Journal of Enterocolitis

Case Report

Development of Crohn's Disease in a Patient with Ankylosing Spondylitis Receiving Etanercept

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Cite this article as: Bodakçı E, Karakaya MF, Er RE, Güvenir ST, Yılmaz V, Soykan Aİ. Development of Crohn's disease in a patient with ankylosing spondylitis receiving etanercept. *J Enterocolitis.* 2023;2(2):34-35.

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Received: June 12, 2023 **Accepted:** August 9, 2023

DOI:1014744/Jenterocolitis.2023.23050

ABSTRACT

Tumor necrosis factor -alpha is an important cytokine that plays a role in inflammation and immune reactions. Tumor necrosis factor-alpha and its receptors are known to play a role in the pathogenesis of numerous immune-mediated diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and inflammatory bowel disease. It is known that anti-tumor necrosis factor agents used in inflammation suppression and remission could lead to a series of paradoxical side effects. In this paper, we presented a case with ankylosing spondylitis in whom Crohn's disease developed during etanercept treatment. A significant improvement was achieved in the symptoms and laboratory values by stopping etanercept treatment and switching to adalimumab.

Keywords: Ankylosing spondylitis, Crohn's disease, etanercept

INTRODUCTION

Anti-tumor necrosis factor (TNF) agents are groundbreaking drugs in the treatment of auto-inflammatory diseases. They bond with TNF cytokine, which is one of the mediators playing a key role in the pathogenesis of the disease, and provide suppression of the proinflammatory pathway. While creating this effect, they may lead to certain paradoxical side effects. Frequently observed side effects are alopecia areata, drug-induced lupus erythematosus,[1] and psoriasis.[2] A less known yet severe side effect is de novo inflammatory bowel disease (IBD).[3] In contrast to other anti-TNF molecules, etanercept is not an effective agent in the treatment of IBD.[4] In addition to being effective in the treatment of Crohn's disease (CD), etanercept has been found to be associated with de novo CD and ulcerative colitis development.[5] In this paper, we present a CD case which developed 13 years after etanercept treatment in a patient followed up with ankylosing spondylitis (AS).

CASE

Our case involves a 57-year-old patient who was diagnosed with AS 13 years ago. As the patient had not responded to conventional therapies, etanercept treatment—25 mg/week—had been started. While in remission for AS, the patient, who had been using etanercept for 13 years, presented with pain in the right lower quadrant of the abdomen and intermittent diarrhea for the last 3 months. In the routine examination of the patient, C-reactive protein (CRP) was 24 mg/L (0-5), hemoglobin was 13.4 g/dL, and sedimentation was 24 mm/h (0-20). A colonoscopy was performed in order to investigate the etiology of the abdominal pain. The colon mucosa evaluated appeared normal, and the 25 cm ileum mucosa starting from the ileocecal valve when evaluated was observed to be diffusely ulcerated and erythematous (Figure 1). Biopsy samples were taken with a pre-diagnosis of CD. In terms of potential proximal intestinal involvement and complications, MR enterography was performed (Figure 2). The patient was not using non-steroid anti-inflammatory drugs. As a result of pathology results and MR enterography results consistent with CD, it was thought that the patient might have paradoxical CD related with etanercept treatment. The patient's fecal calprotectin level was found to be 645 ug/g (0-80 ug/g). Etanercept treatment was terminated, and adalimumab 40 mg/week was started. The patient's fecal calprotectin level examined in the third month of the treatment was 68 ug/g, CRP was 2 mg/L, and sedimentation was 11 mm/h. It was observed that abdominal pain and diarrhea attacks were alleviated in the patient. The patient is biochemically and clinically followed up in remission.

DISCUSSION

Etanercept is an effective anti-TNF molecule in the treatment of spondyloarthropathies and rheumatoid arthritis.[6] Etanercept is not effective in the treatment of CD.[4-6] Etanercept is the anti-TNF molecule that most frequently leads to paradoxical IBD development.[7,8] Paradoxical IBD development following anti-TNF use in AS patients is around 0.15%, and this ratio is 2.2/100 patient years for etanercept and 0.2/100 patient years for infliximab.[5] Paradoxical CD developing under anti-TNF treatment is accepted as an immune-mediated disease.[7]

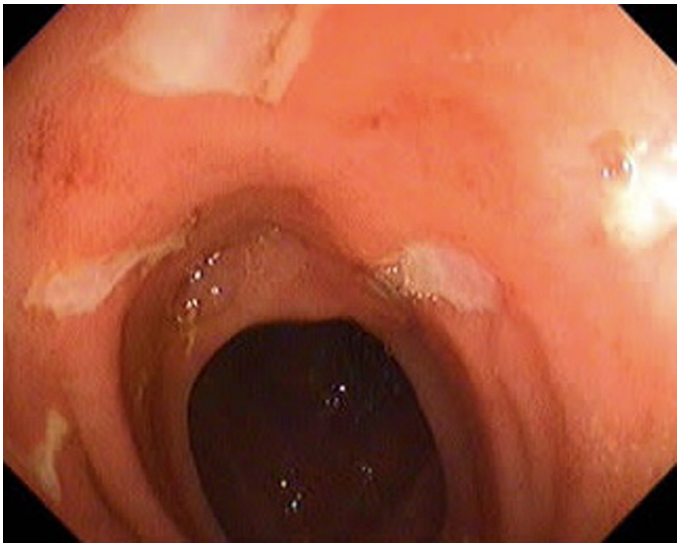

Figure 1. Ulcers in the ileum.

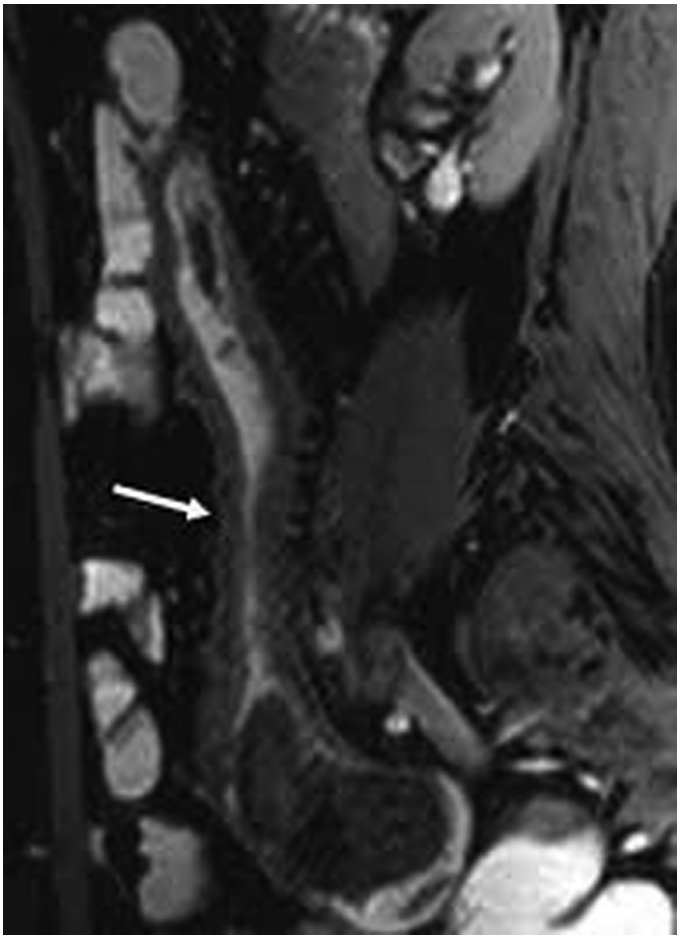

Figure 2. Wall thickening in the ileum.

In a series performed in France, the mean duration between anti-TNF starting time and IBD development was found to be 27 months.[5] In previous studies, it was demonstrated that interferon gamma (IFN-γ) and TNF-α levels increased in AS patients treated with etanercept.[9] It has been stated that increased IFN-γ and TNF-α levels in individuals with genetic tendencies could trigger IBD development.[10]

Patients treated with anti-TNF agents, especially with etanercept, who have bowel symptoms (abdominal pain, diarrhea, and weight loss) should be closely followed up in terms of de novo CD. In patients in whom de novo CD developed, it is recommended to stop etanercept treatment and switch to infliximab and adalimumab.[11] In this paper, a case with de novo CD which developed as a result of etanercept treatment and who went into remission when switched to adalimumab was presented.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.B.; Design – M.F.K.; Supervision – R.E.E.; Funding – S.T.G.; Materials – V.Y.; Data Collection and/or Processing – A.F.S.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: The authors declare that this study has received no financial support.

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