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Upadacitinib in refractory ulcerative colitis

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Dear Editor,

We report the first clinical-practice case to date of treatment with upadacitinib for ulcerative colitis.

A 28-year-old woman presented in 2019 with ulcerative proctosigmoiditis and an endoscopic Mayo score of 2; she received oral and topical mesalazine as well as oral

corticosteroids in order to achieve clinical remission.

Because of dependence on corticosteroids azathioprine was initiated, which resulted in digestive intolerance with no improvement after dose splitting and changing to mercaptopurine, which was then discontinued.

Following a partial response to leukocyte apheresis anti-TNF biologic (infliximab) therapy was initiated, with primary failure to obtain a pharmacodynamic response (normal levels with no antibodies).

Given the urgency, therapy is changed to tofacitinib (a JAK kinase inhibitor), which resulted in clinical remission at 24-48 hours, for 2 months. Then the patient presented with rectal syndrome, and topical steroids and tacrolimus suppositories were administered, which led to partial improvement followed by relapsing disease (6-8 bloody stools a day), which required oral corticosteroids (prednisone).

She then met the criteria for steroid resistance and was admitted to receive i.v. corticosteroids, which provided clinical resolution. Rectoscopy resulted in findings similar to those of previous colonoscopies (Mayo score of 2), overinfection with cytomegalovirus was ruled out by rectal biopsy, and an infectious etiology was excluded by stool culture as well as parasite and *Clostridium difficile* fecal testing.

Treatment was then initiated with an anti-IL12-23 agent (ustekinumab) with neither clinical response nor improvement in calprotectin levels despite intensification; later the patient also failed to respond to vedolizumab (anti-integrin α4β7).

In view of the initial response to tofacitinib, upadacitinib (JAK kinase inhibitor) a 45mg/día was started for compassionate use at 45 mg/day in September 2021, with clinical remission being achieved after 4-5 days. Following induction for 8 weeks, the dose was lowered to 30 mg/day for maintenance, and both endoscopic and histological remissions were ascertained by colonoscopy (endoscopic Mayo score: 0;

rectal, sigmoidal, transverse colonic biopsy samples: no inflammatory activity. Calprotectin values remained normal and the patient remains asymptomatic and steroid-free.

She had an ocular herpes simplex virus on tofacinib that relapsed on upadacitinib, and is now being managed at the ophthalmology department.

Discussion

Upadacitinib led to meet all criteria for clinical, endoscopic, and histological remission (primary and secondary objectives) for ulcerative colitis in currently reported phase-III studies (1), not being approved for such indication yet (2). The safety profile was consistent with prior studies in other indications (3,4).

In our patient, upadacitinib achieved those objectives in real-life clinical practice, following prior refractoriness to all therapeutic options, and preventing proctocolectomy as of today after treatment for 7 months.

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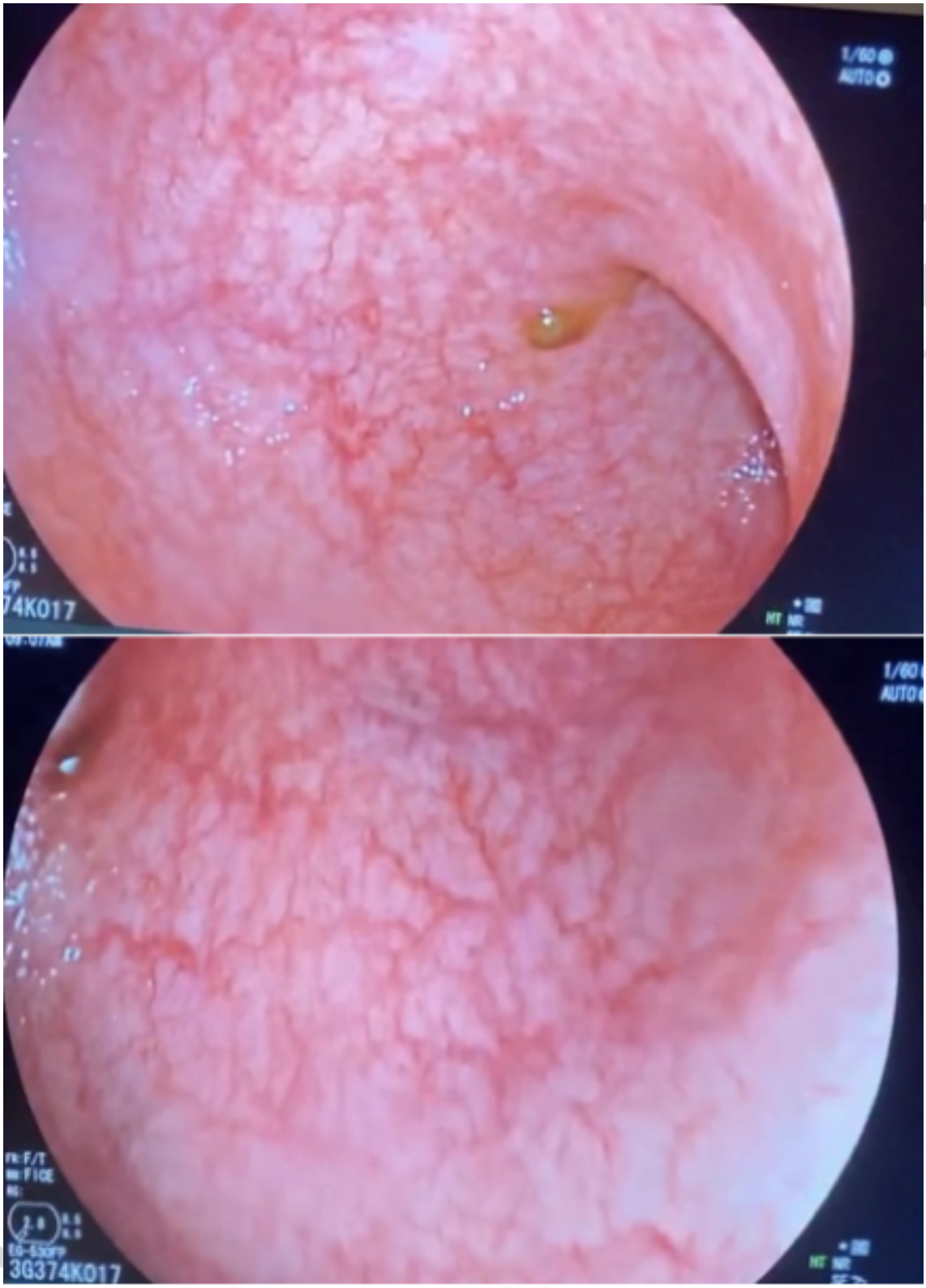

Figure 1, Mucosal healing. A. Rectum. B. Sigmoid colon. Endoscopic Mayo score of 0.