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Infliximab in a patient with refractory mucosal aphthosis

Editor

We report on a 47-year-old woman who presented with recurrent aphthosis of the oral and vaginal mucosal for 3 years due to underlying Crohn's disease. Several aphthous lesions presented at the lips, palate, tongue, and at the introitus vaginae. Genuine aphthosis and Behçet's disease were excluded. The patient's condition was unresponsive to several treatments including retinoids, systemic corticosteroids, and treatment with dapsone. The current immunosuppressive therapy, including prednisone (10 mg/day), isotretinoin (20 mg/day), and dapsone (100 mg/day), did not lead to long-lasting disease remission. As the clinical status of the patient further deteriorated, we had to search for therapeutic alternatives and started treatment with infliximab. The recent finding that tumour necrosis factor- α (TNF- α) antagonist infliximab heals intestinal lesions of Crohn's disease¹ prompted us to initiate a therapeutic regimen with infliximab that was administered at 5 mg/kg/day intravenously at weeks 0, 2, and 6 for induction therapy and then every 8 weeks. Additional systemic immunosuppressive therapy was discontinued, and the patient received only topical treatment with povidone iodine dilution. By week 2, oral and genital aphthosis had an almost complete regression (fig. 1). Clinical remission still persisted 6 months after initiation of infliximab treatment without remarkable side-effects. The patient's clinical status remained stable, leading to a complete regression of the oral and intestinal lesions.

Infliximab is a chimeric monoclonal antibody that contains in both F_{ab} portions a variable murine region that is specifically directed towards human TNF- α and consists of the constant region (F_c) of human IgG1. Infliximab binds with high specificity and affinity to free and

membrane-bound TNF- α on various inflammatory cells. In addition to blocking soluble TNF- α , infliximab also induces lysis of the target cell through activation of complement.² At present, infliximab has been approved for the treatment of severe Crohn's disease, ulcerative colitis, ankylosing spondylitis, active rheumatoid arthritis, psoriatic arthritis, and psoriasis vulgaris.¹ Moreover, infliximab has proven to be effective in several TNF- α -associated inflammatory dermatoses, such as subcorneal pustular dermatosis, pyoderma gangrenosum, and granulomatous disorders.¹

Crohn's disease is a chronic inflammatory gastrointestinal disorder that may also present clinically as mucosal aphthosis. Infliximab has proven as an effective treatment for Crohn's disease in patients with poor response to conventional therapy. Due to the successful application of infliximab in patients with refractory Crohn's disease, the use of TNF- α blockers may be also a therapeutic option for extraintestinal manifestations.^{3,4} Infliximab has been shown to reduce the number of activated mucosal lymphocytes in patients with Crohn's disease,⁴ leading to down-regulation of mucosal inflammation by activated T cells, which are the main producers of proinflammatory cytokines such as TNF- α . Furthermore, there is evidence that up-regulation of matrix metalloproteinases (MMP) is of pathogenetic relevance in patients with inflammatory bowel disease.⁵ Infliximab down-regulates MMP-1, MMP-3, and MMP-9 and also decreases MMP-1 and MMP-3 activities.

Serious adverse events attributable to infliximab treatment include severe bacterial infections, viral infections, and tuberculosis but are generally rare. Regarding the overall safety of biologic agents used for treatment of inflammatory bowel disease, the most accurate data are available for infliximab, which was evaluated in many more clinical trials than any other biologic agent. Moreover, post-marketing experience also provides very valuable information about any side-effects occurring during treatment with infliximab.⁶ Thus, TNF- α blockade by infliximab is a very effective and safe therapeutic option for immediate control of refractory extraintestinal aphthosis in Crohn's disease.

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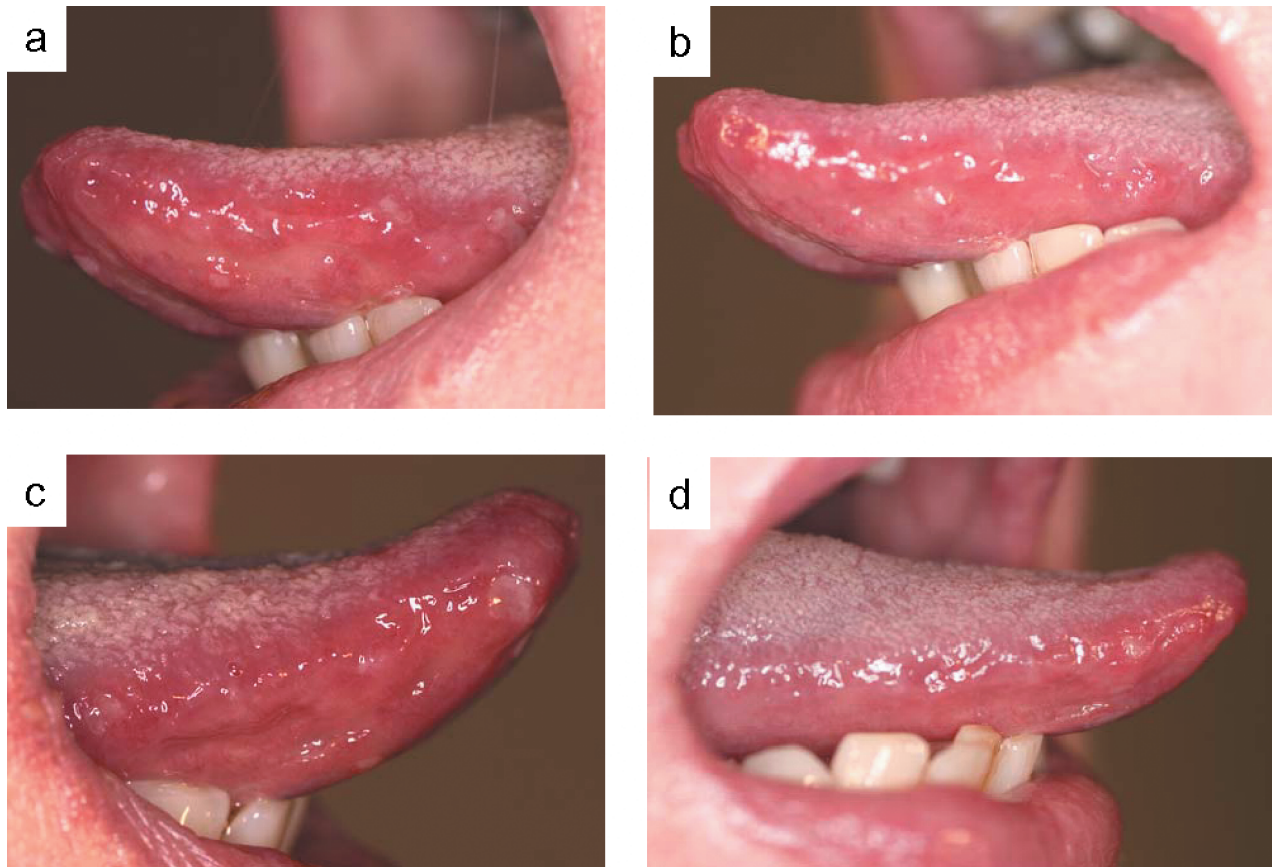


fig. 1 Aphthosis of the lateral tongue before (a and c) and 2 weeks after (b and d) initiation of infliximab. Mucosal lesions showed an almost complete regression.

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Vasculitic leg ulcers in a patient with mixed myelodysplastic and myeloproliferative syndrome

Editor

Ulcerations of the leg are frequently seen in dermatological practice as they have a prevalence of 4% in Western countries.¹ Ninety-five per cent of all leg ulcers have a venous, arterial, or diabetic aetiopathology, display a typical clinical presentation, and are easy to diagnose. However, besides these common forms, leg ulcers can also be the first sign of serious underlying systemic diseases like vasculitis, autoimmune disease, or malignancy.²