Spinal epidural abscess associated with infliximab treatment for psoriatic arthritis

Case report

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Tumor necrosis factor–α inhibitors are used to treat numerous chronic inflammatory and rheumatological diseases, such as Crohn disease, rheumatoid arthritis, and psoriatic arthritis. Because the mechanism of these inhibitors is to decrease the body’s inflammatory response, the primary complication of treatment is infection. The authors present the first case of a spinal epidural abscess in a patient receiving long-term infliximab therapy for severe psoriatic arthritis. Infliximab and its side-effect profile are discussed, along with other associated complications.

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KEY WORDS • infliximab • psoriatic arthritis • spinal epidural abscess

Psoriatic arthritis is an immune-mediated inflammatory disease that affects ~5–7% of people suffering from the chronic skin condition psoriasis. The primary symptoms are nail lesions, joint inflammation, tendonitis, and dactylitis. The disease can occur in patients of any age, however it usually appears 10 years after the first signs of psoriasis. The incidence is equal in men and women.

Psoriatic arthritis is inflammatory in nature, so medications that antagonize natural immune responses are used in its treatment. One such agent is infliximab, a monoclonal antibody directed against TNFα. By dampening immunity, however, the body is less able to battle serious infections, which has raised concerns over the long-term safety of these medications. Some authors have reported infection rates as high as 4–6% during infliximab therapy.

To our knowledge, this is the first report of a spinal epidural abscess occurring in a patient taking infliximab. Clinicians should be aware of this and other potentially serious infectious complications in patients using this medication.

Case Report

History and Examination. This 49-year-old man who had received a diagnosis of psoriatic arthritis in 1992 presented to our emergency department complaining of 3 days of chest pain, shortness of breath, and left-side neck pain. His psoriatic arthropathy had previously been controlled with methotrexate (15 mg weekly) and infliximab (maintenance dose of 7.5 mg/kg every 8 weeks) for 15 years, however his medication regimen was changed to infliximab (maintenance dose of 7.5 mg/kg every 8 weeks) alone for the 5 years prior to this presentation.

On initial presentation, the patient demonstrated no neurological compromise. He denied recurrent pneumonia or respiratory infections, frequent urinary tract infections, intravenous drug abuse, history of endocarditis, or recurrent skin infections. Cardiac origins for his symptoms were explored and excluded, but 2 sets of blood cultures grew methicillin-sensitive Staphylococcus aureus. The C-reactive protein and erythrocyte sedimentation rates were 416 mg/L and >140 mm/hour, respectively. His peripheral white blood cell count on admission was 20.8 × 10³ cells/μL and increased to 27.0 × 10³ cells/μL by hospital Day 2. He was started on a course of intravenous vancomycin. On hospital Day 2, the patient complained of an inability to walk, lower extremity weakness and numbness, and urinary retention. On examination, his lower extremity strength was 3/5 bilaterally with decreased sensation to light touch and elevated postvoid residuals. Emergent MR imaging of the spine was performed and revealed an epidural abscess with cord compression from C2–T7 (Fig. 1left).

Operation and Postoperative Course. The patient was immediately taken to surgery for C3–6 and T3–5 laminectomies with complete evacuation of the epidural abscess. Postoperatively, his weakness improved but he had residual sensory deficits in the lower extremities. Once the blood
cultures and intraoperative cultures definitively grew methicillin-sensitive \textit{S. aureus}, the antibiotic regimen was switched to intravenous cefazolin. Follow-up blood cultures were negative for \textit{S. aureus} once appropriate antibiotics had been initiated. Postoperative MR imaging did not show residual abscess (Fig. 1 right). The patient was discharged on 6 weeks of intravenous cefazolin and oral rifampin. By this time, his white blood cell count had normalized to $6.9 \times 10^3/\mu\text{l}$, and he left the hospital ambulating and with minimal lower extremity sensory deficits. Although he still has some residual lower extremity sensory changes, his strength and urinary function are entirely normal.

\section*{Discussion}

Psoriasis is an immune-mediated inflammatory condition in which T-lymphocytes initiate hyperproliferation of the epidermis.\textsuperscript{17} Various inflammatory mediators, including TNF\textalpha, are overexpressed in the secondary response, which leads to the associated condition psoriatic arthritis.

Tumor necrosis factor-\textalpha is an important factor in the pathophysiology of rheumatological diseases. It is produced by macrophages, lymphocytes, neutrophils, and keratinocytes during the immune response, binding to cell surface receptors of T cells and thereby activating B cells.\textsuperscript{13} When TNF\textalpha is inhibited, the production of interferon-\gamma and the expression of Toll-like receptor-4 are decreased.\textsuperscript{2} This blocks phagocytic recognition of intracellular bacterial and fungal pathogens. Tumor necrosis factor-\textalpha inhibitors may also provide increased susceptibility to mycobacterial and fungal infections, as TNF\textalpha aids in the formation of granulomas.\textsuperscript{11,12,14}

Infliximab is a chimeric mouse–human monoclonal immunoglobulin G1 antibody directed against soluble and cell-associated TNF\textalpha, which blocks the binding of TNF\textalpha with its endogenous cell surface receptor. This drug is slightly different from other TNF\textalpha antagonists, such as etanercept, a TNF\textalpha receptor/immunoglobulin G1 fusion protein.\textsuperscript{11}

Infliximab is approved for use in the treatment of psoriatic arthritis, as well as Crohn disease, RA, ankylosing spondylitis, and ulcerative colitis.\textsuperscript{17} The typical dose is 5 mg/kg, and it may be given with or without methotrexate; dosage may be increased with maintenance infusions given every 8 weeks.

Serious complications associated with long-term infliximab use have been reported, with the most common being upper respiratory infection and rhinitis, as well as bone and joint, urinary tract, and skin and soft tissue complications.\textsuperscript{8} The German Biologics Register in 2001 reported a relative risk of 3.0 (95\% confidence interval 1.8–5.1) for serious infection in patients treated with infliximab after adjusting for other predictive factors of infection risk including patient age and disease severity.\textsuperscript{9} As of 2006, 3 of the 4 randomized controlled trials that randomized more than 600 patients to anti-TNF\textalpha treatment or a placebo have shown a statistically significant increase in serious infections in the patients who received anti-TNF\textalpha.\textsuperscript{4,7,18} The majority of these infections are granulomatous. As such, antagonists like infliximab may reactivate dormant infections such as tuberculosis.

Other potential side effects of infliximab are acute and delayed hypersensitivity reactions, demyelinating disease,
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seizures, aplastic anemia and pancytopenia, intestinal perforation, cutaneous lupus-like rash, various infectious and opportunistic diseases, and even malignant lesions such as skin cancer and lymphoma.

The patient we present here was originally treated with methotrexate and infliximab, but was taking only infliximab at the time of presentation. It is therefore likely that the infliximab alone ultimately contributed to the epidural abscess formation, rather than the combination. Interestingly, most studies examining combination use of infliximab and methotrexate in RA have shown no increased risk of infection compared with the use of a single drug alone. In a study by Maini et al.,
the incidence of pneumonia in patients with RA who received infliximab and methotrexate was not statistically different from that in patients treated with methotrexate alone. To the authors’ knowledge, no such studies exist evaluating the side effect profile of this drug combination specifically in psoriatic arthritis patients. It is likely, however, that use of either drug carries similar risks to those seen in the RA population.

We present the first case of a spinal epidural abscess in a patient receiving infliximab for psoriatic arthritis. We are unable to find any other reference to this particular infectious complication reported for any other chronic inflammatory or rheumatological condition associated with infliximab therapy.

Spinal epidural abscess has been previously reported in patients undergoing treatment with other similar immunosuppressive agents for chronic rheumatological diseases. Harrington et al.
reported on a patient with a history of RA treated with a 7.5-mg weekly methotrexate dose who had an epidural abscess at L2–3 that grew methicillin-resistant S. aureus on culturing. Watabe et al.
also described the case of a 52-year-old man in whom a methicillin-resistant S. aureus thoracic epidural abscess developed while he was receiving plasmapheresis and a course of high-dose oral prednisone for bullous pemphigoid.

The most common pathogen isolated from spinal epidural abscesses is S. aureus. The source of these infections can be quite diverse, however. In a meta-analysis of the international literature on spinal epidural abscesses between 1954 and 1997, Reihaus and colleagues
found that antecedent infectious processes were identified in 377 (44%) of 854 cases. In most of these cases, the infection led to seeding of the epidural space by hematogenous spread. The next most prevalent mechanism was invasive procedures, which led to spinal epidural abscesses in 188 (22%) of the 854 patients. The most common such procedures were the administration of epidural anesthesia and extraspinal operations, with equal frequency of 4.91% each.

In our patient, no antecedent infection was ever identified, and he did not report having undergone any recent invasive procedure. The patient denied any history of intravenous drug abuse, recent or chronic infections, traumatic injury, or history of other chronic immunocompromising conditions such as diabetes. His chest radiographs and physical examination failed to demonstrate any respiratory origin for his disease. He had no open wounds that could have led to skin infection. The only other possible predisposing condition to septicemia and eventual epidural abscess was a prior total hip replacement, but this occurred 5 years before presentation.

It is known that postoperative infections, such as peri-prosthetic septic arthritis, postoperative osteomyelitis, and deep-wound infections are complications of orthopedic surgery.
Furthermore, RA, a chronic inflammatory condition similar to psoriatic arthritis, is an independent risk factor for postoperative orthopedic infection. The infection rate has been reported to be 2–4 times higher after orthopedic surgery when a diagnosis of RA coincides.
However, less is known about the effects of actual TNFα therapy on bacterial infections that arise after orthopedic surgery. Giles and colleagues
found that of 91 patients with RA who underwent 1 or more orthopedic surgical procedures, 7 (70%) of the 10 who experienced postoperative infection were taking TNFα inhibitors. These authors determined that TNFα therapy was significantly associated with the development of a serious bacterial postoperative infection.

Conclusions
Infliximab is a TNFα antagonist commonly used to treat chronic inflammatory and rheumatological conditions such as psoriatic arthritis. When used safely with periodic monitoring, this medication can alleviate many of the symptoms associated with this debilitating disease. However, even patients without common risk factors are still susceptible to infections. This particular case of a large spontaneous spinal epidural abscess was successfully treated with prompt surgical evacuation and appropriate antibiotic therapy, and ultimately resulted in a good neurological outcome. Clinicians must be cognizant of the fact that infections may emerge insidiously in patients taking infliximab and may, as in this patient, affect the spine and nervous system.

Disclaimer
The authors do not report any conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References


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