Case Report Annals of Dermatology 2023;35(Suppl 2):S292-295 • https://doi.org/10.5021/ad.22.101

Ulcerative Colitis Diagnosed through Evaluation of Underlying Diseases in a Pyoderma Gangrenosum Adolescent without Gastrointestinal Symptoms

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Received April 18, 2022
Revised May 4, 2022
Accepted May 26, 2022

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Pyoderma gangrenosum (PG) is a rare, non-infectious, neutrophilic dermatosis characterized by painful ulcers with indistinct borders and peripheral erythema. The diagnosis of PG requires the exclusion of other causes of similar appearing skin manifestations, including vasculitis and infections. The pathogenesis of PG is not clear; however, dysregulation of the immune system has been suggested in previous studies. More than half of the PG patients have underlying diseases; the most common being inflammatory bowel disease (IBD). The progression of PG in IBD patients is seen after the onset of IBD, usually during its exacerbation. On the other hand, PG may follow a course independent of the intestinal disease. We present a case of an 18-year-old young male with PG that presented before being diagnosed with ulcerative colitis as an associated condition. He had a painful ulcerative lesion on his right shin with no previous gastrointestinal symptoms. This case suggests that investigating for underlying disorders is essential in PG patients despite the lack of symptoms other than the skin lesions.

Keywords: Colonoscopy, Inflammatory bowel disease, Pyoderma gangrenosum, Ulcer, Ulcerative colitis

INTRODUCTION

Pyoderma gangrenosum (PG) is a chronic, neutrophilic dermatosis characterized by rapidly evolving painful ulcers with undermined borders and peripheral erythema, which is a very rare disease with an incidence of 58 per million people[1]. It is one of the severe extra-intestinal manifestations of inflammatory bowel disease (IBD)[2-4]. Up to 70% cases of PG are associated with underlying systemic diseases, such as IBD, monoclonal gammopathy, hematologic disease, or malignancy[3-5].

The most common systemic disease associated with PG is IBD. About 20% of the patients with PG have IBD, with similar frequencies of both Crohn's disease and ulcerative colitis (UC)[6]. PG occurs in 0.5%~5% of patients with IBD and tends to appear after the onset of IBD. In only few cases, PG has been reported to precede the onset of the IBD or present in patients with quiescent bowel disease[7].

Here, we report a case of an 18-year-old young male patient who presented with skin ulceration on the right shin, which was diagnosed as PG. Clinically, he did not have any gastrointestinal symptoms such as abdominal pain and diarrhea, but UC was diagnosed by endoscopy during evaluation of underlying disorders.

CASE REPORT

An 18-year-old male adolescent visited our clinic complaining of a painful ulcer on his right leg that had abruptly developed over one week (Fig. 1A). He had no history of trauma, and there were no signs of fever or systemic disease. On physical

examination, there was a 3×3-cm clearly demarcated ulcer with an erythematous base and undermined borders on his right shin. Laboratory tests revealed elevation of white blood cell count (10,620/μl; 4,000~10,800/μl), C-reactive protein (CRP, 51.2 mg/L; 0.1~6.0 mg/L) level, and erythrocyte sediment rate (ESR, 108 mm/hr; 0~15 mm/hr). Serum albumin levels, known to be a sensitive marker of inflammatory activity in IBD, were normal (4.7 g/dl; 3.4~5.3 g/dl), and the liver and renal function tests were also normal. Serum antineutrophil cytoplasmic autoantibodies against myeloperoxidase and proteinase-3 were negative. Wound swab culture was positive for *Pseudoclavibacter* species, a gram-positive bacillus. Histopathologic examination from the border of the lesion revealed a deep dermal abscess with a dense neutrophilic infiltrate (Fig. 2). The cause of the lesion was thought to be infective. The patient was hospitalized and treated with antibiotics (amoxacillin/clavulanate) based on drug sensitivity tests. In the follow-up culture, performed 10 days after the start of antibiotic use, the bacteria did not grow any more. However, the wound did not seem to be healing. Therefore, the lesion was regarded as PG rather than infective ulceration. Oral prednisolone (20 mg/daily) was prescribed, and the ulceration gradually improved with re-epithelialization. As the wound improved, oral steroids were tapered and the patient was discharged (Fig. 1B). However, the values of ESR and CRP remained elevated (CRP; 67.6 mg/L, ESR; 120 mm/hr) on follow-up laboratory tests, although the ulcer showed improvement. Therefore, we decided to perform a thorough systemic evaluation to identify the underlying disease associated with PG. There were no abnormal blood cells on peripheral blood smear performed for the evaluation of hematologic disorders. Considering the high association of PG with IBD, colonoscopy and endogastroduodenoscopy (EGD) were performed, although there were no gastrointestinal symptoms. Colonoscopy revealed periappendiceal inflammation with exudates and erosions, with a reduced vascular pattern in the ascending colon (Fig. 3A).

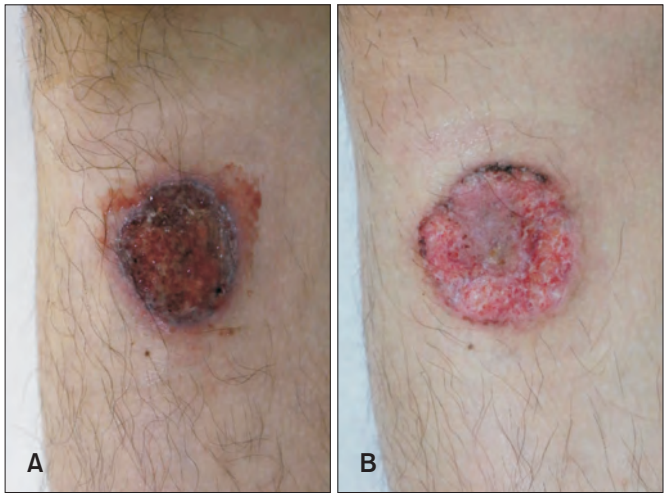

Fig. 1. Clinical features of the patient. (A) Ulcerative lesion on the right shin at initial visit, (B) 30 days after treatment.

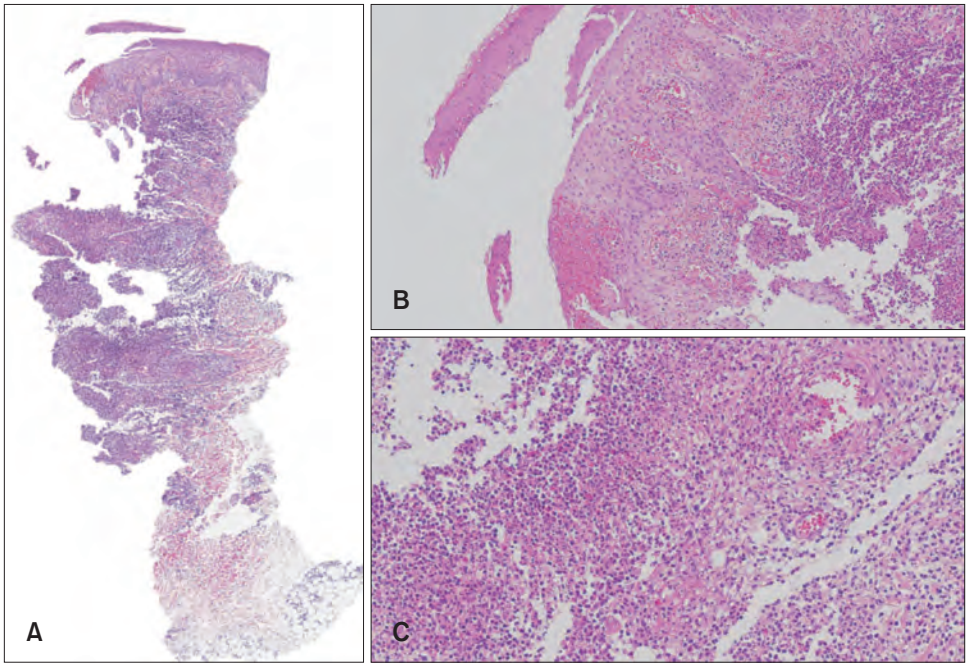

Fig. 2. Histopathologic findings of the lesion: (A) H&E, original magnification ×20; (B) epidermal ulceration (H&E, ×100); (C) diffuse infiltrates consisting of neutrophils, lymphocytes, and histiocytes in the entire dermis (H&E, ×200).

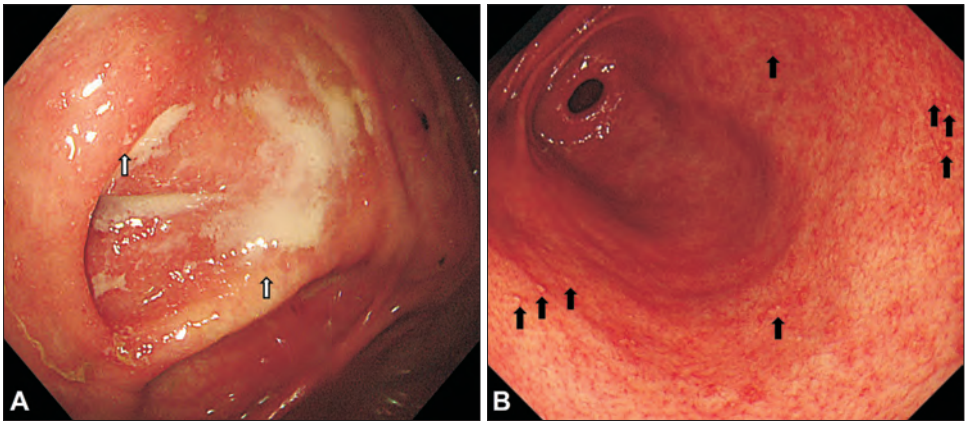

Fig. 3. Images of endoscopy. (A) Multiple aphthous ulcers, erosions, and exudates on colonoscopy suggestive of ulcerative colitis (white arrows). (B) Numerous aphthous ulcers were observed on endogastroduodenoscopy (black arrows).

EGD showed numerous gastric erosions, suggestive of atypical findings in UC (Fig. 3B). The patient was diagnosed with UC. Shortly after, the patient developed gastrointestinal symptoms such as frequent diarrhea and abdominal pain. The patient was referred to a gastroenterologist for UC and was started on mesalamine and azathioprine. His ESR, CRP level, gastrointestinal symptoms, and dermatologic manifestation improved with the medication. We received the patient's consent form about publishing all photographic materials.

DISCUSSION

The pathogenesis of PG is still unknown. It was previously thought to be related to latent bacterial infection and circulating autoantibodies; however, abnormalities in neutrophil function, genetic mutations, and dysregulation of the innate immune system are now considered to be the main causes[8].

PG clinically presents as a painful nodule, plaque, or pustule that evolves into well-demarcated violaceous ulcers or necrotic plaques with undermined or raised borders. It develops on apparently normal-looking skin, with the most common site being the leg. It can also occur at sites of previous trauma or surgery, which is known as pathergic phenomenon[9]. PG is diagnosed clinically and it is important to exclude other causes for skin manifestations such as vasculitis and infections. There is no specific finding or laboratory test that establishes the diagnosis of PG. Histolopathologic findings are not diagnostic but can be supportive of the diagnosis[3,4,8].

There are no clear guidelines for patient care due to the lack of data on interventions for PG. In general, patients are treated with a combination of local or systemic therapies including anti-inflammatory drugs and wound management[10,11]. Early and localized PG is mainly treated with wound care and topical agents such as steroids and calcineurin inhibitors, whereas progressive and severe cases are best treated with systemic agents such as steroids, cyclosporine, methotrexate, and azathioprine[12,13]. Anti-neutrophilic therapies such as colchicine and dapsone are generally used as adjunct agents[8,11]. It is also important to ensure proper wound care along with the topical or systemic treatments. It can often take weeks to months to achieve complete ulcer healing[10]. Biologics, including anti-tumor necrosis factor agents such as infliximab and adalimumab, and anti-interleukin (IL)-12/IL-23 agents such as ustekinumab can be used as second-line treatment[9,14]. More than half of the patients with PG are associated with underlying systemic diseases, most commonly IBD, arthritis, and hematologic disease or hematologic malignancy[3,10,15]. Therefore, when PG is diagnosed, gastrointestinal symptoms such as persistent fever, abdominal pain or diarrhea, joint pain or swelling should be checked as well as the laboratory findings including complete blood count with differential count, inflammatory markers and antibodies such as ESR, CRP, fecal calprotectin, antineutrophil cytoplasmic antibodies, and anti-Saccharomyces cerevisiae antibodies.

PG is known to usually manifest after the onset of UC and around the time of an exacerbation[7,15]. Therefore, we assume that our patient was suffering from IBD at the time of presentation with PG, although he did not have any gastrointestinal symptoms or signs and the diagnosis of UC was made during the evaluation for underlying disorders. In conclusion, systemic evaluation is very important to determine the underlying disorders in PG patients who show continuously high titers of ESR and CRP, suggesting systemic inflammation, even though there are no other symptoms except skin lesions.

In summary, we report a case in which an 18-year-old young male patient diagnosed with PG was later found to have UC as the underlying disease. Therefore, even if there are no other symptoms except skin lesions, it is important to evaluate for underlying systemic diseases through appropriate tests.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

None.

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