparin and was instructed to continue infliximab infusions on an outpatient basis. She was later transitioned from enoxaparin to a direct oral anticoagulant and continued to do well, without recrudescence of tender, cutaneous purpura.

DISCUSSION

Cutaneous gangrene resulting from thrombotic vasculopathy is a rare and poorly understood extra-intestinal manifestation of inflammatory bowel disease, most commonly ulcerative colitis.¹⁻⁵ Hypercoagulable states and thromboembolism are more common in patients with inflammatory bowel disease compared to control subjects, possibly because of thrombocytosis, abnormal platelet

function, endothelial dysfunction, elevation of serum procoagulants (ie, fibrinogen, factor V, factor VII, and von Willebrand factor), and depletion of anticoagulants (ie, antithrombin, protein C, and protein S).^{6,7} Depletion of antithrombin may be linked to losses through a damaged enteric barrier, because elevated antithrombin levels have been detected in the stool of patients with ulcerative colitis and acquired antithrombin deficiency.⁸ Losses of antithrombin and resultant thrombosis has also been described in other forms of protein-losing enteropathies.^{9,10}

Selective loss and or depletion of antithrombin seems especially applicable to our case, given the exclusion of other prothrombotic etiologies and consistently low anti-Xa and antithrombin III levels while receiving a high-intensity heparin drip.

Cutaneous thrombotic vasculopathy is a rare but morbid extraintestinal manifestation of ulcerative colitis. Thrombotic vasculopathy should be suspected in a patient with known or occult inflammatory bowel disease who presents with rapidly progressive racemose purpura. Depending on the personal and family history of the patient, workup for acquired and possibly inherited disorders of coagulation may be undertaken to better understand the pathomechanisms of thrombosis in these individuals. Despite enteric blood losses from perturbed mucosal integrity, anticoagulation should not be withheld to limit the extent and severity of cutaneous infarction. Additional measures aimed at controlling underlying inflammatory bowel disease are warranted.

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REFERENCES

1. Komatsu YC. Skin gangrene as an extraintestinal manifestation of inflammatory bowel disease. *An Bras Dermatol*. 2014;89:967-969.
2. Stapleton SR, Curley RK, Simpson WA. Cutaneous gangrene secondary to focal thrombosis—an important cutaneous manifestation of ulcerative colitis. *Clin Exp Dermatol*. 1989;14:387-389.
3. Wackers FJ, Tytgat GN, Vreeken J. Necrotizing vasculitis and ulcerative colitis. *Br Med J*. 1974;4:83-84.
4. Goldgraber MB, Kirsner JB. Gangrenous skin lesions associated with chronic ulcerative colitis. A case study. *Gastroenterology*. 1960;39:94-103.
5. Pollard AB. Acute ulcerative colitis presenting with skin gangrene. *Proc R Soc Med*. 1961;54:814-815.
6. Owczarek D. Inflammatory bowel disease: epidemiology, pathology and risk factors for hypercoagulability. *World J Gastroenterol*. 2014;20:53-63.
7. Ornaghi S, Barnhart KT, Frieling J, Streisand J, Paidas MJ. Clinical syndromes associated with acquired antithrombin deficiency via microvascular leakage and the related risk of thrombosis. *Thromb Res*. 2014;133:972-984.
8. Büller HR, ten Cate JW. Acquired antithrombin III deficiency: laboratory diagnosis, incidence, clinical implications, and treatment with antithrombin III concentrate. *Am J Med*. 1989;87:445-485.
9. Amtage F, Marouf W, Hetzel A, Schubert M. Acquired prothrombotic state due to protein-losing enteropathy as a rare cause for ischemic stroke? *Eur J Neurol* 2007;14:e7-e8.
10. Muntean W, Rossipal E. Loss of inhibitors of the blood coagulation system in protein-losing enteropathy [in German] *Klin Padiatr*. 1979;191:20-23.