
# Pyoderma Gangrenosum after COVID-19 Infection and Vaccination

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*To the Editor:*

**Introduction**

Pyoderma gangrenosum (PG) is a rare, autoinflammatory neutrophilic dermatosis that is characterized by highly painful purulent pustules or deep, enlarging ulcers with purple and undermined edges.[1] PG has been associated with systemic diseases including HIV, hepatitis, systemic lupus erythematosus, ulcerative colitis, inflammatory bowel disease, and Takayasu arteritis;[1] however, there remains limited discussion on occurrences of PG after COVID-19 infection and vaccination despite multiple documented cases. We present a review of PG onset after COVID-19 infection and vaccination and its implications for both adverse effects monitoring and patient counseling.

**Methods**

Literature searches were conducted on PubMed and Google Scholar ranging from 2019 to July 2022. Ten contributions were selected based on subject relevance; novel PG onset, and PG flares after COVID-19 infection and vaccination were included. Citations within the selected papers were also screened for relevance.

**Results**

To date (7/2022), there have been four cases of PG after COVID-19 vaccination and six cases of PG after COVID-19 infection (Table 1, Appendix).

**Discussion**

Multiple authors have hypothesized that exposure to the COVID-19 spike protein antigen via infection or vaccination may trigger an autoimmune response that mediates PG.[2–5] This is due to

the pathogenesis of COVID-19 and PG both involving the activation of proinflammatory cytokines including interleukin-6 (IL-6), IL-8, IL-12, IL-23, and tumor necrosis factor-α (TNF-α).[2,3,5] Both are also associated with elevated neutrophils and dysregulation of the Janus Kinase/signal transducer and activator of transcription (JAK/STAT) signaling pathway.[3,4] Finally, it is hypothesized that COVID-19 vaccination can trigger cutaneous inflammation from the polarization of T-helper 1 cells (Th1) and Th17 cells to induce PG.[2]

The associations between COVID-19 and PG in some of these patients have been challenged by independent risk factors including pressure ulcers from long-term ICU hospitalization,[6] a history of ulcerative colitis (UC),[7] injection of subcutaneous granulocyte colony-stimulating factor (G-CSF),[7] and cocaine use.[5] Risk factors such as UC and G-CSF treatment may predispose patients to PG-inducing autoimmune reactions triggered by COVID-19 infection/vaccination.[7] The patients who developed pressure ulcers and subsequent PG in the ICU were initially hospitalized for severe COVID-19, indicating how COVID-19 infection may mediate conditions that favor PG development.[6]

**Conclusions**

PG is an exceedingly rare complication following COVID-19 infection and vaccination. Given that only 47 incidences of PG have been reported to VigiBase (the World Health Organization's global database for suspected adverse effects) after the administration of over 12.2 billion COVID-19 vaccine doses as of 7/15/2022, the benefits of COVID-19 vaccines still significantly outweigh the risks. We advise healthcare providers to continue advocating for the importance of obtaining the COVID-19 vaccine while monitoring for rare but severe adverse effects such as PG in patients with a history of COVID-19 infection and vaccination.

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**Conflicts of Interest**

The authors have no conflicts of interest to declare.

IRB approval status: Exempt

**Appendix**

*Table 1: Reported Cases of Pyoderma Gangrenosum after COVID-19 Infection and Vaccination*

| Patient Profile | After Infection or Vaccination? | COVID-19 Vaccine Type | Onset (days after vaccine administration/infection) | Location of Lesions | Treatment | Clinical Outcome |
|---|---|---|---|---|---|---|
| 29-year-old male [2] | Vaccination | Tozinameran, 2nd dose | 2 days | Right lower leg | Oral prednisolone 30 mg/day (0.3 mg/kg/day) | Gradual improvement with therapy |
| 73-year-old female [3] | Vaccination | Tozinameran, 2nd dose | 14 days (flare) | Left pretibial region | Infliximab injection, oral prednisone, cyclosporine, biweekly adalimumab injections | Injection reaction to infliximab, unresponsive to all other treatments |
| 49-year-old male [7] | Vaccination | Tozinameran, 2nd dose | 22 days | Upper arm injection site (unspecifie | Topical and systemic corticostero | Resolution after 1 month of therapy |

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|---|---|---|---|---|---|---|
| | | | | d laterality) | ids (prednisone 1 mg/kg/day) | |
| 27-year-old male [8] | Vaccination | Tozinameran, 1st dose | 1 day | Right lower leg and upper posterior thigh, left lower leg, perianal region, dorsal right hand | Intravenous prednisone 1 mg/kg/day | Rapid improvement in 3 days, complete resolution in 21 days |
| 66-year-old male [6] | Infection | Not applicable (N/A) | 33 days | Sacral region | Negative-pressure wound therapy (NPWT) x 1 month, pedicled superior gluteal artery perforator flap for wound closure | No post-operative complications, discharged 33 days after surgery |
| 52-year-old male [6] | Infection | N/A | 42 days | Sacral region | NPWT x 6 weeks, pedicled superior gluteal artery perforator flap for wound closure | No post-operative complications |
| 71-year-old male [4] | Infection | N/A | 10 days | Penis, left scrotum, groin, | Prednisone 60 mg daily, | Prompt improvement with |

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|---|---|---|---|---|---|---|
| | | | | buttocks, and abdomen | topical corticosteroids, and infliximab for long-term treatment | steroid therapy |
| 44-year-old female [9] | Infection | N/A | ~90 days (after bilateral mastectomy) | Nipple areolar complex of both breasts | Steroids, then infliximab | Clinical improvement on steroids, wound dehiscence after discharge. Steady improvement on infliximab. |
| 72-year-old male [10] | Infection | N/A | Unspecified | Left scrotum | Prednisone prior to loose wound edge approximation. Cyclosporine and infliximab for post-procedural therapy. | Improved on prednisone, scrotal prolapse requiring loose wound edge approximation. Complete wound healing at 5-months |
| 41-year-old male [5] | Infection | N/A | Unspecified; 8 days prior to hospital admission (flare) | Upper back, left trunk, right arm | Intravenous methylprednisolone, topical clobetasol dipropionate 0.05% | Unresponsive to in-hospital therapy, referred to the burn center. |