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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Use of Tofacitinib for the Treatment of Arthritis Associated With Ulcerative Colitis

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ABSTRACT

Tofacitinib is a Janus kinase 1–3 inhibitor initially approved for the treatment of rheumatoid arthritis and now approved for the treatment of moderately to severely active ulcerative colitis (UC). We present the case of a patient with UC and seronegative inflammatory arthritis in whom arthritis progressed while on vedolizumab and was successfully treated with tofacitinib. This case provides insight into the use of tofacitinib for the treatment of UC and a concomitant extraintestinal manifestation of joint involvement.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that is confined to the colon and rectum but frequently has concomitant extraintestinal manifestations (EIMs), the most common of which is joint pain.[1] Involvement of the joint in UC is most often characterized by arthralgias without inflammation, but inflammatory arthritis does occur and is characterized by swelling of the joints or synovial tissues.[2] Prior therapeutic options for patients with concomitant UC and joint involvement included aminosalicylates (especially sulfasalazine), concomitant methotrexate, and anti-tumor necrosis factor (TNF) biological therapies.[3] The recent approval of tofacitinib for the treatment of moderately to severely active UC is of great interest as a possible novel treatment in such cases. Tofacitinib is an oral, small-molecule Janus kinase (JAK) inhibitor previously approved for the treatment of rheumatoid arthritis and psoriatic arthritis, and recently demonstrated efficacy in the treatment of moderately to severely active UC.[4–8] There are limited data regarding the efficacy of tofacitinib for the treatment of EIMs in UC. We present the case of a patient with moderate UC and seronegative inflammatory arthritis successfully treated with tofacitinib.

CASE REPORT

A 40-year-old nonsmoking woman presented with a history of UC that was diagnosed with proctitis at age 32 while pregnant. At that time, she was treated with oral and topical 5-aminosalicylic acid with symptomatic improvement. However, during her second pregnancy, her colitis relapsed, and she was found to have an extension of her disease to the left colon. She was subsequently treated with steroids, 6-mercaptopurine, and infliximab with some improvement in her symptoms but was not in stable remission. She then developed intermittent hand and ankle joint pain with joint swelling when her colitis was active, which was treated with intermittent doses of steroids and later with an increased dose of infliximab. Eighteen months later, she failed to respond to infliximab and was found to have developed antidrug antibodies. She was cycled to certolizumab pegol without response. Vedolizumab was initiated at the usual loading and a maintenance dose of 300 mg intravenous infusion every 8 weeks and achieved clinical remission. However, her prior joint pains re-presented with synovitis of her right index finger and right fifth digit distal interphalangeal and proximal interphalangeal joints (Figure 1). Methotrexate was initiated, first at doses of 10 mg oral weekly, and then increased to doses of 20 mg subcutaneous injection weekly. There was some improvement in her arthritis, but not complete resolution, with ongoing exacerbations during menses. Rheumatologic evaluation for rheumatoid arthritis or other seropositive arthropathies only identified an antinuclear antibody >1:1,280. Due to her persistent joint inflammation resistant to methotrexate treatment, methotrexate was discontinued and tofacitinib 5 mg orally twice daily was initiated, followed by an extended-release formulation of 11 mg orally once daily. Vedolizumab was continued with

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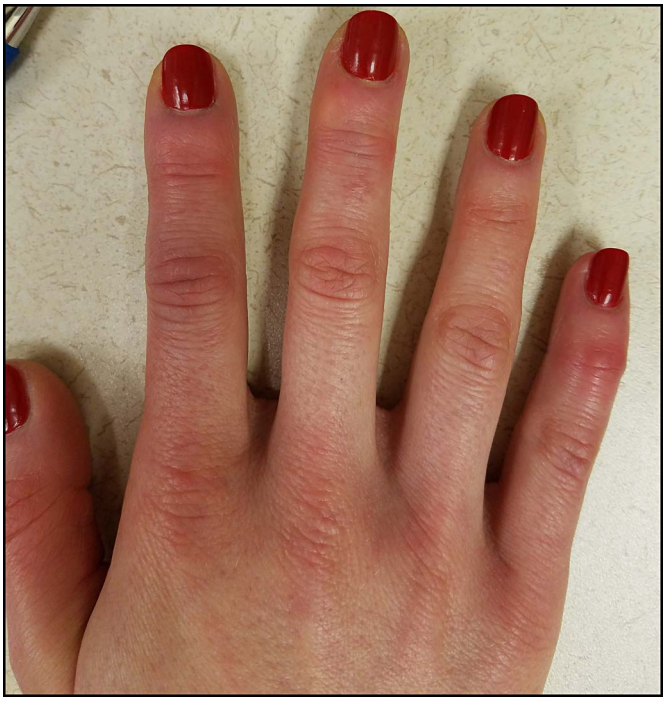

Figure 1. Right index finger and fifth digit synovitis while on vedolizumab and before tofacitinib treatment.

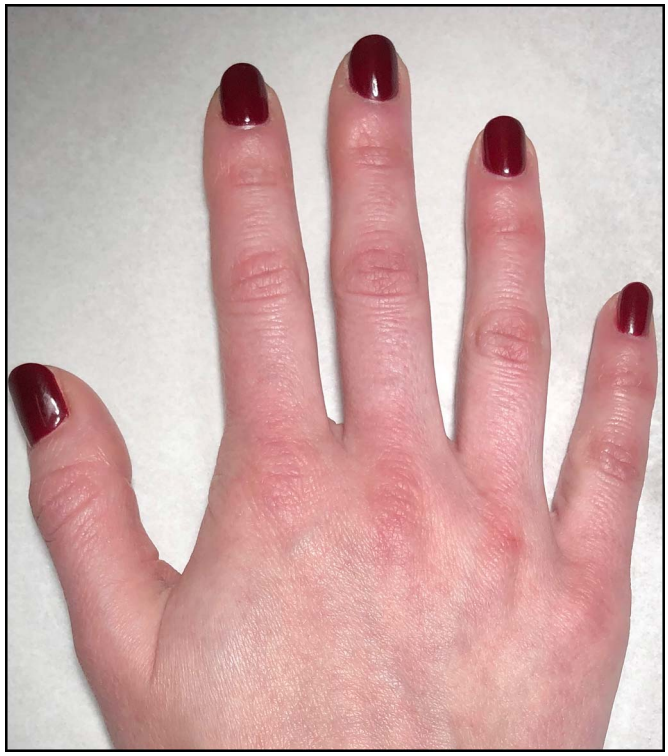

Figure 2. Resolution of joint swelling 8 weeks after tofacitinib treatment.

concomitant tofacitinib treatment for approximately 3 months and then discontinued. During her 3-, 12- and 18-month follow-up, the patient remained in deep remission from her colitis and without any joint symptoms (Figure 2).

DISCUSSION

Joint pain is the most frequent EIM experienced by IBD patients.[2] However, management of this problem remains enigmatic and continues to represent a difficult challenge in clinical practice. In this case, our patient had a history of UC and a predominant EIM of arthritis. Despite the patient's colitis being in remission while receiving vedolizumab, she developed frank asymmetric synovitis. Although her arthritis may have represented an independent process, it is also possible that the gut selectivity of vedolizumab may have further "uncovered" and exacerbated an underlying seronegative arthritis. There have been previous case reports of new onset or exacerbation of arthritis/sacroiliitis in vedolizumab-treated patients, and this phenomenon was also described in a large cohort study that demonstrated a 13.9% incidence of inflammatory arthralgia/arthritis in patients receiving vedolizumab therapy.[9,10] It is of interest, however, that the study did find some efficacy of vedolizumab in managing EIMs, as close to half of the 47 patients with inflammatory arthralgia/arthritis achieved complete remission of their rheumatologic symptoms. Despite these reports and observations, the post-hoc analysis of the pivotal trials of vedolizumab in both Crohn's disease and UC did not demonstrate an increased risk of arthralgias or arthritis.[11]

Tofacitinib acts by preferentially inhibiting JAK1 and JAK3, with reduced inhibition for JAK2 and tyrosine kinase 2. This, in turn, inhibits the signal transduction activity by the surface receptors for multiple cytokines including an important subset of pro-inflammatory cytokines such as interleukin (IL)-2, -4, -7, -9, -15, and -21 and interferon gamma (IFN-y) cytokines, which are integral to lymphocyte activation, proliferation, and function.[12,13] Tofacitinib offers a nonselective anti-inflammatory treatment that, in this case, successfully maintained the patient's colitis while also controlling her arthritis. Tofacitinib is orally taken, has a short pharmacokinetic half-life of 3.2 hours, and is rapidly absorbed and eliminated, with reversibility of pharmacodynamic effects within 14 days of discontinuation.[14,15] Tofacitinib is now recommended as an option for first-line therapy in patients suffering from moderately to severely active UC and would be an appropriate first-line option in similar cases.[16] We believe that this is the first reported case of a patient treated with concomitant use of tofacitinib and vedolizumab and the first patient with UC to receive the extended-release formulation of tofacitinib in the maintenance phase. This case provides insight into the future management options in UC and such EIMs.

DISCLOSURES

Author contributions: W. Wang, NK Clevland, and J. Ollech wrote the manuscript. DT Rubin reviewed and approved the final version of the manuscript and is the article guarantor.

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