

## Long-Term Follow-Up of an HIV-Infected Patient With Reactive Arthritis Treated With Infliximab

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Tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), implicated in the pathophysiology of a variety of rheumatic diseases,<sup>1-3</sup> may also contribute to HIV propagation, and there are data suggesting clinical benefit from anti-TNF- $\alpha$  approaches for treating HIV-associated symptoms in infected patients.<sup>3</sup> Still, TNF- $\alpha$  is an important component of immune responses, and TNF- $\alpha$  suppression is associated with an increased risk of opportunistic infections among patients undergoing treatment for rheumatic or other inflammatory disorders.<sup>4,5</sup> Thus, concern exists about using anti-TNF- $\alpha$  treatments in HIV-infected patients who may have compromised immune function.

We published one of the first investigations into the use of anti-TNF- $\alpha$  therapy for rheumatic disease in an HIV-infected male patient during 18 months of treatment.<sup>6</sup> We present the 10-year follow-up of this same patient who has continued infliximab therapy.

The patient first presented in April 2000 at the age of 41 years, weighing 72.57 kg with a 6-year history of HIV infection. His antiretroviral regimen (initiated in January 2000) comprised zidovudine 400 mg twice daily, lamivudine/zidovudine 150 mg/300 mg twice daily, and saquinavir 400 mg twice daily (switched in June 2007 to a once-daily dose of efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg in a fixed-dose combination). A diagnosis of HIV-associated reactive arthritis was made based on the clinical presentation and medical history, and he was started on a combination of intravenously administered (IV) methotrexate (MTX) 20 mg/wk, oral prednisone 20 mg/d, and a pulse treatment of IV methylprednisolone 1 g.

Approximately 4 months later, infliximab was added to his treatment regimen to address symptom recurrence. The initial dose of IV infliximab was 300 mg (~3 mg/kg body weight). He was then given 2 additional 300-mg doses of IV infliximab at weeks 2 and 6, after which he began receiving single 300 mg IV infliximab every 6 to 7 weeks. He experienced a complete resolution of symptoms, with the rash and swelling resolved, the nails regrowing, no pain, and full range of motion.

By June 2001, corticosteroid use was discontinued, viral titer was less than 400 Qn:US copies/mL, and CD4<sup>+</sup> count was within reference range. He continued MTX 15 mg/wk and IV infliximab 300 mg approximately every 8 weeks and was evaluated monthly. In March 2002, he experienced increased onycholysis of the big toe and inflammation in a fingernail. An

increase in the infliximab to 4 mg/kg resolved the symptoms. He then discontinued MTX and infliximab while traveling for 3 months.

In October 2002, he had a recurrence of necrotic nail changes and synovitis of distal interphalangeal joints and small joints of the hands, along with flare-ups on the back, neck, and ankles. Based on transient severe transaminase elevation (which was attributed to alcohol consumption), we could not restart MTX but were able to start infliximab 4 mg/kg and prednisone 10 mg/d. We administered an additional dose of infliximab 4 weeks later. He returned to an every-8-week schedule and continued daily prednisone, but MTX was not restarted because of liver problems.

In June 2003, his liver enzymes had returned to normal, but he reported arthritis symptoms. Methotrexate 15 mg/wk was added to his regimen, and prednisone was discontinued. In April 2005, after being off the arthritis regimen for approximately 15 months, he had symptoms. He was started on MTX 15 mg intramuscular every week and infliximab 3 mg/kg every 4 weeks. After 1 month, symptoms had improved significantly. In May 2005, infliximab dosage was changed to 3 mg/kg every 8 weeks. Methotrexate was adjusted to oral dosing 2.5 mg every 12 hours for 3 doses each week. As mentioned, in June 2007, his HIV regimen was switched to a once-daily dose of efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg in a fixed-dose combination.

The patient did well until February 2010. After a 5-month lapse in infliximab therapy, he experienced joint discomfort, and his nails were breaking up. After restarting infliximab, his symptoms resolved. The patient's viral load remained low while he was on antiretroviral medication. As of December 2010, the patient was free of symptoms related to his reactive arthritis. His absolute CD2<sup>+</sup> cells were 3189 cells/ $\mu$ L, his absolute CB8<sup>+</sup> cells were 1630 cells/ $\mu$ L, and his absolute lymphocytes were 3952 cells/ $\mu$ L, all of which were above the upper limit of normal. His viral load was undetectable, and his CD4<sup>+</sup> cells were within reference range.

This follow-up is the longest for a patient given infliximab for reactive arthritis associated with HIV infection. A definite pattern to his reactive arthritis symptoms emerged in relation to treatment, with his symptoms worsening if a dose of infliximab was delayed or missed. Dose increases and shorter intervals between infliximab injections were used when his symptoms worsened.

Other studies have shown similar results,<sup>7-9</sup> but this report is the only one demonstrating no increased risk of infection in the long-term treatment of an HIV-infected patient with a TNF- $\alpha$  inhibitor over an 11-year period. Infliximab did not affect our patient's response to HIV treatment, nor did it exacerbate his HIV disease. In fact, when infliximab was discontinued, his viral load increased; when infliximab was restarted, his viral load decreased, usually to undetectable levels.

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