Behcet's Disease: A Satisfactory Response to Adalimumab

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Behcets Disease (BD) is characterized by oral and genital ulcers, ocular manifestations, arthritic, vascular, central nervous system and gastrointestinal involvement and usually affects young adults. A thirty-six-year-old Bahraini female with recurrent ocular panuvieitis presented with history and clinical criteria was diagnosed with Behcets Disease (BD) despite a negative HLA B51. The eye involvement was characteristic of BD and she was managed systemically with Adalimumab and responded satisfactorily.

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Behcet's disease (BD) is an immune-mediated systemic vascular affliction caused by an autoimmune response to an infectious or environmental insult in a genetically predisposed individual[2].

Diagnosis of Behcet's disease is characterized by recurrent oral and recurrent genital ulcers that tend to scar, uveitis, skin lesions or a positive pathergy test[2]. In addition to the skin, rheumatoid arthritis, thrombophlebitis, gastrointestinal disorders, kidney, respiratory system and rarely CNS changes could occur[1].

Ocular disease affecting the retina and uvea could be seen in up to 70% of patients leading to blindness in 25%. In 10%-20% of patients, eye manifestations may present first but they usually appear 2-3 years after the mucocutaneous lesions. Joint involvement is reported in 45-60% of BD and is usually non-erosive and non-deforming. Gastrointestinal manifestations take up to 26%, varying in different populations[1].

Chronic recurrent uveitis could lead to major morbidity including blindness if untreated promptly. Both anterior and posterior uveal tracts can become affected starting with a cold hypopyon and reaching up to the optic nerve with papillitis.

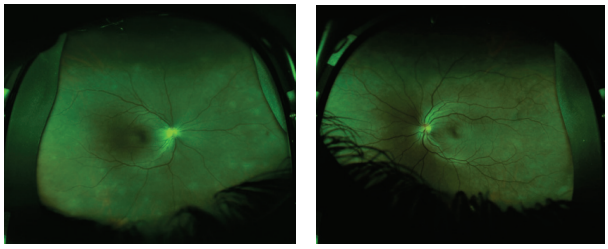
The main objective of BD management is to induce and maintain remission and improve quality of life and prevent irreversible damage to the involved organs. Adalimumab is a biologic anti-TNF α agent. It is approved for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, and psoriasis[8]. Recently, the American Uveitis Society proposed new recommendations for the use of anti-TNF-α biological agents in patients with ocular inflammatory disorders. In these recommendations, infliximab and adalimumab are the best options for the treatment of ocular manifestations of BD[8].

The aim of this report is to present a case of Behcet's disease and its successful management with Adalimumab.

THE CASE

A thirty-six-year-old Bahraini female presented with bilateral eye pain and redness of one-month duration, it was associated with a mild blur in her vision especially in her right eye.

The visual acuity was 6/12 OD and 6/9 OS with iridocyclitis in both her eyes, a cellular reaction of around 4 cells with flare, hypopyon of 2 mm and fresh keratic precipitates on the endothelium of her corneas. Her Intraocular Pressure (IOP) was normal. Fundus examination revealed a swollen appearing optic disc in her right eye and mid-peripheral and peripheral creamy looking lesions with associated flame hemorrhages in some sectors, see figure 1.



A B

Figure 1:Wide Field Fundus Photograph Showing Creamy Coloured Ill-Defined Peripheral Retinal Lesions in All Quadrants A: Right fundus B: Left fundus

Mild vitirits in both her eyes was seen; however, the macula was normal except for mild diffuse thickness revealed on Optical Coherence Tomography (OCT), see figure 2.

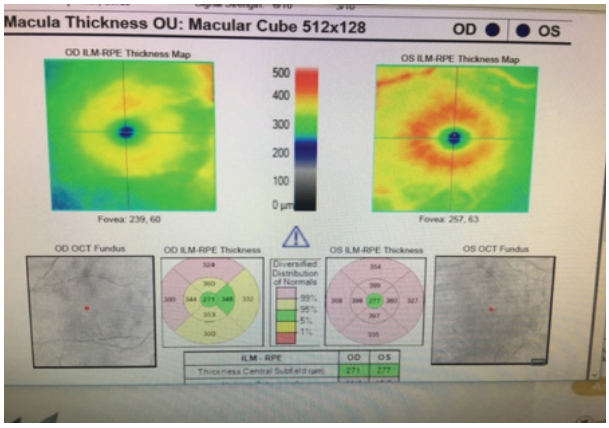


Figure 2: Thickening of the Macula on Optical Coherence Tomography (OCT)

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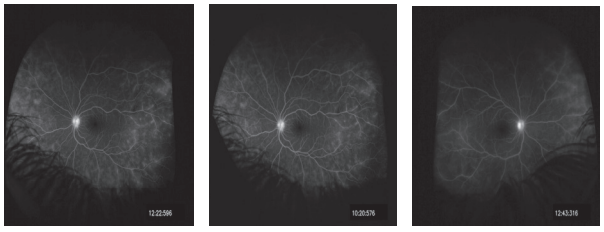
A provisional clinical diagnosis of bilateral non-granulomatous panuveitis was contemplated. History revealed joint pains and oral ulcers since she was a teenager especially around the time of menstruation. She had a rudimentary left cervical rib which showed no stenosis or vascular compromise. She had multiple visits over the past few years to the primary health care facility for non-specific gastritis, myositis and fleeting arthritis symptoms. Hourly topical steroids and cycloplegia were initiated.

The patient had a good response to the topical treatment with resolution of her symptoms and the inflammation in the anterior segment of the eye; also the lesions in her fundus appeared to have faded away, the optic disc swelling remained subtle and no macular edema developed. A wide-field fluorescein angiogram was normal with no leakage or staining. A brain magnetic resonance imaging and clear chest x-ray were normal. She had a negative PPD test. All her serology including her viral screen, ESR, serum ANCA were negative and within normal ranges. She had no HLA B51 allele.

Less than two months later, she presented with a flare-up of uveitis in both her eyes, a small cold hypopyon, minimal vitritis only and no retinal or choroidal signs. She was not keen on starting immunosuppression or biologics due to possible side-effects. A tapering course of oral steroid and regular follow-ups over three months period resulted in a complete resolution of her eye symptoms as well as her frequent joint discomforts. Her visual acuity was 6/6 in the right eye and 6/6p in the left eye, both eyes showed again non-granulomatous type of uvieits, with the same retinal focal creamy lesions and hemorrhages. Macular OCT was normal but on a repeated wide field FFA there appeared to be peripheral vasculitis involving primarily the arteries and veins associated with hot discs in the right eye more than the left eye, see figure 3.



A1 A 2 B

Figure 3: Peripheral Vasculitis and Hot Disc Appearance in the on Wide Field Fundus Fluorescein Angiography (FFA) A1 , A2: Left fundus B: Right fundus

The intensity of topical steroids was increased to hourly and started on Humira (Adalimumab 40 mg SC) twice weekly and remained on the minimum dose of 5 mg prednisolone per day. After one month she showed complete resolution of symptoms and the fundus changes disappeared and the cellular reaction came down to minimal occasional cells. A follow-up FFA in 3 months revealed complete resolution of the vasculitis in the vessels and recovery of the "hot disc" appearance in the right eye and no new-onset cystoid macular edema. She did not complain of any side-effects of Humira.

DISCUSSION

BD is a chronic disease with remissions and exacerbations affecting multiple organ systems through occlusive vasculitis[2]. It is common in the Middle and the Far East along the latitudes 30-45 degrees north in Asia and the Mediterranean basin which corresponds to the Old Silk Route used by traders from the East to Europe and one of the major causes of acquired blindness in the Middle East and Japan[13]. In Bahrain, the prevalence of the disease was not studied; it could be presumed that our prevalence is similar to Saudi Arabia (20%) because of very close and approximate racial and ethnic similarities[12].

Our patient fulfilled some major and some minor criteria of BD, but would be categorized as "Incomplete Behcet's" (2 major criteria - oral ulcers and eye inflammations and 2 minor criteria - arthritis and gastric involvement)[13]. Our patient's retinal findings disappeared spontaneously during her first attack with an only topical steroid which is another feature of BD.

Proper collaboration with rheumatologists is key for managing systemic diseases with uveitis especially as some systemic immune-modulatory drugs could have some side-effects; they are preferred to control the recurrent eye inflammations specifically with BD to prevent serious future implications on the visual acuity. Our patient responded very well to Humira (Adalimumab). Generally, Humira has been proven to be safe and effective in many cases of ocular inflammation[7]. Humira has been proven to be effective in Infliximab refractory BD[6,8]. In a study by Enterlandi et al, Humira showed to be highly effective in 91% of Behcets uveitis[8]. Adalimumab (Humira) has proven to be effective in cases of Behcets with a high safety profile[11].

CONCLUSION

Behcets disease is a systemic vasculitic that affects young people and could present with serious ocular involvement that needs to be managed properly to save the vision. Not all cases of BD are typical and high suspicion is warranted by the ophthalmologist when it comes to eye findings. The patient needs to be treated aggressively. Adalimumab has proven to be effective and safe for Behcet's disease and specifically for ocular involvement and should be considered as first-line management.

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