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Journal
Dermatology Online Journal, 26(5)

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Publication Date
2020

DOI
10.5070/D3265048778

Granulomatous pyoderma gangrenosum in a patient with ulcerative colitis

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Abstract

A 34-year-old woman with a past history of inflammatory bowel disease developed a painful elevated edematous swelling with ulcerations on the dorsum of her left foot. Histopathological examination revealed dense infiltration of neutrophils and mononuclear cells in the lower dermis and subcutaneous tissue. Tumor necrosis factor (TNF) was strongly detected in giant cells. To date, only a few cases of pyoderma gangrenosum with granulomatous changes have been reported. Tumor necrosis factor may have played a role in the granulomatous reaction in our case.

Keywords: granulomatous reaction, inflammatory bowel disease, pyoderma gangrenosum

Introduction

Usually, the histological features of pyoderma gangrenosum do not exhibit granulomatous reactions and granuloma is rarely seen. We report pyoderma gangrenosum with granulomatous changes, along with the relevant literature.

Case Synopsis

A 34-year-old woman was referred to our hospital, complaining of painful leg ulcers on the dorsa of her left foot and right thigh, which had appeared 10 days previously. Simultaneously, she had been having diarrhea. She was suspected of having Crohn disease 12 years previously. At that time, infliximab was started, which controlled her intestinal condition; she self-discontinued infliximab therapy 5 years later. Physical examination showed a painful elevated edematous swelling with ulcerations on the dorsum of her left foot (**Figure 1A)**. The surface had reddish granulation and the ulcer was surrounded with erythema. Cultures for bacteria, deep fungus, and *Mycobacterium* were sterile. Furthermore, an elevated ulcerative plaque was observed on the posterior left thigh. Laboratory examination showed increased white blood cell counts (10,300/μl, with 73% neutrophils) and elevated levels of C-reactive protein (9.17 mg/dl).

A biopsy specimen from the edge of the ulcer showed dense infiltration of neutrophils and mononuclear cells in the lower dermis and subcutaneous tissue (**Figures 1B, C)**. Immunohistochemistry revealed a number of CD3- and CD68-positive inflammatory cells in the dermis (**Figure 1D)**, and tumor necrosis factor (TNF) was strongly detected in giant cells (**Figure 1E)**. Grocott methenamine silver and Ziehl-Neelsen staining were negative. Computed tomography scan showed total colon wall thickening and mural hyperenhancement. Colonoscopy showed erosion and ulcers in the descending colon-rectum and redness and edematous mucosa in the total colon, suggesting a Mayo endoscopic subscore of 3. Histopathologic examination of the colon biopsies revealed extensive infiltration of immune cells in the intestine and dysplasia of the intestinal tract. Ulcerative colitis was diagnosed (total colitis type) and mesalamine (4000mg/day) was administered. The patient was

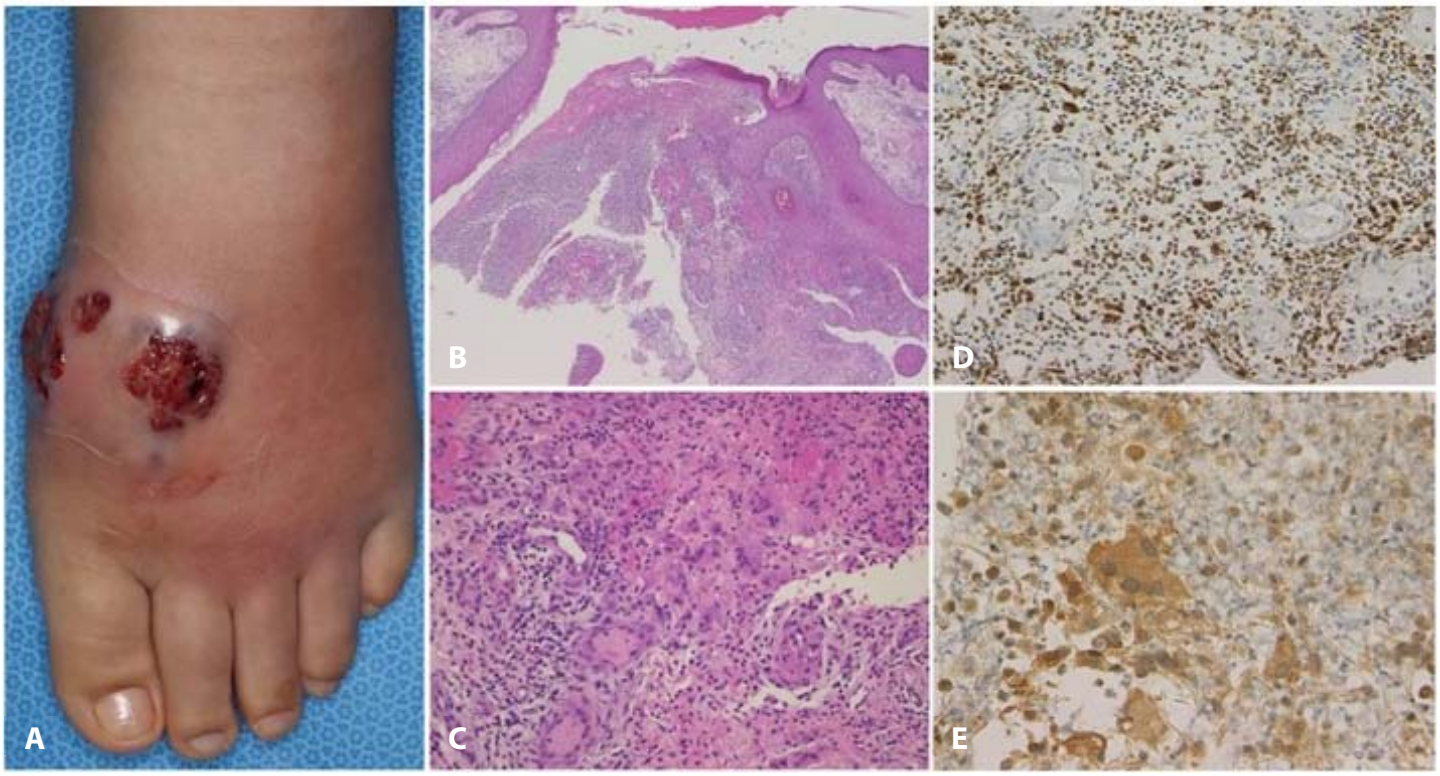

Figure 1. ***A)*** *Ulcerative plaque on the foot.* ***B)*** *Histological features showing prominent infiltration of lymphohistiocytic cells and neutrophils H&E, 100×.* ***C)*** *Higher magnification reveals granulomatous changes with giant cells, H&E, 400×.* ***D)*** *Infiltrating inflammatory cells in the dermis were positive for CD68, 400×.* ***E)*** *Tumor necrosis factor was strongly expressed in giant cells, 1000×.*

initially treated with systemic prednisolone (30mg/day), which was significantly effective and ulcers epithelized four weeks later. However, during tapering at a dose of 15mg/day, a new lesion appeared on the left lower leg. Prednisolone was escalated to 20mg/day and oral cyclosporine (100mg/day) was added. Thereafter, prednisolone and cyclosporine were gradually tapered and successfully ceased 8 months later without remission.

Case Discussion

The present case histologically showed epidermal proliferation and neutrophil infiltration with granulomatous reaction containing multiple giant cells in the dermis. Such histological features require consideration of a diagnosis of superficial granulomatous pyoderma. However, three-layered granulomas consisting of an innermost zone of superficial abscess formation, a midzone of histiocytes and giant cells, and an outer layer of mixed infiltrate of lymphocytes, neutrophils, and plasma cells were not observed. Additionally, clinical features were not vegetative and did not exhibit keratotic plaques. Thus, we believe that the diagnosis was most consistent with granulomatous pyoderma gangrenosum. In cases of granulomatous pyoderma gangrenosum, conducting vessels can exhibit granulomatous giant cell vasculitis, thrombosis, necrosis of the vascular walls, and perivascular infiltration of nuclear dusts and neutrophils.

Usually, the histological features of pyoderma gangrenosum do not exhibit granulomatous reactions and granuloma is rarely seen. To date, only a few cases of pyoderma gangrenosum with granulomatous changes have been reported [1-4]. Among them, cases with either necrotizing granulomatous inflammation with severe vascular changes [2], or granulomatous inflammatory reactions associated with granulomatous giant cell vasculitis [3], have been described. Superficial granulomatous pyoderma is considered the same entity as vegetative pyoderma gangrenosum. It

generally responds to topical agents and does not accompany other systemic disorders. Like our case, there have been few reported cases of pyoderma gangrenosum with vegetative clinical appearances and aggressive clinical behaviors, in spite of histological granulomatous reactions [1, 2]. Tumor necrosis factor, an important cytokine of granuloma formation, has been suggested to play a crucial role in the pathogenesis of pyoderma gangrenosum [5], and thus may have played a role in the granulomatous reaction in our case.

Conclusion

To date, only a few cases of pyoderma gangrenosum with granulomatous changes have been reported. Tumor necrosis factor may have played a role in the granulomatous reaction in our case.

Potential conflicts of interest

The authors declare no conflicts of interests.

References

1. Speeckaert R, de Smet L, de Schepper S, et al. Pyoderma gangrenosum with granuloma formation: not always a benign disorder. *J Eur Acad Dermatol Venereol.* 2016;30:188-189. [PMID: 25174437].
2. Park H-J, Kim Y-C, Cinn Y-W, Yoon T-Y. Granulomatous pyoderma gangrenosum: two unusual cases showing necrotizing granulomatous inflammation. *Clin Exp Dermatol.* 2000;25:617-620. [PMID: 11167975].
3. Kägi MK, Burg G. Pyoderma gangrenosum: an unusual case associated with symmetrical eruptive, nodular and necrotizing granulomatous giant cell vasculitis. *J Cutan Pathol.* 1995;22:68. [DOI: 10.1111/j.1600-0560.1995.tb00739.x].
4. Meier F, Berner D, Scherwitz C, Rassner G, Metzler G. An unusual case of pyoderma gangrenosum with necrotizing granulomatous dermatitis. *J Dtsch Dermatol Ges.* 2003;4:302-305 (in German). [PMID: 16285486].
5. Marzano AV, Borghi A, Wallach D, Cugno M. A comprehensive review of neutrophilic diseases. *Clin Rev Allergy Immunol.* 2018;54:114-130. [PMID: 28688013].