

Successful Treatment of Oral Crohn's Disease by Ustekinumab

Oral lesions, such as cheilitis or ulcerative lesions in the oral cavity, have been reported in a subset of patients with Crohn's disease (CD) and may even precede gastrointestinal involvement.¹ Little has been published regarding therapy of oral CD, but recent case-reports describe a beneficial effect of anti-TNF-alpha antagonists.² Ustekinumab, an antibody targeting the p40 subunit of interleukin-12 and interleukin-23, has demonstrated efficacy in CD.³ However, up to date ustekinumab has not been described as treatment of Crohn's cheilitis. Here we report a case of successful treatment with ustekinumab for a severe refractory oral manifestation of CD.

A 57-year-old female was diagnosed with perforating ileal CD after an ileocecal resection. Six months later, she presented with minor abdominal symptoms but particularly painful lips, mouth, and throat, leading to severe dysphagia. First, she was treated with consecutive topical and then systemic steroids without any response. Subsequently, she responded to infliximab but lost response despite adequate trough concentrations and had a primary nonresponse to vedolizumab. She further deteriorated with progressive dysphagia and a trismus caused by cheilitis and tonsillitis. Laboratory results displayed elevated inflammatory markers (C-reactive protein [CRP]: 18 mg/L, fecal calprotectin: 761 µg/g). Imminent malnutrition required placement of a percutaneous endoscopic gastrostomy (PEG) tube. Biopsy was performed

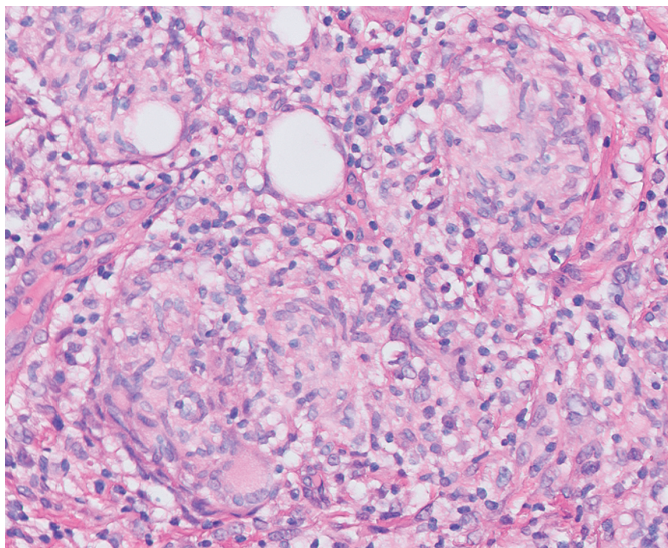


FIGURE 1. Biopsy of cheilous ulcer showing nonspecific active and chronic inflammation with granuloma formation

on a cheilous ulcer to investigate the association with CD. Histology showed active and chronic inflammation and granuloma formation compatible with an oral manifestation of CD (Fig. 1). Finally, therapy was switched to ustekinumab, according to the licensed dose for CD. Thereafter, her symptoms and inflammatory parameters gradually improved up to complete remission of both oral and intestinal CD allowing removal of the PEG tube. She is in sustained remission up to the writing of this article (follow-up 15 months).

Oral CD remains a clinical challenge with the lack of controlled clinical studies. It has been hypothesized that oral CD may represent a distinct phenotype⁴ and genotype.⁵ This may support the role of biological therapies targeting other immunological cascades than the conventional drugs that are used for intestinal CD. In this case, we report a beneficial effect of targeting the IL-12/23 pathway with ustekinumab for the treatment of cheilitis and tonsillitis as oral manifestations of CD. Currently several drugs selectively targeting a part of the same immunological pathway, such as anti-IL-12/23p40 (briakinumab) and anti-IL-23p19 (risankizumab, brazikumab) antibodies, are studied for CD. Future studies may also investigate the therapeutic potential of these drugs for oral manifestations of CD.

Jelmer B. Jukema, MD^{id},
Johannan F. Brandse, MD, PhD,
and Nanne K.H. de Boer,
MD, PhD

From the Department of Gastroenterology and Hepatology, Amsterdam UMC, VU University Medical Center, Amsterdam, the Netherlands

Conflicts of Interest: NKHDB has served as a speaker for AbbVie and MSD and as a consultant and principal investigator for TEVA Pharma BV and Takeda. He has received unrestricted research grants from Dr. Falk, TEVA Pharma BV, and Takeda.

Address correspondence to: Nanne K. H. de Boer, MD, PhD, Department of Gastroenterology and Hepatology, Amsterdam University Medical centers, Vrije Universiteit Amsterdam De Boelelaan 1118, Amsterdam, the Netherlands. E-mail: khn.deboer@amsterdamumc.nl.

REFERENCES

1. Tan CX, Brand HS, de Boer NK, et al. Gastrointestinal diseases and their oro-dental manifestations: part 1: Crohn's disease. *Br Dent J*. 2016;221:794-799.
2. Bokemeyer A, Tentrop N, Barth PJ, et al. Successful treatment of oral Crohn's disease by anti-TNF-alpha dose escalation - a case report. *BMC Gastroenterol*. 2018;18:88.
3. Feagan BG, Sandborn WJ, Gasink C, et al.; UNITI-IM-UNITI Study Group. Ustekinumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2016;375:1946-1960.
4. Gale G, Sigurdsson GV, Östman S, et al. Does Crohn's disease with concomitant orofacial granulomatosis represent a distinctive disease subtype? *Inflamm Bowel Dis*. 2016;22:1071-1077.
5. Turkcapar N, Toruner M, Soykan I, et al. The prevalence of extraintestinal manifestations and HLA association in patients with inflammatory bowel disease. *Rheumatol Int*. 2006;26:663-668.

© 2020 Crohn's & Colitis Foundation. Published by Oxford University Press on behalf of Crohn's & Colitis Foundation. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com.

doi: 10.1093/ibd/izz321
 Published online 7 January 2020