Peripheral Neuropathy with Infliximab Therapy in Inflammatory Bowel Disease

To the Editor:
Antitumor necrosis factor alpha (anti-TNFα) agents have provided an important breakthrough in the management of patients with inflammatory bowel disease (IBD), leading to high remission rates, fistula closure, and improved quality of life. However, they are not without serious adverse effects, including lymphoma, infection, bowel obstruction, and neuropathy.¹ This case report illustrates a rare and clinically significant side effect of peripheral neuropathy occurring with anti-TNFα therapy for Crohn’s disease (CD).

A 57-year-old woman with longstanding ileocolonic CD presented with a flare characterized by frequent (up to 10 times per day), loose stool, with nocturnal diarrhea and crampy abdominal pain. Investigations revealed a culture-negative stool with erythrocytes and white blood cells, raised inflammatory markers (C-reactive protein [CRP] 113, platelets 550) and evidence of active ileocolonic inflammation on endoscopic and histological inspection. The patient’s medical management had previously been limited because of adverse reactions to thiopurines (pancreatitis with merthotrexate, nausea, vomiting, and headaches). Oral steroid therapy failed to control this flare and the patient was hospitalized for ongoing symptoms.

Subsequently, the patient was started on anti-TNFα therapy (infliximab 5 mg/kg) and after 2 doses the patient had significant clinical improvement. Her bowel symptoms resolved, inflammatory markers normalized (CRP 3.6, platelets 372), with endoscopic evidence of healing and reduced histological activity.

On day 3 after the initial infusion she suffered from flu-like symptoms and developed a dry, pruritic rash on her upper limbs which resolved over a week. Day 6 after the second infusion the patient reported aching of the low back and lower limbs, with numbness and paresthesia of the toes, and burning of the feet. Examination revealed a tandem gait ataxia, reduced power, and loss of light touch with diminished pain, proprioception, and vibration sense to the level of the ankles. Her lower limbs were areflexic, with nonresponsive plantars and a positive Romberg sign. Nerve conduction studies revealed a severe sensory motor neuropathy. Investigations including antinuclear antibodies (ANA), extractable nucleic acid (ENA), erythrocyte sedimentary rate (ESR), anti neutrophil cytoplasmic antibody (ANCA), double stranded DNA (dsDNA), anti-neuronal nuclear 1 (anti-Hu), anti-neuronal nucleus 2 (anti-Ri), purkinje cell antibody (anti- Yo), purkinje cell antibody (anti-PCA-2), thyroid stimulating hormone (TSH), glucose, vitamin B₁₂, folate, anti tissue transglutaminase (anti-TTG), and chest computed tomography (CT) were within normal limits. Serum protein electrophoresis on several occasions over 6 months demonstrated an IgG kappa monoclonal band of <2.0 g/L. The patient’s clinical presentation was consistent with a generalized axonal neuropathy, and following withdrawal of the anti-TNFα agent her neurological symptoms and signs resolved over a period of 4 months.

The time course of this adverse event makes it very likely that it was due to the infliximab therapy. Axonal polyneuropathy has been reported with TNFα antibody treatment of rheumatoid arthritis but as far as we are aware it has not been reported with treatment of CD or ulcerative colitis.²

Despite the high levels of TNFα found in the cerebral spinal fluid and brain plaques of multiple sclerosis patients, anti-TNFα therapy is not effective in this condition. In a randomized, placebo-controlled trial involving 168 multiple sclerosis patients, Lenerecept, a p55 TNF receptor fusion protein, resulted in increased disease activity with higher relapse rates.³ Moreover, infliximab therapy is associated with an increased number of new gadolinium-enhancing lesions on magnetic resonance imaging (MRI) in multiple sclerosis patients.⁴ Case reports of peripheral neurological complications arising in patients with rheumatoid arthritis include Guillain–Barre syndrome, chronic demyelinating polyradiculoneuropathy, multifocal motor neuropathy with conduction block, and mononeuritis simplex/multiplex.⁵⁻⁷

In summary, central and peripheral neuropathies are rare but recognized side effects of TNFα monoclonal antibody therapy. However, neuropathies are not commonly mentioned with regard to complications of TNFα monoclonal antibody treatment in the IBD literature. Axonal neuropathy in particular has not been reported with TNFα monoclonal antibody treatment of IBD, and we draw this to the attention of our gastroenterology colleagues.

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REFERENCES