


Multiple Orocutaneous Extraintestinal Manifestations in Ulcerative Colitis Patient: Complete Response to Ustekinumab

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Key Words: extraintestinal manifestations, multiple orocutaneous extraintestinal manifestations, ustekinumab, ulcerative colitis

Case

Pyostomatitis vegetans (PV) is characterized by exophytic-erythematous pustules with superficial erosions of the oral mucosa, while pyoderma gangrenosum (PG) is a rare skin disorder characterized by the development of painful and deeply ulcerated necrotic areas.¹ The diagnosis of PV and PG is based on clinical features while histology is unspecific and not always required.²

We report a case of a 73-year-old woman with steroid-dependent, long-standing pancolonic ulcerative colitis (UC) previously treated with azathioprine and naïve to biologics. She was admitted to hospital for sepsis (fever 39 °C, white blood cell count 18 000, C-reactive protein >200 mg/dL, procalcitonin 0.75 ng/mL) and moderate UC relapse (partial Mayo score 10, Mayo endoscopic subscore 1) with multiple painful, ulcerated, vegetative and purulent lesions in the oral cavity and skin (leg and sacral regions) (Figure 1).

Intravenous (IV) piperacillin-tazobactam was started and sepsis resolved after 3 days. After dermatological assessment a diagnosis of multiple PG and oral PV was made, IV methylprednisolone 60 mg/d was started. Remission of intestinal symptoms and improvement of orocutaneous lesions were observed until steroid tapering, when orocutaneous lesions worsened. Due to the age of the patient and the recent septic event, anti-tumor necrosis factor (TNF) treatment was considered not indicated and IV ustekinumab 390 mg was started followed by a maintenance regimen with 90 mg every 8 weeks. Complete healing of the orocutaneous lesions and clinical and biochemical remission (partial Mayo score 0, C-reactive protein normalization, fecal calprotectin <150 µg/g) was obtained by the

end of induction and maintained off of steroids during the following 10 months.

Discussion

PG and PV are rare orocutaneous extraintestinal manifestations complicating inflammatory bowel disease. The unclear pathogenesis and the insufficient data on their clinical management make inflammatory bowel disease-associated PG and PV therapeutically challenging. We describe a case of multiple PG and PV in a 73-year-old woman with active ulcerative colitis, naïve to biological therapy, refractory to steroids, successfully treated with the anti-interleukin-12/interleukin-23 monoclonal antibody ustekinumab. Both PV and PG are characterized by a sterile infiltrate of neutrophils and lymphoid cells.³ Defects in neutrophil chemotaxis, inflammasome activation, and excessive expression of interleukin (IL)-1 β, TNF-α, and IL-8 have been implied in the pathogenesis of PG.⁴ Ustekinumab is a monoclonal antibody targeting IL-12 and IL-23 approved for the treatment of moderate-to-severe UC with an improved safety profile as compared with anti-TNFs.⁵ Data reporting efficacy of ustekinumab in this setting are based on cases of isolated PG or PV.^{6–9}

IL-23 upregulation in PG implies T helper 17 cells in the inflammatory process sustaining skin lesions. In contrast, cytokine expression in PV has not been yet reported.¹⁰ Acknowledging that PG and PV might have a partially overlapping pathogenic mechanism, ustekinumab-dependent block of the IL-23–T helper 17 axes might explain the rapid healing of the orocutaneous lesions. However, we cannot exclude that the improvement of the intestinal inflammation could have contributed to the resolution of the orocutaneous lesions.



Figure 1. Oral pyostomatitis vegetans and pyoderma gangrenosum before (left) and 6 months after (right) ustekinumab start.

Acknowledgments

The authors thank the patient for her permission to document her treatment course and outcome.

Funding

None.

Conflicts of Interest

S.O. has received speaker fees from AbbVie, Janssen, Galapagos, and Takeda. M.C.F. has received consulting fees

from Roche, Takeda, Janssen-Cilag, Pfizer, Sandoz, Biogen, and Galapagos; and research economic support from AbbVie. The other authors disclose no conflicts.

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