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Nodular Vasculitis in a Patient With Crohn's Disease on Vedolizumab

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Abstract

Erythema induratum (EI), or nodular vasculitis (NV), is a type of panniculitis that is often associated with vasculitis affecting various-sized veins, venules, and arteries in reaction to various causative factors. Historically, EI was highly linked to tuberculosis, but in 1946, Montgomery first proposed the term NV to describe cases of EI not associated with tuberculosis. Only 2 reports of NV associated with inflammatory bowel disease have been reported in the literature. The authors report a 60-year-old woman with Crohn's disease presenting with exacerbation of NV in the setting of vedolizumab therapy.

Keywords

nodular vasculitis; erythema induratum; vedolizumab

CASE REPORT

A 60-year-old woman with a history of Crohn's disease, controlled on vedolizumab, presented to dermatology clinic with tender, erythematous subcutaneous nodules on bilateral lower extremities (Fig. 1). Before starting vedolizumab, the patient endorsed similar firm nodules that evolved to ulcerated plaques. Use of topical clobetasol had provided some improvement, and she had complete resolution with oral prednisone. Initiation of biologic therapy 3 months before presentation had caused the lesions to became much more numerous and persistent. The patient denied a history of Bacillus Calmette-Guerin, tuberculosis, or recent tuberculosis exposure.

Cutaneous biopsy showed a mixed lobular and septal granulomatous inflammatory infiltrate composed of large histiocytes, lymphocytes, and neutrophils, accompanied by fat necrosis. Medium-sized vessels in the septa demonstrated fibrinoid necrosis and intramural inflammation (Fig. 2). These findings were consistent with a pathological diagnosis of nodular vasculitis (NV). No microorganisms were identified on PAS-F, Fite, and Gram special stains. Immunoperoxidase studies for cytomegalovirus were negative.

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The authors declare no conflicts of interest.

DISCUSSION

Cutaneous complications of autoimmune colitis, including Crohn's disease and ulcerative colitis, are seen in approximately 15% of patients.[1] Panniculitis is commonly seen in patients with Crohn's disease and can be subcategorized based on the location of inflammation. Panniculitis associated with Crohn's disease is commonly septal, as seen in erythema nodosum, or lobular, as seen in neutrophilic lobular panniculitis with granulomas. However, NV or erythema induratum (EI), in association with Crohn's disease is exceptionally rare. To date, there are only 2 reported cases in the literature of EI/NV associated with inflammatory bowel disease—1 Crohn's disease and 1 ulcerative colitis.[1,2] Histologically, granulomatous vasculitis with discrete granulomas involving the venules and veins in association with lobular panniculitis, or a mixed septal and lobular panniculitis, is a reported feature of EI/NV in association with Crohn's disease.[2]

Of interest, our patient experienced exacerbation of cutaneous symptoms with initiation of vedolizumab. This is an anti-α4β7 integrin humanized monoclonal antibody used for the treatment of severe inflammatory bowel disease in patients' refractory to therapy, including treatment with tumor necrosis factor (TNF)-α antagonists. The mechanism of action of vedolizumab is through the blockage of mucosal addressin cell adhesion molecule-1, an adhesion molecule specifically expressed on blood vessels of the gastrointestinal tract. This interaction inhibits leukocyte adhesion and migration, counteracting the lymphocyte trafficking seen in inflammatory bowel disease.[3] Vedolizumab is considered to have a good side effect profile inasmuch as it has few reported gastrointestinal side effects. It has a high affinity for the gastrointestinal tract, but there is little published data on its role in the treatment of the cutaneous Crohn's disease.

Of note, we do not suspect that vedolizumab caused a drug-induced NV in our patient. This has been reported in association with the TNF-alpha inhibitor etanercept and propylthiouracil.[4] However, our patient's skin findings preceded initiation of vedolizumab. Therefore, we suspect that the etiology of our patient's NV was most likely due to her underlying inflammatory disease rather than a drug-induced etiology. Given vedolizumab's gastrointestinal selectivity, and poor activity on skin epithelial inflammatory pathways, we hypothesize that patients who were previously well controlled on biologic drugs with broader selectivity (eg, TNF-α inhibitors) may see flares and intractable cutaneous Crohn's disease symptoms with vedolizumab. Just as our patient saw exacerbation of her EI/NV with transition of vedolizumab from a TNF-α antagonist, Yeh and Tsiaras[5] reported a case of worsening pyoderma gangrenosum after the initiation of vedolizumab in a patient with Crohn's disease. These cases serve as examples that although vedolizumab is effective for treating moderate to severe inflammatory bowel disease, initiation of the drug may conversely exacerbate, or inadequately treat, cutaneous symptoms.

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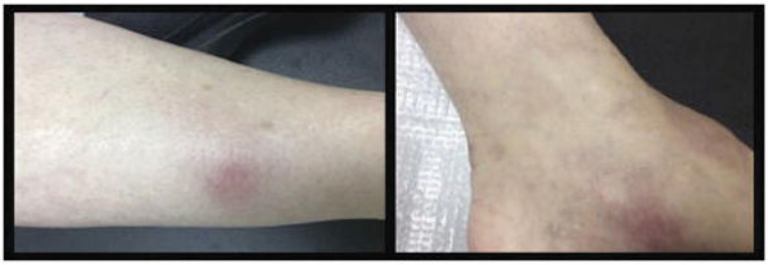

FIGURE 1.
NV. Tender erythematous subcutaneous nodules on bilateral lower extremities.

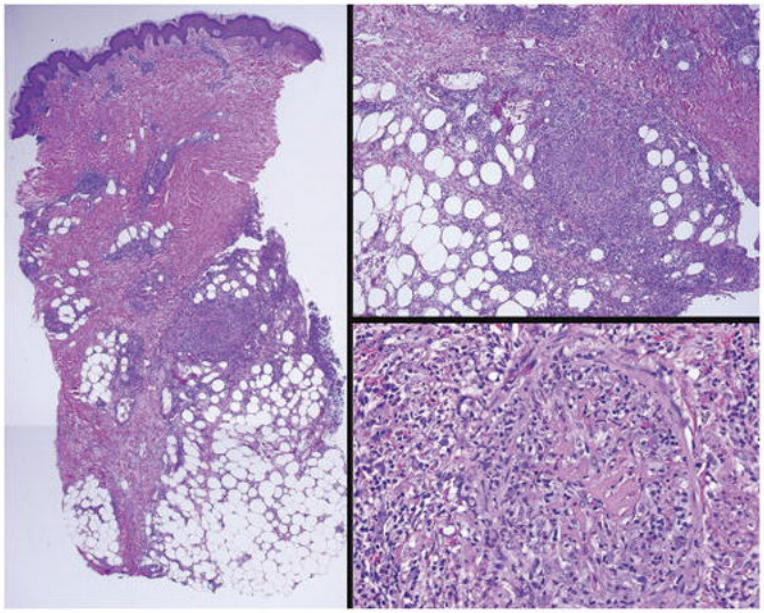

FIGURE 2.

Pathology. Hematoxylin and eosin (H&E) staining of at ×20 (left), ×100 (upper right), and ×200 (lower right) showing a mixed lobular and septal granulomatous inflammatory infiltrate with fat necrosis. Medium-sized vessels show fibrinoid necrosis and intramural inflammation.