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**Case Report**

# A neglected pyoderma gangrenosum following COVID-19: A case report

**Thamir Abdulmajeed Kubaisi**

Department of Dermatology, College of Medicine, University of Anbar; Ramadi, Anbar, Iraq.

**Abstract** COVID-19 infection is related to many skin problems. The pathogenesis is under search, but mainly involves inflammatory and vasculopathic injuries. Pyoderma gangrenosum is an ulcerative sterile inflammatory reaction of the skin. The etiology is unknown in around 50% of the cases. This article reported a 47-years old soldier man with COVID-19 who developed big, very painful, indurated ulcers on his abdomen and another small one at back, treated as pyoderma gangrenosum and established very good improvement on prednisolone and azathioprine. In conclusion, patients of COVID-19 may be at increased risk for emerging pyoderma gangrenosum with significant overlap in disease pathogenesis. Medical doctors should suspect pyoderma gangrenosum in an individual with coronavirus infection who has non-healing ulcers.

***Key words***
Pyoderma gangrenosum, dermatological manifestations, prednisolone, azathioprine.

## Introduction

COVID-19 infection is related to many skin problems, but the main ones include perniosis-like lesions, urticaria, viral exanthema, vesicular like varicella, purpuric papules, and livedoid skin disease. The pathogenesis behind coronavirus cutaneous manifestations is under search, but mainly involves inflammatory and vasculopathic injuries.[1,2] Pyoderma gangrenosum (PG) is an uncommon non-infectious auto-inflammatory skin problem, characterized by painful ulcers that grow rapidly on the skin.[3] Several literatures reported PG after severe COVID infection involving lower extremities in unhealthy adults.[4,5] Alongside few reports spoke about PG following coronavirus vaccination.[6,7] This case study presents an adult, otherwise healthy, who developed a mistreated PG as a rare skin reaction following COVID-19, and highlight on the presentation and treatment.

**Address for correspondence**
Dr. Thamir Abdulmajeed Kubaisi
FIBMS (Dermatology)
Department of Dermatology,
College of Medicine, University of Anbar;
Ramadi, Anbar, Iraq
Email: med.thamer.alkubaisi@uoanbar.edu.iq

## Case report

A 47-years old soldier man presented with big, very painful, indurated ulcers with surrounding erythema and an unequal base and border. The ground of the ulcer is black, necrotic and undermined edge. One lesion exist on the abdomen had a surface area of 135 $cm^2$ **(Figure 1A)** and another smaller lesion (surface area 25 $cm^2$) on the back **(Figure 1B)**. Condition proceeded before 3 weeks of illness, as a sore throat, fevers, and dyspnea, and positive test for COVID-19 by RT-PCR. Simultaneously, the patient's family had similar complaints with positive RT-PCR for SARS-CoV-2 infection. He did not need admission and was advised to self-quarantine for 14 days. At that time and within a few days, he developed tender 2 pustules that rapidly ulcerated. On that day, he went to a hospital where the initial examination did not cause great worry to the general practitioner


**Figure 1** PG on the abdomen had a surface area of 135 $cm^2$ (A). Smaller lesion (surface area 25 $cm^2$) on the back (B).

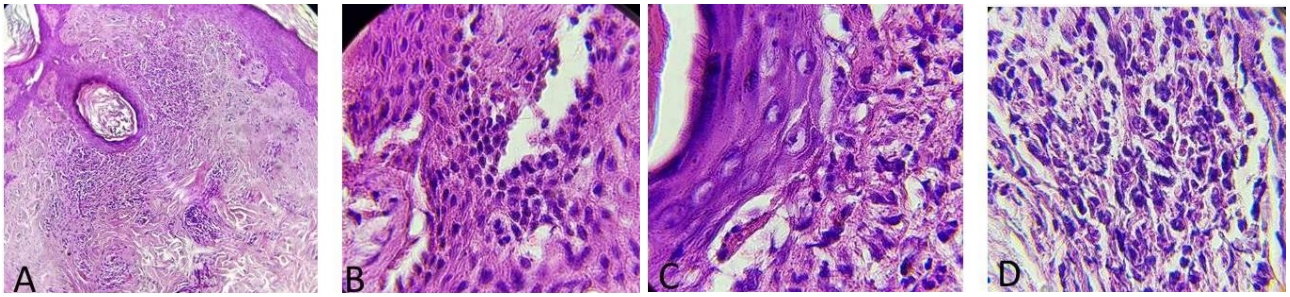


**Figure 2** Hematoxylin & Eosin stained parts presenting marked neutrophils infiltration at the upper and deep dermis. (A-x100- C& D- x400) with special periadnexial and perivascular concentrations. (B-x400).

doctors and diagnosed him as necrotic ecthyma treated with topical detergents, oral paracetamol and parenteral injection of ceftriaxone for 10 days, but the pain increased and the condition surge in the depth and edge. Then the patient decided to look for medical advice from a private dermatology clinic in Al-Anbar City, where a thorough clinical examination was done, general laboratory works were within normal ranges, and no pathogens were detected after direct microscopical check and culture of the purulent and hemorrhagic discharges and a biopsy of lesion's border were taken.

He had no detectable past medical history or drug allergy. He denied recent travel, trauma, contact with animals, or insect bites. Workups for PG associated diseases including inflammatory bowel disease, rheumatoid arthritis, haematological malignancies and major autoimmune diseases were all negative. A written consent was obtained from the patient before publication.

Depending on the Delphi exercise, the diagnosis of ulcerative PG was made.[8] The major criterion is the histological finding of the ulcer's border that shows neutrophils infiltration at the upper and deep dermis with special periadnexial and perivascular concentrations **(Figure 2)**. Patient had five minor criteria including "history of pustule rapidly ulcerating within few days; the exclusion of infection; peripheral erythema, undermining border, and tenderness at ulceration site; decreased ulcer size within 1 month of initiating immunosuppressive medications; and cribriform scars at healed ulcer sites".

After the diagnosis of PG, the patient was started on 40 mg of prednisolone daily (0.5mg/kg) and 50 mg twice daily of azathioprine tablets added as "steroid-sparing agent drug". Good clinical improvement appeared within 2 weeks, with healing of necrotic wound boundaries and development of granulation tissue. Subsequently, two weeks follow up; he established very good improvement **(Figure 3)**.


**Figure 3** after one month treatment, PG of the abdomen (A), PG of the back (B).

The prednisolone dose was regularly tapered by 5 mg each 2 weeks, while continue on azathioprine only. At the 3-month follow-up, there were perforated marks at cured sites.

## Discussion

Pyoderma gangrenosum is a noninfectious inflammatory disease characterized by repeated painful skin ulcers with undermined bluish boundaries and erythema at the margin and distinguish by neutrophil infiltration including the skin and further organs. The clinical characteristics of PG in this study are similar to published data, with a dominance of the classical ulcerative type, and the disease usually affects the age group of 20–50 years.[9,10] Any part of the body can involve in the disease, but the classical ulcers affect the lower extremities in up to 85.7% of the cases and the cause for this specific place is unknown.[11-13] while the present report showed ulcers with peripheral erythema, undermining border, and tenderness involved the abdomen and back. This may be related to an otherwise healthy, sporty soldier patient and he did not complain of chronic peripheral vascular and neurological diseases.

Owing to COVID-19 and its roles of a hyperactive immune response, complement activation and microvascular injury have been hypothesized in the vasculopathy and vasculitic lesions.[14-16] During viral infection, the neutrophils express an intense response, stimulating cross-talk with T cells.[17] Neutrophils also exhibit a complex layout of receptors and attachment molecules for several ligands, including inflammatory markers and immunoglobulin.[18] In this sense, severe COVID-19 seems to be related to a surge in the neutrophil-to-lymphocyte ratio (NLR) levels.[19]

The histopathology of PG is nonspecific, and many studies show the presence of neutrophilic infiltrate and leukocytoclastic vasculitis, and come to an agreement with the present report which found a vasculitis and neutrophilic infiltrate in the border of PG ulcer and reflected a major criterion. These abnormal immunological likenesses overlap between COVID-19 and PG and can play an important role in the pathogenesis of both problems. In addition, many case reports of PG following coronavirus infections, besides a few cases of a rare adverse episode associated with the BNT162b2 vaccine.[4-7]

The patient established very good improvement within a month of the treatment regimen without recurrence. This may be related to site of involvement where the abdomen and back are affected and not the lower extremities, also he is a healthy man and did not complain of chronic immunological problems like malignancy, SLE and diabetes mellitus. The quick response to management was considered a minor criterion

and approval of PG diagnosis.

The goal of the treatment is to decrease pain and to encourage wound healing, thereby promoting the quality of life of subjects. General practitioner doctors misdiagnose PG and consider it as a secondary bacterial infection following COVID-19 as a result of disturbed immunity. The culture and sensitivity were negative growth for bacteria; this goes parallel as a minor criterion of PG.

The treatment of PG is challenging and no single effective therapeutic regimen is present. This study shows very good, safe response and quick healing end with perforated marks of ulcers, using daily oral prednisolone (0.5mg/kg) plus twice daily of 50 mg azathioprine tablets added as "steroid-sparing agent".[20]

## Conclusion

To the best of our knowledge, no previous case report of abdominal PG in patients with COVID-19. Medical doctors should suspect PG in an individual with coronavirus infection who has non-healing ulcers. Early diagnosis and adequate treatment often produce a satisfactory prognosis and will shorten treatment time and prevent PG-associated complications,

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