Case Letter

Pyoderma Gangrenosum and Tumor Necrosis Factor α Agents

To the Editor:

Pyoderma gangrenosum (PG) is a rare, ulcerative, neutrophilic, noninfectious dermatosis of unknown etiology seen in 1% to 5% of patients with inflammatory bowel disease (IBD).[1] It has been reported in all age groups but usually affects women aged 40 to 60 years. Pyoderma gangrenosum often is associated with systemic diseases in approximately 50% of patients affected; however, it is not considered a manifestation or complication of these diseases and its clinical course usually is unrelated to the disease severity or activity.[2,3]

Anti–tumor necrosis factor α (TNF-α) agents have improved and broadened the therapeutic options for IBD.[1] Etanercept is a fusion protein that binds to and inactivates TNF-α; it also has been proposed as an alternative treatment option for patients with refractory ulcers due to PG.[4] We present a case of PG associated with Crohn disease (CD) that was refractory to infliximab treatment.

A 64-year-old man presented with an ulcerating lesion on his left ankle of 6 months' duration. The lesion was painful with red borders surrounding a necrotic base (Figure 1). A 4-mm punch biopsy was performed and histologic examination showed neutrophilic infiltration of the dermis, with microabscess findings compatible with PG.

According to his medical history, he also had insulin-dependent diabetes mellitus with impaired renal function and a 20-year history of refractory active CD. The patient previously had been treated with oral methylprednisolone and azathioprine with poor results. Two doses of infliximab (at baseline and 2 weeks) infused at 5 mg/kg body weight were administered for CD and PG, but therapy failed and the agent was discontinued because the patient experienced abdominal pain and nausea. Cyclosporine was not administered because of renal insufficiency.

At the time of presentation, the patient was being treated with intramuscular methotrexate 25 mg once weekly for CD and PG. He received 4 weekly doses without resolution and was advised to receive etanercept. He underwent routine laboratory tests including a human immunodeficiency virus test, tuberculin test, and chest radiograph, which did not show abnormalities. Etanercept was initiated at a dosage of 50 mg twice weekly without discontinuing methotrexate treatment. The patient showed remarkable improvement after the fourth week of treatment and satisfactory results at week 12. After 3 months, a reduced dose of 50 mg was given once weekly. By week 22, CD and PG satisfactorily responded (Figure 2). No side effects were reported.

Pyoderma gangrenosum may present as ulcerative (the classic form), bullous, pustular, vegetative, peristomal, genital, infantile, and extracutaneous lesions.[3] Currently, there are no diagnostic tests for this dermatosis. The histopathologic changes are not specific and the diagnosis is usually made by exclusion of other conditions, such as infection, vascular disease, and malignancy.

Pyoderma gangrenosum is a rare disease and most treatment recommendations are based on a small

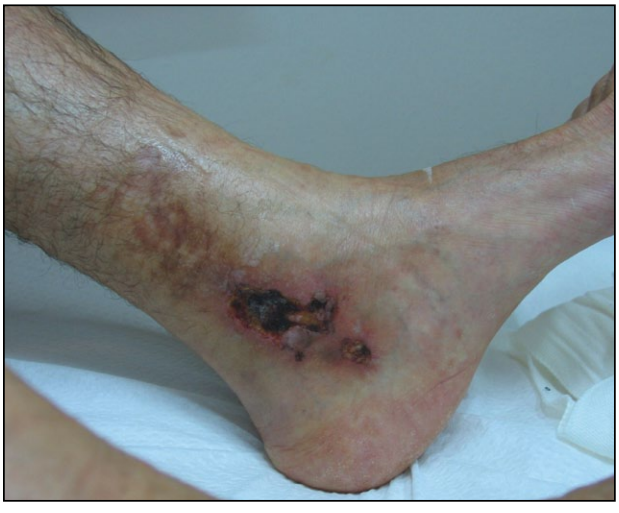

Figure 1. Painful ulcerating lesion on the left ankle.

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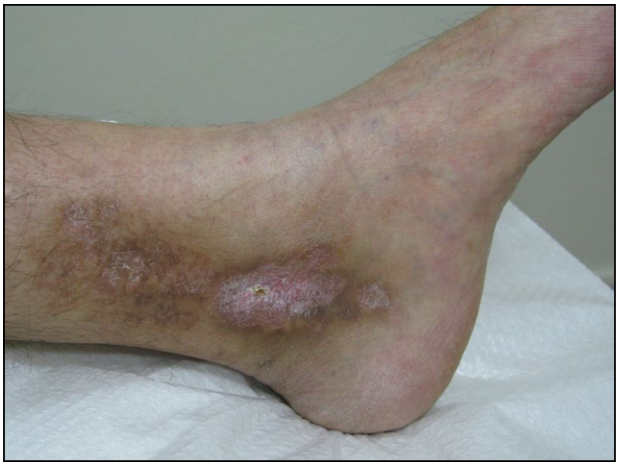

Figure 2. Pyoderma gangrenosum responded after 22 weeks of etanercept administration.

series of patients studied.[2] The management includes systemic immunosuppressive agents, and recently anti–TNF-α agents have been used. Data have shown that infliximab is highly effective in the treatment of PG, with or without an association with IBD.[1] Etanercept and adalimumab also have been proven efficacious for the treatment of PG[4,5] in the majority of reported cases.[6]

Our patient with long-standing CD and refractory PG did not respond to immunosuppressive drugs and infliximab but was successfully treated with etanercept. It seems that a gap still exists in the understanding of the pathogenesis of PG and the exact mechanism of action of the anti–TNF-α agents. Physicians must acknowledge the latter and individualize the administration of TNF-α inhibitors.

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