

## Onset of Inflammatory Bowel Disease Following Interleukin-17A Inhibitor Treatment

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Secukinumab, anti-interleukin (IL)-17A, is a new agent for treating spondyloarthritis. Some cases of new-onset or flare of inflammatory bowel disease (IBD) during secukinumab treatment have been reported.<sup>1-6</sup> In this article, we present a case of new-onset IBD following secukinumab treatment.

A 45-year-old female patient was diagnosed with ankylosing spondylitis (AS) eight years before. She had symptoms and complaints related to the AS although she had taken non-steroidal anti-inflammatory drugs and certolizumab pegol at therapeutic dosages for long-term. Certolizumab pegol was switched to secukinumab (150 mg/week for four weeks, followed by 150 mg/four weeks). At the sixth week of secukinumab treatment, the patient returned to the hospital and was admitted according to symptoms of abdominal pain, diarrhea, tenesmus, increased bowel movements, and a 3 kg weight loss in the last 20 days. Abdominal examination showed widespread tenderness in the abdomen and increased bowel sounds. Laboratory test results were presented in Table 1.

Flexible colonoscopy showed aphthous ulcers and erosions in the distal 3 cm segment of the terminal ileum and deep ulcers in the colon wall and mucosa for each segment, accompanied by

normal looking protected areas. After biopsy, findings from the histologic evaluation were consistent with chronic active ileitis and focal active colitis.

New-onset IBD related to secukinumab was diagnosed. The secukinumab treatment was stopped and replaced with methylprednisolone (24 mg/day). Five days after receiving methylprednisolone treatment, her symptoms decreased, and all abnormal clinical findings resolved within three weeks.

Secukinumab failed to reduce disease activity in Crohn's disease (CD) and phase IIa study was terminated prematurely due to higher rates of adverse events compared with placebo.<sup>7</sup> New-onset or activated IBD cases have also been observed in clinical trials evaluating the efficacy of secukinumab in patients with AS and psoriatic arthritis. A pooled safety analysis showed that events of IBD were uncommon with secukinumab treatment.<sup>8</sup> Post-marketing registries have found 18 new-onset IBD patients among 1,721 patients using secukinumab.<sup>9</sup> Also, the incidence of new-onset IBD in biologic databases was higher in patients treated with ixekizumab, another IL-17A inhibitor.<sup>9</sup>

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**Table 1.** Laboratory test results

	Patient's sample	Normal
Hemoglobin	8.6 g/dL	12-16 g/dL
White blood cell	16.710 mm <sup>3</sup>	4,500-8,500 mm <sup>3</sup>
Platelet	434,000 mm <sup>3</sup>	150,000-450,000 mm <sup>3</sup>
Erythrocyte sedimentation rate	47 mm/hr	0-20 mm/hr
C-reactive protein	14.8 mg/dL	0-0.5 mg/dL
Albumin	4 g/dL	3.5-5.4 g/dL
Stool (microbiological examination)	Enrichment of erythrocytes and leukocytes. No parasites	No erythrocytes leukocytes and parasites.
Stool culture	Normal colonic bacterial flora	Normal colonic bacterial flora
<i>Entamoeba histolytica</i> antigen	Negative	Negative
<i>Clostridium difficile</i> toxins	Negative	Negative

Interleukin-21 and IL-22 produced by T-helper 17 (Th17) cells have protective and regenerative effects on epithelial cells.<sup>10</sup> Th17 cells can contribute to CD progression by dysregulating mucosal immunological response.<sup>11</sup> While Th17 cells have been shown to contribute to the progression of CD, it is interesting that IL-17 blockade drugs have been ineffective in the treatment of that disease.

The therapeutic use of biological agents produces some adverse, undesirable and paradoxical effects. The new onset of IBD in patients taking IL-17A antagonists may similarly result from imbalance in cytokine levels in the bowel. An increasing number of case reports and studies show that IL-17 blockade may have no place in the treatment of IBD.

In conclusion, it should be kept in mind that before starting an IL-17 antagonist on a patient with spondyloarthritis, signs of subclinical bowel disease should be carefully investigated. Additionally, new-onset IBD may develop in patients using IL-17 blocking drugs for the treatment of other inflammatory diseases.

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