Case Report

Efficacy of Infliximab on the acute attack of uveitis

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ABSTRACT

يعد التهاب حدقة العين من أعظم سمات مرض بهجت مع نمط الانتكاسة و الخمود. قد يكون الظهور الشديد للمرض مقاوم للمعاجلة التقليدية. تم استخدام الستيرويد في معالجة التهاب حدقة العين الحاد الناجم عن مرض بهجت، على الرغم من أن لديه مضاعفاته العينية الخاصة عند استخدامه على جرعات عالية. لقد وصفناه للمرضى الذين حضروا وهم يعانون من التهاب حدقة العين، حينما كانوا على المعالجة، وتمت السيطرة على التهاب حدقة العين عن طريق إضافة مضادات (TNF) وعقار انفليكسيبام

Uveitis is one of the major features of behcet's disease with relapse and remission pattern. Severe presentation can be resistant to the conventional treatment. Steroid has been used in the treatment of acute behcet's uveitis, although it especially has its own ocular complications when used in large doses. We describe to patients presented with acute uveitis while on treatment, uveitis was controlled by adding anti-tumor necrosis factor (TNF) and Infliximab.

Saudi Med J 2010; Vol. 31 (1): 82-85

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Received 17th October 2009. Accepted 20th December 2009.

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Behcet's disease is a chronic multisystem disorder with relapsing inflammation. The main pathology is vasculitis of both arteries and veins of different sizes in all organs. The ocular involvement occurs in 56%,[1] usually in the form of non-granulomatous. Panuveitis also can present with retinal vasculitis.[2] The cause of Behcet's disease is unknown, but the inflammatory reaction in Behcet's disease is mediated by cytokines derived from T-helper type lymphocytes, including tumor necrosis factor (TNF). The concentration of TNF and soluble TNF receptors is increased in the serum of patients with active diseases.[3] Recent studies showed the effect of using infliximab to treat Behcet's uveitis. In some disorders, all types of TNF antibodies have similar efficacy, but that does not appear to be the case of uveitis when infliximab is at present looking to be more effective than etanercept.[4] We report the effect of infliximab as steroid sparing when used to treat acute Behcet's uveitis be of more effective than etanercept.[5] We report the used of infliximab to treat 2 patients with acute Behcet's disease presented with uveitis.

Case Reports. *Patient One.* A 36-year-old gentleman diagnosed to have Behcet's diseases 2 years ago, diagnosis was based on the recurrent purified oral ulcers, uveitis with 3 attacks over the last 2 years, and genital ulcer (only once) and Folliculities, in addition he has an off and on arthritis in both knees with occasional effusion. He was on cyclosporine 150 mg; and he stopped prednisolone one year ago. He was presented with active uveitis no history tuberculosis (TB) or TB contact. The mantoux test was negative and the chest x-ray was normal. He was given Infliximab 5 mg/kg stat (anti-TNF) alone without adjusting cyclosporine dose or adding steroid. Our intention was to repeat infliximab infusion after 2 weeks if showed any improvement, and if no response, the patient should receive methyl prednisolone infusion. Interestingly, the patient started to show improvement after 2 days of infliximab infusion. The patient was evaluated in the clinic after 3 weeks when they reported a significant improvement after the single infliximab infusion (**Table 1**).

Patient 2. A 22-year-old gentleman, diagnosed to have Behcet's disease one year ago, diagnosis was based on recurrent painful oral ulcers, uveitis, and recurrent genital ulcers. He was receiving prednisolone 20 mg once daily tapened from 60 mg OD and cyclosporine 150 mg OD "to treat uveitis," and was admitted to the hospital when he decreased vision and pain in the right eye, after prednisolone tapened to 20 mg OD, he was diagnosed with severe uveitis. He received infliximab 5 mg/kg without altering any of his current treatment and

there was improvement after single infliximab infusion (**Table 2**). On 23 May, 2003 it was documented that all signs of retinitis have disappeared. Patients developed posterior sub-capsule cataract in both eye.

Patient 3. A 26-year-old lady known to have Behcet's disease for the last 3 years with severe uveitis as the main problem, she required large doses of steroid that was complicated by cataract. She has undergone a cataract extraction of the right eye (**Figure 1**); seen in ophthalmology clinic 2 weeks ago. The patient was complaining of decreased visual activity and red eyes. She was diagnosed with severe uveitis and was started on Prednisolone 60 mg and cyclosporine 300 mg (5 mg/kg/day). Despite this, she was still having the same symptoms and examination of the eyes showed the same previous finding. She was given Infliximab 3 mg/kg infusion. She had partial improvement, and Infliximab dose was repeated after 2 weeks then after 4 weeks then 6 weeks. She had a significant response after the second dose. Examination findings pre- and post- Infliximab treatment are shown on (**Table 3**).

Discussion. Inflammatory eye disease is one of the serious manifestation of Behcet's disease that has high morbidity and may lead to blindness. Patients with high risk complication are young men. Acute attacks of both posterior uveitis and retinal vasculitis are usually treated with corticosteroid and cyclosporine, or azathioprine, or cyclophosphamide, and inferferon.[5-7] Anti-TNF has been tried to treat Behcet's uveitis in 5 patients, some of the patients had increment in the prednisolone dose and addition of azathioprine and this will influence the response of uveitis to treatment, namely, it may not be purely due to infliximab, but findings generally indicate that infliximab lead to rapid and effective suppression of ocular inflammation.[8] Lindstedt[9] studied the effect of infliximab on 13 patients with uveitis, 6 had Behcet's disease, and they received infliximab 3 mg/kg with a variable number of doses according to the severity; a good clinical response was observed regarding inflammation in most of patients without serious side effect.[9] The severity and frequency of uveitis attacks in Behcet's disease determine the extent of permanent damage to the intraocular structures and resultant visual loss. The main goals in the management of patients with Behcet's uveitis are rapid resolution of intra-ocular inflammation. Prevention of recurrent attacks, achievement of complete remission, and preservation of vision. The effect of infliximab on the frequency of uveitis attacks, and the visual prognosis was studied on

Table 1 - Clinical features before and after infliximab infusion. Infliximab was administered on 10th May 2003) (patient 1).

Infliximab 3 mg/kg	Right eye					Left eye				
	Visual acuity	Anterior chamber activity	Vitreous haze	Retinal lesions	Vasculitis	Visual acuity	Anterior chamber activity	Vitreous clarity	Retinal lesions	Vasculitis
0	6/12 6/9 with pinhole	-	+	-	-	CF 0.5 M Mac oedema	+	+++	-	-
2 weeks later	6/20 on cyclopentolate	-	+	-	-	1/60		++ Pigmented cells only	-	-

On 23rd May 2003, it was documented that all signs of retinitis has disappeared. Patient developed posterior sub-capsular cataract in both eyes.
- = negative, + = mild, ++ = moderate, +++ = severe

Table 2 - Received infliximab on 11th November 2003 (patient 2).

Infliximab 3 mg/kg	Right eye					Left eye				
	Visual acuity	Anterior chamber activity	Vitreous haze	Retinal lesions	Vasculitis	Visual acuity	Anterior chamber activity	Vitreous clarity	Retinal lesions	Vasculitis
0	6/80	++	+++	+ macular edema	+	6/7.5	±	-	-	-
2 weeks later	6/60	-	-	-	-	6/6	-	-	-	-

- = negative, + = mild, ++ = moderate, +++ = severe, ± = doubtful

Table 3 - Examination findings pre- and post- infliximab treatment (patient 3).

Infliximab 3 mg/kg	Right Eye					Left eye				
	Visual acuity	Anterior chamber activity	Vitreous haze	Retinal lesions	Vasculitis	Visual acuity	Anterior chamber activity	Vitreous clarity	Retinal lesions	Vasculitis
0	0.5/60	++	Vitiritis ++	Retinitis macular edema ++	+	6/6	±	-	-	-
2 weeks later	6.5/60	-	-	-	-	6/6	-	-	-	-

- = negative, + = mild, ++ = moderate

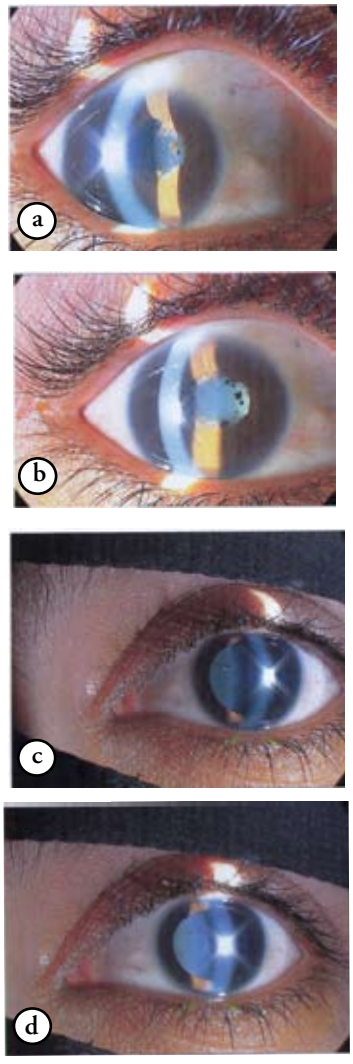

Figure 1 - **a & b**) Right eye - intraocular lens, synechia, vitreous haze, and no active inflammation. **c & d**) Left eye - nothing remarkable.

13 male patients and the results suggest that infliximab is effective in suppressing the occurrence of uveitis attacks and that it has a corticosteroid sparing effect with favorable implication for the visual prognosis of patients with resistant Behcet's uveitis.[10] The long term efficacy and safety of infliximab in patients with Behcet's disease were addressed by Niccoli et al.[11] Twelve patients with refractory posterior uveitis. Their baseline medication includes prednisolone (1 mg/kg) with rapid tapering and 9 infliximab infusions (5 mg/kg) over 12-month period. After they were reassessed and found that 7/12 patients (75%) achieved full remission. All the patient had dramatic improvement of ocular inflammation. Infliximab was well tolerated with no side effects. Another study by Lopez-Gonzalez,[12] describe the use of infliximab in patients with refractory uveitis in 11 patients (17 eyes) with 7 years follow-up. After infliximab, 6 eyes mentioned their basal visual acuity, 9 eyes improved, and 2 eyes worsened and they were those with coroiditis and active retinal vasculitis. There was no infliximab related adverse event. In our patients, we used infliximab 3 mg/kg in acute attack of uveitis without adding any other agents or altering their current treatment and it showed good effect in suppressing acute uveitis without complications. Our experience is consistent with the other reports, which indicate the safe and good effect of infliximab use in acute uveitis, which may replace the use of high dose corticosteroid to avoid the side effect on the long term especially cataract formation. However, these are all small number of patients; clinical trials are necessary to determine the optimal therapeutic strategy in patients with uveitis with regard to the dosage and duration of treatment.

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