Case Report

Biological agent in prevention of ocular recurrence in Behçets disease: a case report

Adnan Ismail A[1], Kharel Sitaula R[2], Biswas J[3]
[1]Indira Gandhi Memorial Hospital, Male' Maldives,
[2]Department of Ophthalmology, BP Koirala Lions Centre for Ophthalmic Studies, Institute of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal
[3]Medical and Vision Research Foundations, Sankara Nethralaya, Chennai, India

Abstract

Introduction: Ocular involvement in Behçets disease (BD) is characterized by recurrent inflammatory attacks leading to poor long-term visual prognosis. The development of biologic agents has heralded a new era in the management of BD uveitis enabling more targeted immune modulation with greater efficacy and has now become the first line agents.
Objective: To report a case of young gentleman with Behçets disease whose ocular recurrence was controlled with injection Adalimumab.
Case: A 31-year-old male with recurrent oral and genital ulcers with bilateral recurrent uveitis was diagnosed as bilateral ocular Behçet's disease based on positive HLA B51 typing and ferning pattern in FFA. He was on oral Prednisolone and Cyclosporine and was advised for biological agents. On presentation to us, he had anterior uveitis with pseudophakia and secondary open angle glaucoma in right eye and posterior subcapsular cataract in left eye. After starting Inj Adalimumab with oral Methotrexate, the ocular inflammation was under control and patient underwent uneventful cataract surgery in left eye. Over 1-year follow-up, the patient is on remission, on injection Adalimumab with the steroid tapered off.
Conclusion: Biological agents like Adalimumab is effective in controlling recurrences in Behçet's disease

Key words: Behçets disease, biological agents, Adalimumab

Introduction

Behcet's disease (BD) is a rare immune-mediated systemic vascular disorder characterized by relapsing and remitting episodes of inflammation (Yurdakul S et al, 2004). Presentation varies, depending on the organ involved and the severity. (McNally TW et al, 2017). Non-infective uveitis is rare, affecting 25-50 people per 100,000 in the UK (McNally TW et al, 2017). However, it is the most frequent ocular manifestation of BD and may involve anterior, intermediate and posterior uveal tract or either in isolation, or in combination as panuveitis. While there are no pathognomonic symptoms or signs, uveitis in BD usually presents with acute onset hypopyon and occlusive retinal vasculitis, with

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Corresponding author
Dr. Almas Adnan Ismail
Indira Gandhi Memorial Hospital, Kanbaa Aisarani Rani Hingun, Male', Republic of Maldives, 20402.
E-mail: almasadnann@gmail.com

predominant inflammation of retinal veins rather than arterioles. Although Uveitis due to BD is commonly bilateral, inflammatory flares commonly occur unilaterally and alternate between eyes (McNally TW et al, 2017).

In the treatment of BD, there are no widely accepted gold standards due to the variation in presentation and severity. Treatment is usually initiated and monitored by a multi-disciplinary team, that requires collaboration between dermatologists, ophthalmologists and rheumatologists, with input from cardiologists, genitourinary physicians and neurologists depending on presenting features (McNally TW et al, 2017).

Corticosteroids, Colchicine, and traditional immunosuppressive agents, including Azathioprine and Cyclosporine, have been used for treating Behçet's disease (Ryo Rokutanda et al, 2015). Recently, considerable published data suggest that TNF inhibitors such as Adalimumab represent a significant therapeutic advance for patients with severe and resistant disease, as well as for those with contraindications or intolerance to these treatments (Ryo Rokutanda et al, 2015).

Here we report a first case of young Nepalese gentleman with Behçets disease whose ocular recurrence was controlled with injection Adalimumab.

Case report

A 31-year-Nepalese gentleman presented with recurrent oral (Figure 1A) and genital ulcers with bilateral recurrent uveitis since 2 years when he was studying in Australia. The patient was treated on long term oral steroid for which he had developed cataract and glaucoma. His right eye underwent phacoemulsification at Australia, retinal lasers and was under topical antiglaucoma agents for IOP management.

When he returned back to Nepal, he had attack of hypopyon anterior uveitis in RE (Figure 1B). Vision was 6/9 and 4/60 in right and left eye respectively. Posterior chamber intraocular lens was present in right eye while posterior subcapsular cataract (PSCC) was present in left eye. Fundus examination (Figure 3A & B) found cup-to-disc ratios of 0.7 and 0.4 in right and left eye respectively, with laser marks of pan-retinal photocoagulation in both eyes. As his etiology was not confirmed and was steroid responder, he was referred to a tertiary eye care centre of India. In India, he was thoroughly evaluated with detailed history and extensive work-up including complete blood count (CBC) with differential counts, blood sugars, ESR, serum Angiotensin Converting Enzyme (ACE), serum calcium and phosphorus, HRCT chest which are all within normal limits. He had negative serum ANA, rheumatoid factor, cANCA, Quantiferon TB gold test, VDRL, FTA-Abs, PCR for viral, microbial and protozoal causes. OCT macular showed macular edema, right more than left (CRT 322µm and 286 µm in right and left eye respectively). He had positive HLA B51 typing and ferning pattern in widefield fluorescence fundus angiography (Figure 2A & B). Automated visual field showed moderate and mild visual field defect in right eye and left eye respectively. He was diagnosed as active bilateral ocular Behçet's disease and was started on oral Prednisolone and Cyclosporine along with antiglaucoma agents and was advised for biological agents in Nepal.

After rheumatologist consultation, investigations were repeated to rule-out any systemic infections, including CBC and differential counts, platelets, blood sugars, ESR, CRP, liver and kidney function tests, Interferon Gamma Release Assay (IGRA), VDRL, chest x-ray. After proper counselling about the side effects including the risk of TB in patients on biological agents and importance of regular follow-up, he was started on Inj. Adalimumab 40mg subcutaneously every 3-4 weeks, only with oral Methotrexate 20mg with Folic Acid 5mg once a week. The ocular inflammation

was under control and topical medications were tapered. After 6 months, patient underwent uneventful phacoemulsification with posterior chamber intraocular lens with pars plana vitrectomy with endolaser in left eye, along with perioperative coverage of oral steroids. Regular OCT was done every 3-6 monthly to rule out any macular edema or any other secondary changes.

Over 1-year follow-up, the steroid was tapered off and the patient is on remission, with 6/9 vision in each eye and had received 12 doses of Adalimumab injection. He had no attacks of uveitis over the last 1 year follow-up.

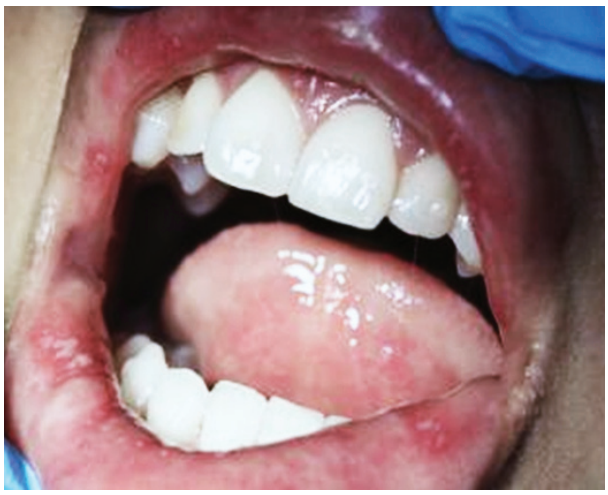

Figure 1 A: Oral ulcers at the time of diagnosis.

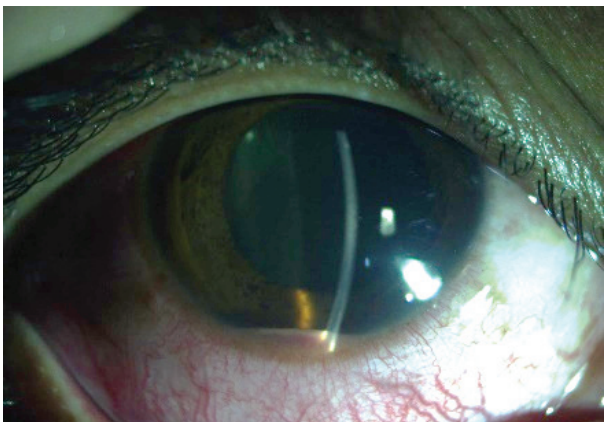

Figure 1 B: Acute anterior uveitis with hypopyon at the time of diagnosis.

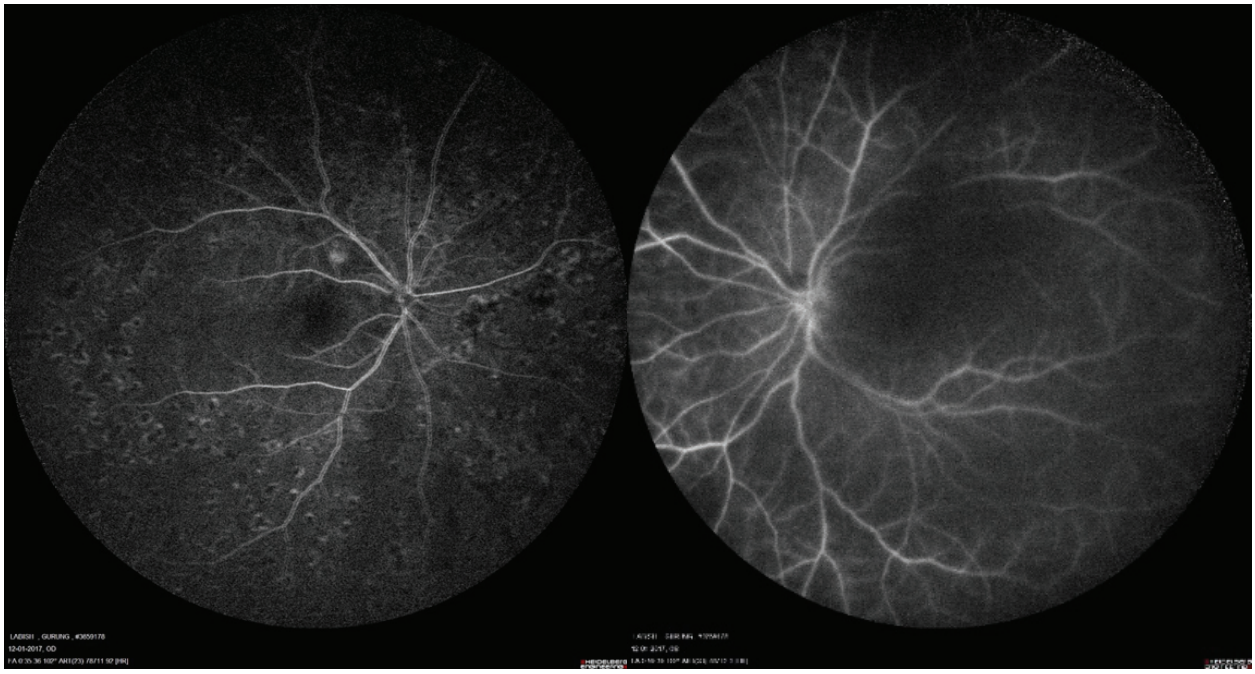

Figure 2A & B: widefield FFA showing ferning pattern in Right eye (fig. A) and left eye (fig. B). Note the presence of laser marks of panretinal photocoagulation in right eye.

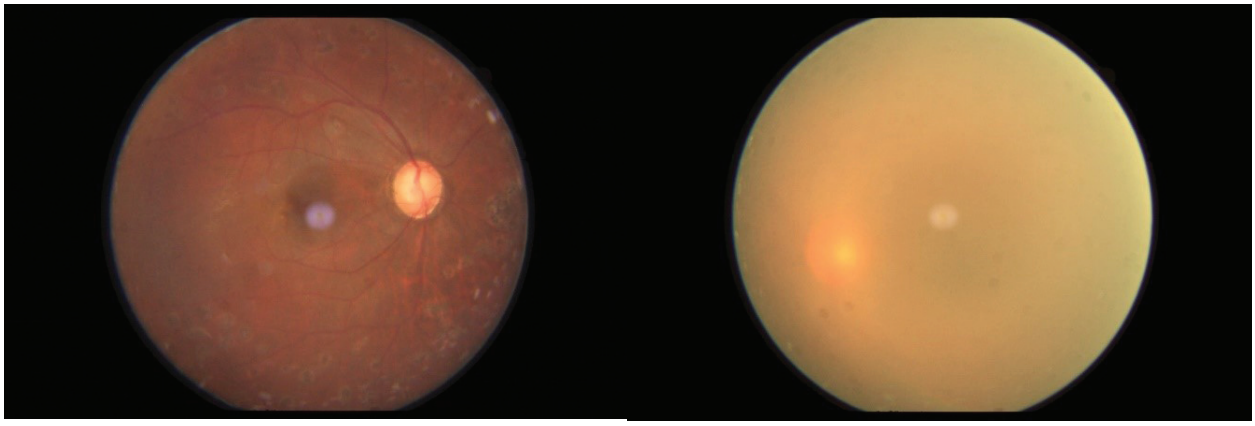

Figure 3A & B: Fundus photo showing enlarged cup with peripheral laser marks in right eye (fig.3A) and hazy view of fundus of left eye due to PSCC (fig.3B)

Discussion

Behcet's disease (BD) is a rare immune-mediated systemic vascular disorder, named after the Turkish Dermatologist, Hulusi Behcet in 1937, which is characterized by relapsing and remitting episodes of ocular inflammations, genital and oral apthae, gastrointestinal disease, skin lesions, mucosal ulcers, neurologic disease, arthropathy, and pulmonary, renal and vascular disease and musculoskeletal involvement (Yurdakul S et al, 2004; McNally TW et al, 2017)).

It is believed to exist in many parts of the world with high incidences in the Middle East, Far East, and Mediterranean region and in an area of the ancient trade route known as "Old Silk Road" in Asia and Europe between latitudes 30° and 45° north (Davatchi F et al 2014). In Nepal, Behçet's disease was reported from tertiary hospital in 0.3% of all uveitic patients (Baba SJ et al, 2017).

Evidence suggests that the pathogenesis of BD requires an unusual immune response in patients who are genetically predisposed to the disease following exposure to an exogenous agent, probably infective, supporting the involvement of human leukocyte antigen B51 (HLA-B51) (McNally TW et al, 2017). Infectious agents, such as Streptococcus sanguis, Herpes simplex virus, hepatitis viruses, and parvovirus B19 have been implicated as causes of Behçet's disease (Ryo Rokutanda et al, 2015).

BD can involve the anterior, intermediate and posterior uveal tract or either in isolation, or in combination as panuveitis. Up to 30% of patients with uveitis due to any cause experience significant visual impairment or legal blindness. Uveitis, therefore, has a significant impact on quality of life (Sirichai P et al, 2014).

The aim of treatment of ocular BD is to control the inflammatory process in order to preserve sight and to prevent the recurrence of the disease (McNally TW et al, 2017).

Although systemic corticosteroids are commonly prescribed, the occurrence of unwanted side effects and associated detrimental impact on quality of life limit the long term usage. Potential side effects include weight gain, hypertension, glucose intolerance, osteoporosis and disturbance of mood. Used as adjunctive immunosuppressive therapy, the Steroid Sparing Agents (SSA) allow reduction of corticosteroid dose, reducing adrenocorticotrophic side effects, but may have serious side effects and require close monitoring. Biological agents allow more targeted immune modulation and thus appear

to have a more desirable side-effect profile, while offering a greater efficacy.

Tumor Necrosis Factor (TNF) inhibitors have become available for several rheumatic diseases, and substantial published data indicate that TNF inhibitors represent a significant therapeutic advance for patients with severe and resistant disease, as well as for those with contraindications or intolerance to these treatments (Ryo Rokutanda et al, 2015). But these are not much in practice in Nepal due to high cost. Tumor Necrosis Factor - α (TNF-α) inhibitors like Infliximab, Adalimumab and Etanercept have been shown to significantly improve the outcome of uveitis in BD (McNally TW et al, 2017). Adalimumab (Humira; AbbVie, Inc., North Chicago, IL, USA) is a human-derived monoclonal antibody directed against TNF-α, which has been demonstrated as a successful first line treatment (McNally TW et al, 2017). A 40mg injection once every two weeks has been proven to be well tolerated, however potential side effects such as hypersensitivity reactions, infections, heart failure, risks of TB and demyelination have been reported (McNally TW et al, 2017).

In our case, the patient with multiple recurrences of ocular Behçet's disease had controlled the inflammation after the biological agent, Adalimumab has been started. The patient did not have any side effects of the medication and was on regular follow-up with good compliance, with complete awareness and understanding of the manifestations of his ailment.

Ocular BD, a disease of waxing and waning nature, the patient compliance in terms of regular follow-up and adherence to medications, is utmost important. This requires proper counseling so as to avoid ocular morbidity and blinding complications of the disease. Adalimumab is very costly drug for average Nepalese patient as there is no provision of insurance coverage. But, it proved to be effective in controlling the recurrence of the uveitis in our community too.

Conclusion

Adalimumab is effective treatment for refractory BD uveitis with sparing effects of conventional immunosuppressants and corticosteroids. However, repeated injections are required to maintain long-term remission of the *typically waxing and waning* course the disease.

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