# **Title Page**

# **A rare case of Pyoderma Gangrenous as a Complication of Ulcerative Colitis: A Case Report**

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# **Statement of Contribution**

Amin Shah played a central role in the research, contributing to conceptualization, data curation, formal analysis, and methodology. Anubhav Sharma, Agnimshwor Dahal, Prinsa Shrestha, Rahul Parajuli, Rebicca Pradhan and Bibek Shrestha were involved in the supervision, validation, and investigation phases of the project, ensuring the study's accuracy and credibility.

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None

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None

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Written informed consent was obtained from the patient for publication of this case image and accompanying images, complying with the requirements as mentioned in Wiley’s CCR Consent Form.

# **Ethical Approval**

The institutional review board (IRB) of Kathmandu Medical College and Teaching Hospital does not mandate ethical approval for Case Image.

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# **Case Report: Manuscript**

# **A rare case of Pyoderma Gangrenous as a Complication of Ulcerative Colitis: A Case Report**

# **Key Clinical Message**

This case highlights a rare and severe complication of ulcerative colitis, pyoderma gangrenosum, in a 79-year-old male. The patient presented with acute symptoms of UC, including severe bloody diarrhea, abdominal pain, fever, and a progressively worsening ulcerative lesion on the left shin following minor trauma. The diagnosis of PG was supported by clinical findings, a history of UC, and the pathergy phenomenon, alongside exclusion of differential diagnoses like cellulitis and erythema nodosum. Investigations revealed anemia, elevated inflammatory markers, and colonoscopy findings consistent with severe ulcerative colitis, confirmed by histopathology. Management included systemic corticosteroids, immunosuppressive therapy and wound care, which led to significant improvement in the ulcer and overall condition. This case underscores the importance of early recognition and multidisciplinary treatment of pyoderma gangrenosum to prevent complications and improve outcomes. It also highlights the need for further research into the mechanisms linking ulcerative colitis and its rare complication.

# **INTRODUCTION**

Ulcerative colitis (UC) is a chronic, idiopathic inflammatory bowel disease characterized by a continuous mucosal inflammation extending proximally from the rectum and confined to the submucosa of the colon. This condition arises from a complex interplay of genetic, environmental, and immunological factors, resulting in a compromised colonic epithelial barrier. The annual incidence of UC ranges from 9 to 20 cases per 100,000 individuals worldwide. [1] Among patients with UC, 0.5% to 5% develop pyoderma gangrenosum (PG), a rare, severe, neutrophil-mediated dermatological condition. PG typically manifests on the extensor surfaces of the legs following minor trauma and begins as painful pustular lesions with poorly defined borders. Without prompt intervention, these lesions can progress to necrotic ulcers, causing significant cosmetic disfigurement, functional impairment, and permanent scarring. [2,3]

Here, we present a rare case of 79-year-old male with UC complicated by PG. This article underscores the intricate association between UC and PG, emphasizing the need for early recognition and interdisciplinary management to prevent severe complications and improve patient outcomes.

# **CASE REPORT**

A 79-year-old male with a known case of ulcerative colitis presented to the outpatient department of our hospital with chief complaints of blood in stool for 20 days and a wound on the anterior shin of the left leg for 15 days. The stool was liquid in consistency (Bristol stool type 7), initially occurring 8-10 times a day, which later progressed to become uncountable, small in quantity (1-2 teaspoons), containing mucus, offensive in smell, and associated with crampy lower abdominal pain. The patient also complained of stool incontinence without pain during defecation. The wound on the anterior shin of the left leg was sustained from a bamboo stick injury 15 days before the onset of the symptoms. Initially, the wound presented as redness and swelling, which later progressed to a bloody discharge with mucus and a foul smell. Despite multiple dressings at home, the wound did not subside in size but instead increased in size and later became extremely painful. Two weeks after the injury, the patient developed a fever with a maximum recorded temperature of 103°F associated with chills and rigors, which was relieved with antipyretics. The patient also complained of weight loss, decreased appetite, back pain, and easy fatigability. The patient also gave a history of ulcerative colitis with previous recurrences despite compliance with medication. He discontinued his medication two months ago, following which there was a reappearance of symptoms. He gave no history of preexisting comorbidities such as diabetes mellitus or hypertension.

During the physical examination, the patient appeared conscious, cooperative and well-oriented regarding time, place, and person. Pallor and localized edema were observed over the left lower leg. Moreover, a 10 x 6 cm ulcerated lesion with active oozing of blood and mucus was observed on the anterior shin of the left leg (Figure 1). The lesion had irregular edges, surrounding erythema, and an increased local temperature, suggesting inflammation. On abdominal examination, it was unremarkable, with normal bowel sounds and no tenderness. From the clinical history and examination findings, several differential diagnoses were considered for the ulcerative lesion on the patient's anterior shin. Cellulitis was initially suspected due to localized erythema, swelling, and warmth; however, the lack of systemic signs of infection such as bacteremia or positive blood cultures, along with the lesion’s progression despite antibiotic treatment, ruled it out. Venous leg ulcer was another consideration, but the lesion’s location on the anterior shin, its irregular borders, and the absence of clinical features of venous insufficiency, such as varicose veins or hyperpigmentation, made this unlikely. Erythema nodosum, a common dermatologic manifestation of UC, was excluded as it typically presents as tender, non-ulcerative nodules rather than ulcerative lesions. Necrotizing fasciitis was also contemplated due to the lesion's severity, but the absence of crepitus, rapid necrosis, or gas on imaging studies negated this possibility. The presentation of an ulcer with undermined edges following minor trauma, coupled with the patient's history of UC and the pathergy phenomenon, strongly supported the diagnosis of P). For further confirmation, laboratory and radiological investigations were done. Routine laboratory tests showed anemia and leukopenia, while the iron profile revealed iron deficiency with reduced ferritin and transferrin saturation, which can be attributed to significant blood loss due to frequent passage of bloody stools. Moreover, inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), were elevated, indicating inflammation. A contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis revealed circumferential thickening in the rectum, sigmoid, and ascending colon, along with fat stranding and enlarged vasa recta, indicative of inflammatory bowel disease (IBD), most likely ulcerative colitis. A colonoscopy was done, which revealed a complete loss of vascular pattern, deep ulcers, luminal bleeding, and pseudo polyps in both the rectum and sigmoid colon (Figure 3). Along with the colonoscopy, a biopsy was also done, whose histopathological examination confirmed chronic moderately active colitis with crypt abscesses, architectural distortion, and basal lymphoplasmacytosis. These findings established the diagnosis of acute flare of UC. Based on clinical history, examination and laboratory findings along with lesion’s characteristic presentation at the site of minor trauma, coupled with its significant improvement following systemic corticosteroids and immunosuppressive therapy, confirmed PG as a rare extraintestinal complication of UC.

The patient was managed with Mesalazine 400 mg, Azathioprine 100 mg, and Prednisolone 50 mg for UC due to their anti-inflammatory and immunosuppressive properties. For PG, treatment included Fusidic acid with Betamethasone valerate cream, Dapsone 100 mg, and Prednisolone 50 mg, which have anti-inflammatory effects and promote wound healing. Following management, the wound showed a reduction in size and inflammation with visible granulation tissue, decreased erythema, and no bleeding or mucus. These findings indicated significant improvement from the presentation, and the patient was discharged after 9 days (Figure 2).

# **DISCUSSION**

UC is an idiopathic chronic inflammatory illness that is characterized by recurrent and remitting inflammation of the mucosal lining affecting the colon. It can cause several complications, not only limited to the intestine but also extraintestinal complications in the skin, joints, pericardium, and so on. Among the extraintestinal dermatological manifestations, PG is the second most common after erythema nodosum. [4] PG is a non-infectious, ulcerative, inflammatory condition linked with systemic illness like inflammatory bowel disease. [5,6] PG typically presents with painful, rapidly progressing skin lesion with violaceous edge. It can affect various body parts including the chest, limbs and perianal region. [10] According to the European Crohn’s and Colitis Organization (ECCO), the prevalence of PG is 0.6% to 2.1% in ulcerative colitis patients, which is higher than that of Crohn’s disease patients. [7] Despite its name, PG is neither caused by infection nor gangrene. Its pathophysiology involves multifactorial causes. It is primarily thought to be caused by abnormal neutrophilic infiltration, which causes neutrophilic dermatosis. Immune system dysregulation involving pro-inflammatory cytokines such as IL-1β, IL-8, IL-17, and TNF-α are thought to contribute to its pathophysiology. Genetic predisposition and genetic mutation involving pathways like PTPN6 and PSTPIP1 are also believed to lead to an autoinflammatory process that resembles pyoderma gangrenosum. [8]

Here we present a case of a 79-year-old male with a known case of UC for the past four years with previous recurrences, who currently presented with intestinal symptoms after discontinuing his medication for two months and a progressively worsening wound on the anterior aspect of his left shin following injury from bamboo stick 15 days back. This presentation aligns with the typical pattern of pyoderma gangrenosum, which appears at sites of trauma as described in various studies, including a descriptive cohort study by Weizman et al., which showed the lower extremities as the most common sites for PG. [2] Furthermore, a number of studies demonstrate a strong correlation between UC flare-ups and the development of PG, which is supported by active and aggravated bowel symptoms at the time of PG onset. This case further supports this link. [2,4,6] The initial investigation revealed a low hemoglobin level, most likely caused by blood loss in the stool. Further, colonoscopy showed complete loss of vascular pattern, deep ulcers, luminal bleeding, and pseudo polyps in both the rectum and sigmoid colon. These findings are consistent with typical ulcerative colitis presentations, as documented in multiple sources. [1,5,6] Additionally, colonic and rectal biopsies showed crypt abscesses and architectural distortion, which further confirmed the diagnosis of UC, as these are hallmark features of the disease. [1,5,6] Stool examination and culture revealed no enteropathogenic organism after 48 hours of incubation at 37 degrees, as suggested by many texts in literature, a requirement to rule out colonic infection, which can produce similar clinical findings. [1,5] The patient was classified as having the severe type of UC based on Truelove and Witts criteria, which is a set of clinical criteria used to evaluate the severity of ulcerative colitis. This classification was due to his presentation of more than eight episodes of bloody stools per day with fever and anemia. With suggestive clinical presentation and positive investigation findings, including endoscopy and biopsy as recommended, the diagnosis of acute ulcerative colitis in relapse with extraintestinal manifestation, pyoderma gangrenosum, was made. [1,5] Corticosteroids are the cornerstone of treatment for pyoderma gangrenosum, particularly in cases associated with ulcerative colitis. They are effective in reducing inflammation and promoting healing of skin lesions. Systemic corticosteroids are recommended as a first-line treatment, especially during acute exacerbations of pyoderma gangrenosum. [12] In cases where corticosteroids are insufficient or where long-term use is not advisable due to potential side effects, other immunosuppressive agents may be utilized. These include calcineurin inhibitors and biological agents such as infliximab and adalimumab, which have shown efficacy in treating both ulcerative colitis and pyoderma gangrenosum. [13,14]

Here, the patient was hospitalized, and treatment was initiated in the line of acute severe UC with a systemic corticosteroid, which also happens to be the most commonly initiated therapy for PG, as potent immunosuppression is needed for PG irrespective of underlying intestinal disease activity. [2,4,5] In addition, the patient received 2 pints of packed red blood cells (RBC) to treat his anemia. First-line agent Mesalazine, with a remission rate of 50%, was also initiated, which shows its anti-inflammatory effect by inducing peroxisome proliferator-activated receptor-gamma (PPAR-γ) gene expression and activating nuclear factor kappa-B (NFκB), while also inhibiting the synthesis of prostaglandin and interleukin-1. [1,6] Mesalamine which is a 5 amino salicylic acid, has shown efficacy in treating and maintaining remission in ulcerative colitis and has shown to be superior to sulfasalazine in treating ulcerative colitis. If used with probiotics, mesalamine has improved symptom score and reduced disease activity. [11] The lowest level of hemoglobin reported was 6.4 mg/dl, after which two pints of packed RBC were transfused 1 day apart with successive improvement in hemoglobin levels, 8.5mg/dl after the first transfusion and 9.9 mg/dl after the second transfusion. With the improvement of clinical symptoms and endoscopic evidence of healing, remission was achieved, and medications were continued and adjusted to sustain the remission. Since the patient responded well to intravenous corticosteroids, the need for early use of biologics like infliximab was eliminated. [5] This positive response to treatment demonstrates an encouraging treatment outcome in managing such cases. Proper wound care in the hospital and counseling the patient on wound care and management also significantly helped to improve the patient’s outcome, enhancing early wound healing and enabling the patient to be discharged early. The patient was discharged after nine days of hospital admission. Treatment of pyoderma gangrenosum poses a significant challenge due to the phenomenon of pathergy, which is described as an amplified response to minimal skin trauma or degrading status of the existing wound on minimal insult, thus minimizing the prospect of performing any surgeries or elaborate procedures. [9] In lack of proper treatment comprising primarily of simple wound care and debridement, complications like deep ulcers, permanent scarring, cosmetic disfigurement, and bacterial super-infections could develop, significantly impacting a patient’s life. [2,9]

This rare association of pyoderma gangrenosum and ulcerative colitis highlights the need for further research to enhance understanding, diagnosis and management. While current treatment strategies, such as systemic corticosteroids and immunosuppressive therapies, have shown efficacy, the variability in individual responses and the risk of adverse effects underscore the importance of exploring alternative therapies, including biologics and targeted treatments. Additionally, the pathophysiological mechanisms linking pyoderma gangrenosum and ulcerative colitis, particularly the role of immune dysregulation and genetic predisposition, remain incompletely understood and warrant deeper investigation. Large-scale studies and clinical trials focusing on identifying predictive markers for pyoderma gangrenosum in ulcerative colitis patients, as well as comparative studies evaluating different treatment modalities, could improve early detection and optimize patient outcomes. Advancing knowledge in this field could also provide valuable insights into other neutrophilic dermatoses and inflammatory bowel disease manifestations, contributing to the broader scope of evidence-based medicine.

# **CONCLUSION**

This case underscores the importance of recognizing PG as a rare but severe extraintestinal manifestation of UC. Prompt diagnosis, a multidisciplinary approach, and tailored management, including systemic corticosteroids and immunosuppressive therapies, were pivotal in achieving a favorable outcome for the patient. This case also highlights the pathergy phenomenon as a key diagnostic clue in PG and emphasizes the critical role of careful wound management in avoiding complications. By presenting this case, we aim to increase awareness among clinicians about this challenging complication, advocating for early intervention to improve patient outcomes. Further studies are warranted to better understand the pathophysiology of PG in UC and to optimize treatment strategies.

# **Figures**

1. Figure 1: Pyoderma gangrenosum lesion on the left shin at presentation with 10 x 6 cm ulcerated lesion with active oozing of blood and mucus
2. Figure 2: Pyoderma gangrenosum (PG) lesion on the left shin after treatment
3. Figure 3: Colonoscopy showing areas of active colitis with loss of vascular pattern in the colon, consistent with findings of ulcerative colitis

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