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Case report

Successful treatment of Behçet's uveitis with Tocilizumab

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Abstract

A 33-year-old man with history of lymphoma was misdiagnosed as multiple sclerosis (MS) 18 months previously, developed intermediate uveitis, unresponsive to interferon, and corticosteroids. A diagnosis of Behçet's disease (BD) was made on the basis of recurrent orogenital ulceration, erythema nodosum, and a positive pathergy test. The patient was started on Tocilizumab and experienced an improvement in visual acuity and intraocular inflammation over the following 2 weeks. In patients with BD-related uveitis, Tocilizumab can be an effective alternative to anti-tumor necrosis factor alpha medications.

Keywords: Behcet's syndrome, Vasculitis, Uveitis, Tocilizumab

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Introduction

Behçet's disease (BD) is characterized by recurrent inflammation of the oral and genital mucosa, uveal tract, vasculature, skin, and central nervous system. Ocular involvement occurs in 20–70% of patients, and can lead to visual loss in up to 90% of untreated individuals.[1] The cause and pathogenesis of BD remain unknown. Corticosteroids remain the first-line of treatment. Azathioprine, infliximab, and interferon have been shown to be effective in treating BD and reducing dependence on corticosteroids and relapse rate over the past decade.

Case report

A 33-year-old man was diagnosed with multiple sclerosis (MS) 18 months previously based on the recurrent neurological symptoms (paresthesia, ataxia) and uveitis. Neuroimaging revealed multiple lesions in the frontal deep white matter, left thalamus, left cerebellar peduncle, body of corpus callosum, and the pons. He also had a number of lesions within the medulla. He was given systemic steroids and was subsequently started on Interferon β 8 million unit subcutaneous injection every other day; his neurological symptoms recovered completely, but uveitis remained refractory. On clinical examination, the visual acuity in the right eye was 20/25 and that in the left eye 20/30. The intraocular pressure was 13 mm Hg in both eyes. He had bilateral anterior non-granulomatous uveitis with 1^{+} cells in both anterior chambers, extensive synechia, and bilateral visually significant steroid induced posterior subcapsular cataracts. Initially, the view of the posterior pole was limited, but the optic nerves were normal and showed no evidence of optic neuritis or vitritis. He was started on topical prednisolone acetate 1% eye drops and then given trans-septal steroids, which gave temporary good control of the inflammation. It was only after temporarily controlling the ocular inflammation and performing cataract surgery on the left eye and synechiolysis that we were able to visualize the mid- and far periphery of the fundi and perform fundus fluorescein angiography (Fig. 1), which revealed the snow balls and active peripheral vasculitis; despite being on Interferon β. The patient subsequently reported recurrent orogenital ulceration and was found to have erythema nodosum, folliculitis, a positive pathergy test

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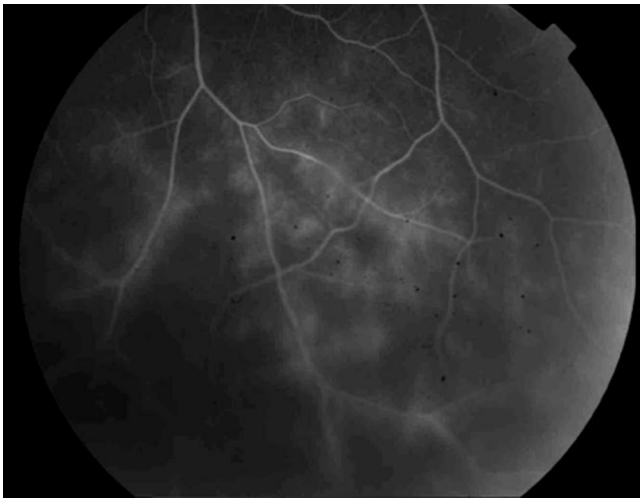

Figure 1. Fundus fluorescein angiography before treatment.

on examination, and recurrent vitritis. We think that the patient presented with neuro-BD and was misdiagnosed as MS. The diagnosis of MS was therefore revised to BD and interferon β was stopped. Of note, the patient had been treated for Non-Hodgkin's Lymphoma (NHL) with both radiotherapy and chemotherapy 5 years previously; he maintained remission from lymphoma and under regular follow-up by oncologist. Given the history of NHL, the decision was made not to offer anti-tumor necrosis factor alpha (TNF-α) medication due to the reported increased risk of NHL associated with the drug class.[3] The patient was given 4 mg/kg Tocilizumab intravenous infusion. Two weeks later, the vitritis was reduced and the vasculitis resolved (Fig. 2). A second dose of 8 mg/kg was given 4-weeks after the first dose. He subjectively noticed improvement in the quality of vision because the floaters subsided in the left eye, but the visual acuity in the right eye did not change due to cataract. His fundus fluorescein angiography showed decreased leakage peripherally (Fig. 1). His uncorrected visual acuity in the right eye was 20/25 and that in the left eye was 20/20, and his intraocular pressure remained within normal range. Throughout treatment, although for a short period, the patient's full blood count, renal and liver function tests remained stable. The patient was assessed 2 weeks after the second dose of Tocilizumab (Fig. 3), and then unfortunately, he lost to follow-up.

Discussion

There is a growing body of research investigating the effect of interleukin-6 (IL-6) receptor blockade in uveitis. There is also evidence that uveitis resistant to anti-TNF-α treatment can be sensitive to drugs, such as Tocilizumab. [4,5]

In Calvo-Rio et al's study,[4] 3 patients (one has rheumatoid and 2 have BD) with uveitis refractory to conventional immunosuppressive therapy and at least one anti-TNF-α drug were treated with Tocilizumab. After they were followed up for 1–12 months, the patients experienced ocular improvement.[4]

While IL-6 receptor blockade is not routinely used in the treatment of BD, there is some evidence that it may be effective in reducing the duration and severity of BD-related flares.[6,7]

Our patient received 2 doses of Tocilizumab with 4-week interval. A subjective response was noted after 2 weeks. Tocilizumab, a humanized anti-IL-6 receptor monoclonal antibody immunoglobulin G1 class, demonstrated significant efficacy in rheumatoid arthritis patients. There is a growing interest in IL-6 blockade for its therapeutic potentials in immune-medicated inflammatory diseases. Interleukin-6 has been found to be elevated in the blood of BD patients with active disease compared with those in remission or healthy individuals.[4] In clinical practice, Tocilizumab was used in a patient with neuro-BD syndrome, who was refractory to conventional treatment and showed secondary failure of the anti-TNF-α agent infliximab. He presented as a progressive weakness of the legs and reduction in walking distance. The cerebrospinal fluid showed signs of inflammation including a vastly elevated IL-6 concentration. Given this result, the anti-IL-6 receptor antibody Tocilizumab was administered and a good improvement of inflammatory parameters and a satisfactory increase of the walking distance were achieved.[8] Hirano et al.[7] reported a patient with BD who

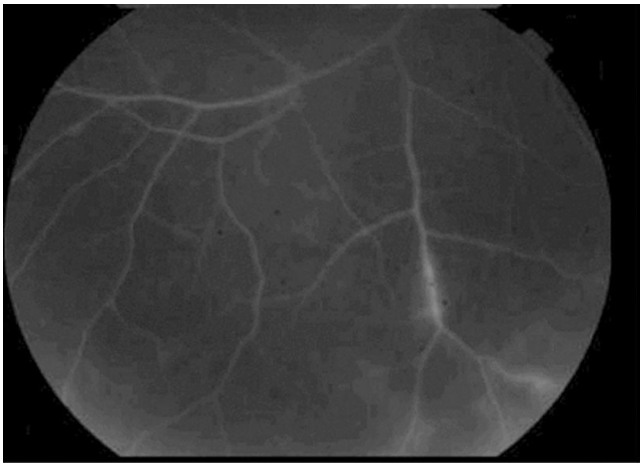

Figure 2. Fundus fluorescein angiography 2 weeks after the first dose of Tocilizumab.

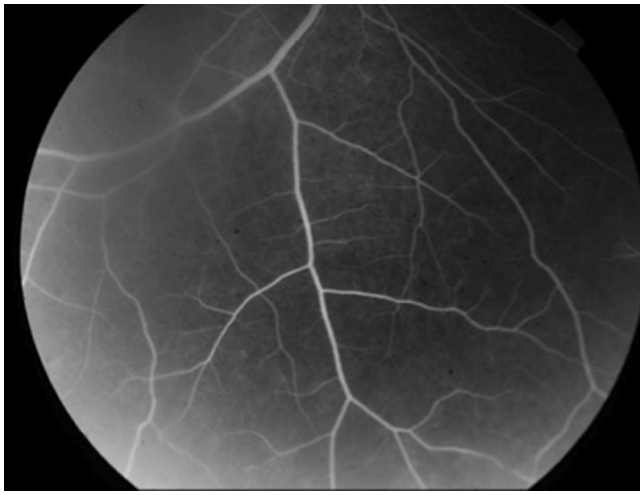

Figure 3. 2 weeks after the second dose of Tocilizumab, there is complete recovery and no vascular leakage.

was treated with cyclosporine A, steroids, and infliximab, and her disease flared up and she presented with recurrent oral ulcers, erythema nodosum, and uveitis with worsening of visual acuity. She was treated with Tocilizumab 8 mg/kg every 4 weeks, and after 6 infusions her symptoms improved markedly and there were no adverse events.[7]

Our case adds to the body of evidence suggesting that patients with BD-related uveitis respond well to IL-6 receptor blockade with no immediate side effects. It also highlights the importance of access to a different class of biologic agents, if anti-TNF-α medications are relatively contraindicated as in this case.

Conclusion

Tocilizumab is an alternative agent for controlling BD-related uveitis refractory to steroids and interferon treatment.

Conflict of Interest

The authors declare that there is no conflict of interest.

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