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Vedolizumab in Patients with Common Variable Immune Deficiency (CVID) and Gut Inflammation

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We present three patients with common variable immune deficiency (CVID) and gut inflammation treated with vedolizumab (IgG1 monoclonal antibody to $\alpha 4\beta 7$ integrin).

Patient 1: a 24-year-old male with CVID receiving intravenous immunoglobulin (IVIG) with abdominal pain and diarrhea. Infectious work-up was negative. Push enteroscopy showed extensive jejunal ulceration consistent with Crohn's disease. He was treated with budesonide and vedolizumab 300 mg at 0, 2, and 6 weeks and then every 8 weeks, with symptomatic remission, discontinuation of steroids, and endoscopic healing on push enteroscopy 5 months after starting vedolizumab. There were no infectious adverse events.

Patient 2: a 40-year-old female with CVID receiving IVIG with progressive diarrhea and weight loss. Infectious work-up was negative. Push enteroscopy showed villous atrophy and scalloping in the duodenum and jejunum without ulcers, and biopsies showed increased intraepithelial lymphocytes and villous blunting (lymphoproliferative disorder excluded by flow cytometry). Serology and genetic testing not consistent with celiac disease. She was treated with vedolizumab induction and maintenance, with symptomatic remission, and endoscopic and histologic healing on push enteroscopy repeated 4 months after starting vedolizumab. There were no infectious complications.

Patient 3: a 67-year-old female with CVID and pancytopenia receiving IVIG and filgastrim, with profuse diarrhea. Serologic and genetic testing was negative for celiac disease, autoimmune enteropathy, and infection. Push enteroscopy showed scalloping in the duodenum and jejunum without ulcers, and biopsies showed increased intraepithelial lymphocytes and villous atrophy. Colonoscopy showed patchy villous atrophy in the terminal ileum and loss of vascular pattern in the colon, and biopsies showed mild active

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chronic inflammation in the ileum and right colon. She was treated with budesonide and vedolizumab induction and maintenance without symptomatic improvement over 52 weeks of therapy. There were no infectious complications.

CVID, an immune deficiency disorder, is frequently associated with paradoxical autoimmune manifestations, including persistent diarrhea with gut inflammation in up to 60% of patients. The associated gut histopathologic findings are diverse and may include intra-epithelial lymphocyte infiltrate, lymphoid aggregates, and crypt distortion[1, 2]. The infectious risks associated with conventional medical therapies for inflammatory bowel disease (IBD) are of significant concern in the context of patients with CVID. While the topical steroid enteric-coated budesonide can be used, toxicity limits use of conventional steroids. Treatment with tumor necrosis factor (TNF) inhibitors has been described and has been clinically effective; but may significantly increase the risk of opportunistic infections and therefore was not used [3].

Vedolizumab selectively blocks leukocyte trafficking to the gut, and is approved for treatment of ulcerative colitis and Crohn's disease[4]. The gut selective mechanism of action has not been associated with an increased risk of opportunistic infections, making this a potentially appealing medication to use in the setting of CVID; however, the safety and efficacy in vedolizumab in this patient population has not been described. We report the use of vedolizumab in anti-TNF naive patients with CVID and gut inflammation without infectious complications during therapy. Furthermore, vedolizumab was effective, leading to clinical and endoscopic remission in 2 of 3 patients.

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