A Case Where Administration of Ustekinumab Maintained the Intestinal Patency After Balloon Dilation for Small Intestinal Stenosis Caused by Crohn's Disease

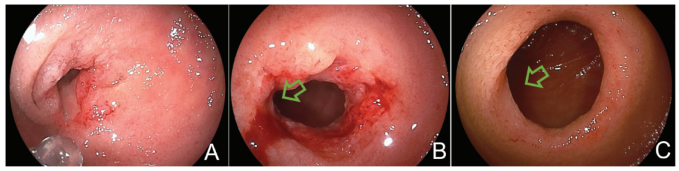

FIGURE 1. Circumferential and severe stenosis, through which the endoscope could not pass (A). Immediately after balloon dilation, a split ulcer with bleeding was observed at the arrow (B). Six months after balloon dilation, a split ulcer had changed the flat area with a whitish surface, and the lumen was larger than just after EBD (C).

To the Editors:

Ustekinumab (UST) has been reported to exhibit some therapeutic effects clinically as an anti-inflammatory agent for Crohn's disease (CD). Ustekinumab may also have antifibrotic effects on stenotic lesions; however, it remains at the animal experimental stage.[1] Stenosis is a serious complication of CD that often leads to subjective symptoms such as abdominal pain and may need further interventions including surgery. We experienced the CD patient with UST induction after endoscopic balloon dilation (EBD) for stenosis, which resulted in long-standing intestinal patency.

A 20-year-old female with ileocolonic-type CD developed severe abdominal pain and underwent computed tomography scan, which showed wall thickness and partial dilatation of the pelvic ileum, about 30 cm in length. Subsequent double-balloon endoscopy (DBE) with a retrograde route revealed several ulcerative lesions with edema and 4 stenotic sites in the middle to lower ileum (Fig. 1A). Two stenoses, which were not passable by endoscope, were dilated by balloon up to 10–11 mm (Fig. 1B), and DBE was finally able to pass through all 4 stenotic sites. Because DBE revealed not only the stenotic sites but multiple inflammatory sites, UST was administered as a remission induction therapy. After 24 weeks, retrograde DBE was performed to evaluate the therapeutic effects. The endoscope easily passed through all stenotic sites, including the 2 sites with previous EBD (Fig. 1C). The lumen at those 2 sites further dilated beyond what had been observed immediately after EBD.

This report describes a patient who was able to maintain intestinal patency and increased lumen width after treatment with UST after EBD. We considered that an anti–tumor necrosis factor–alpha (anti-TNF-α) agent and UST may have different effects on the healing of a split-ulcer post-EBD. Infliximab and adalimumab, commonly used anti-TNF-α agents, have been reported to improve the prognosis of patients after EBD, although such treatments sometime cause an acute small bowel obstruction owing to rapid healing of the split-ulcer. Ustekinumab downregulates TNF-α expression indirectly, which slows the healing of ulcerations as compared with anti-TNF-α agents.[2] Ustekinumab also blocks interleukin (IL)-23 and decreases the expression of IL-17A downstream, which may lead to suppression of fibrogenesis and stenotic formation.[3] Therefore, we hypothesized that UST could heal a split ulcer without re-stenosis and further expand the lumen after EBD (Fig. 1B, C). If this hypothesis is accurate, UST could be an effective treatment for preventing re-stenosis of the small bowel after EBD in CD patients.

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REFERENCES

1. Guan Q, Ma Y, Hillman CL, et al. Targeting IL-12/IL-23 by employing a p40 peptide-based vaccine ameliorates TNBS-induced acute and chronic murine colitis. *Mol Med.* 2011;17:646–656.
2. Verstockt B, Dreesen E, Noman M, et al. Ustekinumab exposure-outcome analysis in Crohn's disease only in part explains limited endoscopic remission rates. *J Crohns Colitis.* doi: 10.1093/ecco-jcc/jjz008.
3. Ogino T, Nishimura J, Barman S, et al. Increased th17-inducing activity of CD14+ CD163 low myeloid cells in intestinal lamina propria of patients with Crohn's disease. *Gastroenterology.* 2013;145:1380–1391.e1.

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