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Regression of severe Behcet's eye disease with infliximab therapy; first two cases treated in Pakistan

Saliha Ishaq
Aga Khan University, saliha.ishaq@aku.edu

Anum Saeed

Majid Jawad

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Saliha Ishaq,[1] Anum Saeed,[2] Majid Jawad[3]

Department of Medicine, Aga Khan University Hospital,[1] Ziauddin University Hospital,[2,3] Karachi.

Corresponding Author: Saliha Ishaq. Email: saliha.ishaq@aku.edu

Abstract

We present two cases of Behcet's Disease with severe eye problems along with oral and genital ulcerations. Both cases, initially were treated with steroids and oral immunosuppressive agents, but did not show a response and ocular disease became worse. Both the cases were kept on Infliximab therapy. an immediate positive response with improvement in vision and symptoms was seen. After initial infusions the ocular damage in both the cases stopped.

Keywords: Behcet's disease, Ocular disease, Uveitis, Infliximab, Anti TNF-alpha drugs.

Introduction

Behçet's Disease (BD) is rare chronic multisystem immune-mediated inflammatory disorder, characterized by recurrent oral and genital mucocutaneous ulcerations with articular, neurological, gastrointestinal and ophthalmological and neurological disease involvement. Ocular involvement presents as bilateral non granulomatous panuveitis, retinal and choroidal vasculitis, optic neuritis and retinal vascular occlusion. Although, BD has a worldwide distribution, it is rare in North American population and Europe. Prevalence is higher in Turkey, Middle and Far East region, affecting mainly young adults, having more severe vascular complications.[1]

According to the International Study Group criteria, the diagnosis of BD requires the presence of recurrent oral ulceration along with any two conditions: recurrent genital ulceration, eye lesions, skin lesions or a positive skin test. The diagnosis is clinical because there is no specific evidence, pathognomonic symptoms or specific laboratory findings.[1]

Behçet's entails recurrent attacks of acute inflammation and generally, does not run a chronic persistent course. Involvement of gastrointestinal tract, central nervous system, and large vessels is occasional, and can be life-threatening.[1] The most feared complication of BD is irreversible vision loss. Susceptibility to BD is associated with HLA-B51 allele. Environmental factors such as infectious agents have been implicated in its pathogenesis.

Corticosteroids and immunosuppressants are the mainstay for treating this disease, however, an increasing number of refractory cases occur. Recently, Infliximab and other tumour necrosis factor inhibitors have shown dramatic results in treating various manifestations of BD.

Case Presentation

Case-1:

A 23-year male, presented with history of recurrent ulcers in mouth and genital tract, blurring of vision and arthralgias, since one year. The patient had apthous ulcers in the mouth, on glans penis and scrotum. He also complained of occasional redness in the eyes along with gradual decrease in vision and arthralgias. A diagnosis of BD was made. On eye examination patient was found to have a low visual acuity (V/A). The left eye had a V/A of 20/400 while right eye V/A was worse at, "counting fingers at 2 feet" secondary to severe panuveitis. The IOP was normal at 14 mmHg bilaterally. ESR was 51, CRP was high 23. He was kept on Prednisolone and Azathioprine. In the next few months, his follow up visits showed worsening V/A secondary to repeated attacks of uveitis in both eyes despite getting Azathioprine, three bilateral intraocular injections of Bevacizumab and, systemic as well as intraocular steroids. The patient's V/A detoriated further during therapy, patient had "Perception of Light" bilaterally a month ago, before referral to Rheumatology clinic. He was then switched to Infliximab therapy. An immediate effect was seen after the first dose leading to stabilized vision. He received three doses of Infliximab over a period of seven months (total time for his treatment at AKU was two years) until his uveitis attacks got settled. Patient's V/A improved to "Counting Fingers at 4 feet" bilaterally, he was continued on Azathioprine and low dose Steroids for maintenance therapy.

Case-2:

A 29-year-old male presented with history of recurrent oral and genital ulcers, vision problems and low

grade fever for few months. His major complaint was decreased vision with redness and pain in both eyes. On examination, the patient had numerous apthous ulcers in the mouth and on glans penis. Eye exam showed diffuse anterior uveitis and V/A of "counting fingers at 2 feet" and "20/400" in right and left eye, respectively. The IOP was measured to be at 18 mmHg (within normal range of 10-21 mmHg). Diagnosis of BD was made. His ESR was 62, CRP was 12 and a positive ANA was present. Oral steroids with Azathioprine were started. Despite high dose therapy for a few months, his V/A continued to deteriorate with relapses of anterior uveitis. He was then started on intravenous Infliximab therapy. After the first two doses the intensity of ocular inflammation weaned off gradually. However, after the second dose of Infliximab, the patient developed reactivation of pulmonary Tuberculosis thus the drug was withheld. Confirmed by a Purified protein derivative (PPD) test and a chest radiograph, acute tuberculous treatment (ATT) was given for 6 months. He recovered from pulmonary tuberculosis successfully, Infliximab was then started. Patient's Intraoccular pressure (IOP) remained at baseline 18 mmHg throughout his treatment. Patient's right eye vision was lost due to recurrent attacks of Uveitis and retinal vasculitis, however, the left eye vision (V/A 20/400) has been sustained after treatment with Infliximab.

Discussion

BD was first depicted in 1937 by a Turkish dermatologist named Hulusi Behçet. Behçet referred to BD as a "complex of recurrent oral ulcers, genital sores, and hypopyon uveitis that could lead to blindness."[2] Ocular involvement of BD, which is basically in the form of anterior and posterior uveitis, cataracts, conjunctivitis or retinal vasculitis, is the most feared symptom of the disease. Eye inflammation, which occurs in 70% of cases,[1] is considered one of the major criteria upon which the diagnosis is based. The ocular disease is characterized by repetitive and explosive inflammatory attacks, which can subside spontaneously or with treatment. Disease affecting the back of eye, is sight threatening, may produce macular oedema, retinal swelling and haemorrhage, and inflammation of blood vessels. Despite therapeutic intervention, about 25% of people with ocular lesion become blind.[3] Early age of onset and male gender are bad prognostic factors for ocular disease.[4] In a study of BD, ocular disease was bilateral in 78.1% and panuveitis was the most common finding. Risk of losing vision within 10 years was 30% for men and 17% for women.[5]

Corticosteroids and immunosuppressants have been the drugs of choice for BD. Topical mydriatic agents and corticosteroids are used initially for mild disease with recurrences if steroids are used as a monotherapy. Trials have shown that Azathioprine and Cyclosporine, Colchicine are effective for treatment of Behcets uveitis.[6,7]

Recent advances in medical treatment of BD have shown TNF-Alpha inhibitors as a new effective drug.[8,9] Infliximab, a chimeric monoclonal antibody to TNF-α, was initially developed to treat systemic inflammatory disorders such as rheumatoid arthritis and Crohn's disease. Levels of TNF-α (as well as other pro inflammatory cytokines) are elevated in active BD thereby suggesting that anti-TNF-α therapy is valuable. Clinically, significant improvement of various BD manifestations with infliximab therapy, and other Anti-TNF therapies, has been reported in literature.[9]

Biologics like Infliximab have successfully been reported to treat resistant Neuro- Bechets disease, eye threatening panuveitis and severe mucocutaneous lesions.[8,10] The success of this drug in treating acute uveitis in patients with BD is secondary to high serum levels the drug can achieve. A Japanese study of relationship between serum Infliximab levels and acute uveitis, done in 2010, concluded that serum concentration of Infliximab in each patient was significantly correlated with its effectiveness in settling recurrent episodes of uveitis.[11] An Open Label Trial conducted recently, showed that infliximab is effective in suppressing the occurrence of uveitis attacks and also has a significant corticosteroid sparing effect.[12]

Here, we reported two cases of severe Bechets eye disease treated successfully with Infliximab.

Despite one of our patients developing reactivation of Pulmonary Tuberculosis after second Infliximab was withheld and resumed after 6 months, which was the duration for which ATT was given.

Conclusion

BD can be incapacitating if not treated aggressively, its complications, include complete blindness. There is a severe need to assess patients by a multi-disciplinary team to start and adjust therapy on time to prevent complications. As per our reports, Infliximab is an effective therapeutic choice for steroid and other immunosuppressant resistant ocular involvement of BD.

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