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Case Report
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Upadacitinib in Concurrent Severe Pyoderma Gangrenosum and Crohn's Disease: Case Report and Literature Review

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Abstract

Pyoderma Gangrenosum (PG) is a neutrophilic dermatosis characterized by skin infiltrations of polymorphonuclear leukocytes in the absence of vasculitis and infection [1]. Its main clinical features include the presence of inflammatory papules or pustules that usually progress to painful ulcers with a violaceous and undermined border. Commonly located on lower limbs, lesions typically seem as tender pustules or nodules that rapidly progress to ulcers with violaceous undermined borders [2]. Most cases occur in patients with an underlying systemic disorder, such as IBD in 0.4% to 2%, inflammatory arthritis, or hematological malignancies.

Keywords: Pyoderma gangrenosum; Upadacitinib; Crohn's disease

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Case Presentation

We present the case of a 30-year-old patient with a one-year history of severe Crohn's Disease (CD) (Montreal classification A1, L3, B3) [3]. The patient had been on infliximab therapy with partial clinical benefit for one year. Afterwards, an erythematous and painful nodule at the level of the middle third of the posterior surface of the leg was observed. After one week, the lesion looked ulcerated, with a necrotic base and a violaceous. The patient underwent dermatologic assessment and a diagnosis of PG was made (Figure 1A); in particular, clinical evaluation showed a pustular subtype PG, a variant of pyoderma that is most related to IBD [4]. The patient started oral corticosteroid therapy and infliximab therapy was discontinued. A couple of weeks after the start of the therapy, the patient showed a slight resolution of the lesion; however, a similar lesion appeared at the level of the left gluteal region (Figure 1B). Therefore, tapering of corticosteroid therapy was planned and off-label treatment with upadacitinib at a dosage of 45 mg in daily single administration for twelve weeks was started. At week 12, both lesions showed an important degree of improvement (Figures 2A and 2B). In addition, the patient reported clinical benefits in bowel activity. Therefore, it was decided to continue Upadacitinib therapy with a maintenance dosage of 30 mg daily. At week 20 of therapy, lesion resolution and healing were noted with only residual pigmentation (Figures 2C and 2D).

PG involves dysregulation of both innate and adaptive immunity, leading to a neutrophil-rich autoinflammatory process with the elevation of multiple cytokines [1,2]. Some of these cytokines act through the JAK (Janus kinase)/STAT (Signal Transducer and Activator of Transcription) pathway [5]. The importance of the JAK/STAT pathway in PG has also been demonstrated through immunohistochemistry in skin biopsy specimens [4]. Upadacitinib is JAK-1 selective inhibitor [6] and is approved for the treatment of other immunologically mediated disorders, including ulcerative colitis, rheumatoid arthritis, psoriasis arthritis, axial spondyloarthritis, ankylosing spondylitis, and atopic dermatitis. Recently, a case report showed an improvement in PG and spondyloarthritis (SpA) activity in a 65-year-old woman who suffered from HLA-B27-negative SpA and PG, who was treated with Upadacitinib [7]. The patient had failed multiple therapies including systemic corticosteroids, immunosuppressants, tumor necrosis factor α inhibitor, etanercept, secukinumab

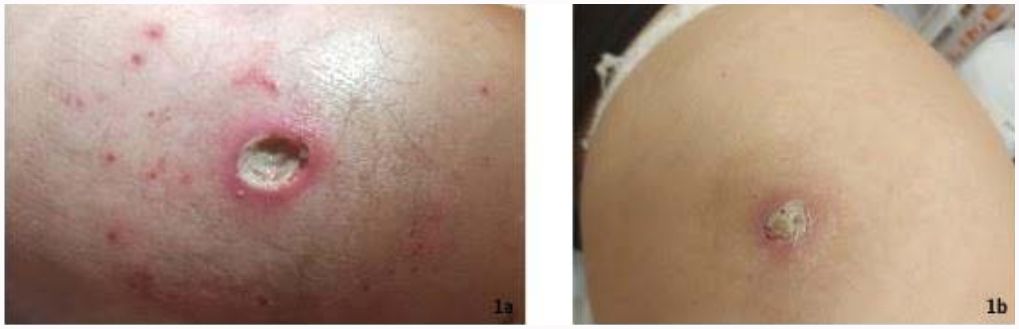

Figure 1: A 30-year-old patient with severe Crohn's disease showed an erythematous and painful nodule at the level of the middle third of the posterior surface of the leg (a) and left gluteal region (b).

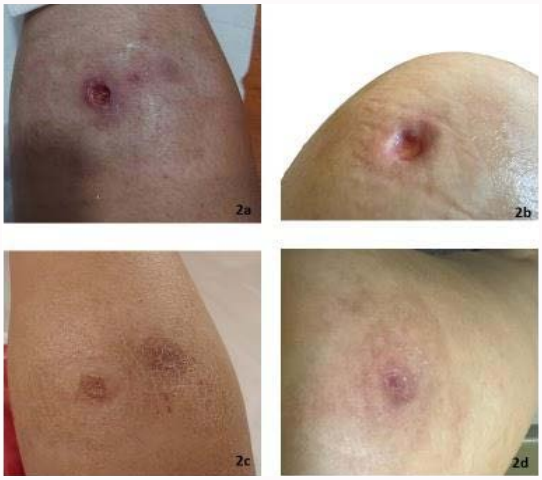

Figure 2: After treatment with upadacitinib for 12 weeks, PG of the posterior surface of the leg (a) and left gluteal region (b) showed clinical improvement. At week 20 of therapy, resolution and healing of both lesions were found, with only residual pigmentation (c and d).

and apremilast. Complete remission was observed at follow-up after 12 weeks and persisted after 24 weeks [8].

Conclusions

With our case report, we hope to broaden the therapeutic options for PG and motivate further research to determine whether JAK inhibitors could play a role in PG treatment. Moreover, upadacitinib may cause relevant changes of our current treatment algorithms for Crohn's disease. Further real-world studies and head-to-head comparisons are needed to position Upadacitinib in our current treatment algorithms for CD.

Author Contributions

Conceptualization, C.M.P. and L.P.; methodology, M.R.D.P.; validation, D.N., M.R.D.P., V.B. and C.M.P.; formal analysis, F.S.; investigation, A.D.L.; resources A.M.S.; data curation, T.S.; writing—original draft preparation, C.M.P.; writing—review and editing, C.M.P.; visualization, M.R.D.P.; supervision, D.N.; project administration, S.C.; funding acquisition, D.N.

All authors have read and agreed to the published version of the manuscript.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient to publish this paper.

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