

Eye Loss by Exogenous Endophthalmitis Following Anti-Tumor Necrosis Factor Therapy: A Report of 3 Cases

To the Editor:

Infectious endophthalmitis is a serious infection of intraocular fluids and tissues, which often leads to loss of vision¹. It can be classified as exogenous or endogenous according to the mechanism of infection. Endogenous endophthalmitis results from hematogenous spread of organisms to the eye, whereas exogenous endophthalmitis occurs due to direct infection of the eye following surgery or penetrating trauma². Anti-tumor necrosis factor- α (TNF- α) drugs are a highly effective treatment for rheumatoid arthritis (RA) and ankylosing spondylitis (AS) but increase the rate of soft tissue and skin infections³. However, only a few cases of severe eye infection have been reported⁴⁻⁸. We describe 3 patients who developed exogenous endophthalmitis during treatment with anti-TNF- α .

Patient 1. A 36-year-old woman had a history of 11 years of erosive RA. She had right facial palsy secondary to facial trauma, leading to difficulty completely closing her right eye. Her RA remained active despite conventional disease modifying antirheumatic drugs (DMARD). Infliximab (3 mg/kg) was therefore started in January 2003, together with methotrexate (MTX; 15 mg/wk) and prednisolone (10 mg/day). This led to a marked improvement of RA. In May 2004, 10 days after the eleventh infusion, she complained of an acute pain in her right eye associated with vision loss. She had a red eye upon examination, associated with a corneal ulceration and hypopyon. Infliximab was discontinued and a vitreous biopsy was performed. Gram staining of vitreous fluid was positive for *Pseudomonas aeruginosa*. Despite intravenous and intraocular antimicrobial therapy, she developed a corneal opacification leading to complete loss of vision (no light perception; Figure 1). She underwent further evisceration and received an eye prosthesis.



Figure 1. Slit-lamp examination of Patient 1, 3 months after emergency corneal patch graft and antibiotic treatment. Note (above right) an area of scleromalacia and corneal opacification with neovessels suggesting severe previous infectious ocular disease.



Figure 2. Slit-lamp examination of Patient 3. Endophthalmitis with hypopyon and corneal abscess spreading from the suture incision (upper right).

Patient 2. A 64-year-old man had severe and active RA for 10 years. He had a history of hematochromatosis and congenital blepharoptosis of his right eye, which had been surgically treated in his childhood. As a result, he experienced difficulty closing his eye. MTX and leflunomide failed to control his RA. Treatment with adalimumab was started in May 2005 (40 mg every 2 wks) together with MTX and prednisone, followed by etanercept after 6 months (50 mg/wk). Four months later, he suddenly complained of a painful red right eye, associated with photophobia and vision loss. He reported onset with subconjunctival hemorrhage 2 days before. Ophthalmological examination revealed a corneal ulceration with destruction of the eye. Neither analysis of vitreous culture nor histological examination were undertaken, but purulence of the eye was highly suggestive of infection. He had necrosis of the eye and no light visual acuity. Evisceration was performed, immediately followed by an ocular prosthesis in April 2006.

Patient 3. A 68-year-old man presented with a 6-year history of severe seropositive and erosive RA. His history included diabetes mellitus and cataract surgery in 1999 with suture of the corneal incision. Infliximab therapy was started in February 2002, associated with MTX 15 mg/week and prednisone 15 mg/day. In March 2004, while receiving treatment with 4 mg/kg (300 mg)/6 weeks of infliximab, he suddenly complained of ocular discomfort. Ocular examination revealed inflammation of the corneal suture, which was removed. Two days later, the pain worsened and he noticed blurred vision. Examination revealed a deep corneal abscess and a hypopyon in the anterior chamber. Corneal scraping was performed and culture showed presence of *Streptococcus pneumoniae*. Despite antimicrobial therapy, he rapidly developed endophthalmitis (Figure 2). Outcome was unfavorable, with retinal detachment resulting in visual loss.

Endophthalmitis is an infection of the posterior segment of the eye that frequently results in loss of vision. In our 3 cases, the contamination was exogenous and occurred after the development of bacterial keratitis. Indeed, none of our patients demonstrated systemic infection, positive blood culture, or distant infection reminiscent of an endogenous origin. Bacterial keratitis is rare in the absence of predisposing factors such as ocular trauma, ocular surface diseases, or use of contact lenses⁹. In our first 2 cases, difficulty closing the eye resulted in exposure keratopathy; in the third case, infection occurred after the removal of a corneal suture. Moreover, bacterial keratitis is rarely complicated with endophthalmitis.

In a retrospective study of 300 cases of bacterial keratitis, Bourcier, *et al* found 2 cases complicated with endophthalmitis⁹. Scott, *et al* showed that this type of contamination was associated with corticosteroid use and immunodepression¹⁰. However, only 1 case of exogenous endophthalmitis has been reported in RA patients treated with corticosteroid or DMARD¹¹. The potential role of anti-TNF- α therapy in the unfavorable and rapid development of infection in our 3 patients should thus be considered.

These 3 cases highlight the possible risk of exogenous endophthalmitis in patients being treated with TNF blockers. Thus, rheumatologists should consider asking for ophthalmological advice before beginning TNF- α treatment, at least in patients with a history of risk factors for bacterial keratitis or undergoing ocular surgery.

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