How challenging can it be to treat Behçet uveitis?

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Abstract:

A 20-year-old male Behçet uveitis (BU) patient presented with visual acuities (VAs) of hand movement in OD and counting fingers at 1 m in OS following treatment with corticosteroid monotherapy elsewhere. He had active intraocular inflammation OU along with macular hole and retinal detachment in OS. Infliximab (IFX) was started and vitreoretinal surgery was performed. He had infusion reaction with IFX, hepatotoxicity and depression with interferon, and resistance to adalimumab and tocilizumab therapies. Cytomegalovirus retinitis developed in OD following intravitreal dexamethasone implant and endophthalmitis developed in OS. At the 33rd month of follow-up, the patient was in clinical remission; however, there was persistent angiographic inflammation under certolizumab pegol, cyclosporine, mycophenolate mofetil, and low-dose prednisolone treatment. The left eye was phthisical and VA was 0.4 in OD. Immunomodulatory treatment is given based on the severity of inflammation in BU and needs to be closely monitored for efficacy and adverse effects.

Keywords:

Adverse effects, Behçet uveitis, immunomodulatory treatment

Introduction

Behçet uveitis (BU) is characterized by bilateral nongranulomatous panuveitis and retinal vasculitis with a relapsing–remitting course. The frequency and severity of uveitis attacks vary during the course of the disease and may be asymmetrical between the two eyes.[1] The ultimate goals in treating BU are to control the intraocular inflammation promptly, to prevent recurrences, and to achieve angiographic remission with favorable visual outcomes.[2] Herein, we report a case of BU with therapeutic challenges.

Case Report

A 20-year-old male patient presented to our clinic with a complaint of visual loss in both eyes. He had a history of recurrent uveitis attacks and oral ulcers, arthralgia, and human leukocyte antigen-B51 positivity. He had been treated with local and high-dose systemic corticosteroid (CS) for 1 year elsewhere. He had a Cushingoid appearance and was still on oral prednisolone 80 mg/day at presentation. Initial ocular examination revealed visual acuities (VAs) of hand movement in OD and counting fingers (CFs) at 1 m in OS. There were 0.5+ cells in the anterior chamber and 1+ cells in the vitreous of both eyes and posterior synechiae in OS. Fundus examination revealed mild vitreous haze, a retinal infiltrate with hemorrhage at the macula and inferior pearl-like precipitates in OD, and macular hole and inferior retinal detachment in OS [Figure 1]. Laser flare measurement was 31/29 ph/ms and intraocular pressures (IOPs) were 11/18 mmHg. Optical coherence tomography (OCT) showed foveal atrophy and juxtafoveal local inner retinal thickening, hyperreflectivity causing shadowing, and juxtapapillary subretinal fluid in OD, and macular hole and retinal detachment in OS [Figure 2]. There were bilateral optic disc staining and diffuse fern-like retinal capillary leakage on fluorescein angiography (FA) [Figure 2]. The patient was diagnosed with severe BU and immediately started on infliximab (IFX) 6.5/mg/kg infusions with a loading dose along with cyclosporine-A (CsA) 3 mg/kg/day and azathioprine (AZA) 1.6 mg/kg/day. Systemic CS was tapered. Pars plana vitrectomy with silicone oil tamponade and scleral buckle surgery was performed on the 2nd day of admission, 1 day after IFX infusion. Intravitreal dexamethasone

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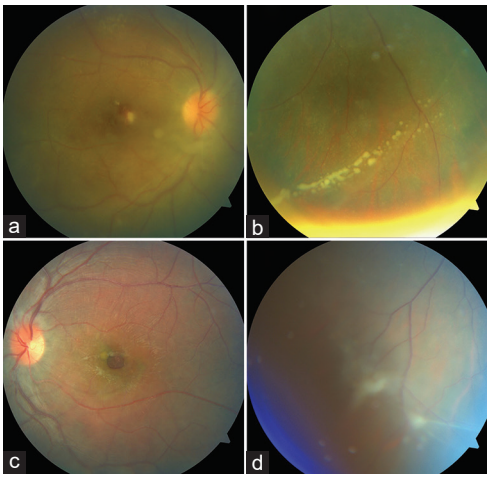

Figure 1: Color fundus photograph at presentation shows mild vitreous haze, a retinal infiltrate with hemorrhage at the macula (a) Inferior pearl-like precipitates in the right eye (b) Macular hole (c) Inferior retinal detachment in the left eye (d)

implant was injected in OD on the 5th day. At week 2 of follow-up, VA was 0.15/CF at 1 m. He showed severe infusion reaction on the 2nd IFX infusion. We discontinued IFX, AZA, and CsA and switched to Interferon (IFN) 3 miU/day treatment. Topical antiglaucomatous medication was started due to the right IOP rise (26 mmHg). IFN-induced hepatotoxicity and depression were noticed on the 10th day of IFN therapy. IFN was stopped and liver function tests returned to normal limits within 2 weeks. VA at 3rd month was 0.4/CF at 1 m. FA revealed optic disc hyperfluorescence OU, peripheral mild vascular and capillary leakage OD, and diffuse fern-like retinal capillary leakage OS. OCT showed foveal atrophy and juxtafoveal scar OD and mild cystoid macular edema and disruption of the outer retinal layers OS. Adalimumab was started at a loading dose of 80 mg. However, at the 12th week, we observed cytomegalovirus retinitis [Figure 3] in OD which was confirmed with aqueous humor polymerase chain reaction analysis, and adalimumab treatment was interrupted for 2 weeks. A single dose of intravitreal ganciclovir injection was performed and intravenous ganciclovir 5 mg/kg twice daily was given for 12 days followed by oral valganciclovir for 2 months. At 6th month of follow-up, there was persistent leakage on FA and cystoid macular edema on OCT while on adalimumab treatment. Therefore, CsA 200 mg/day was added to the treatment. The replacement of emulsified silicone oil was performed and the patient was diagnosed with *Haemophilus influenzae* endophthalmitis 2 months after the replacement surgery and 10 days after a febrile illness [Figure 4]. Lensectomy and silicone oil removal was performed, and based on the antibiogram, intravenous meropenem was given for 3 weeks. Then, we switched to intravenous tocilizumab 8 mg/kg/month due to severe angiographic inflammation. Mycophenolate mofetil 2 g/day was also added to the treatment and CsA was continued as well. However, recurrent uveitis attacks occurred in OD at the 11th month of tocilizumab therapy. We switched to certolizumab pegol initially with a loading

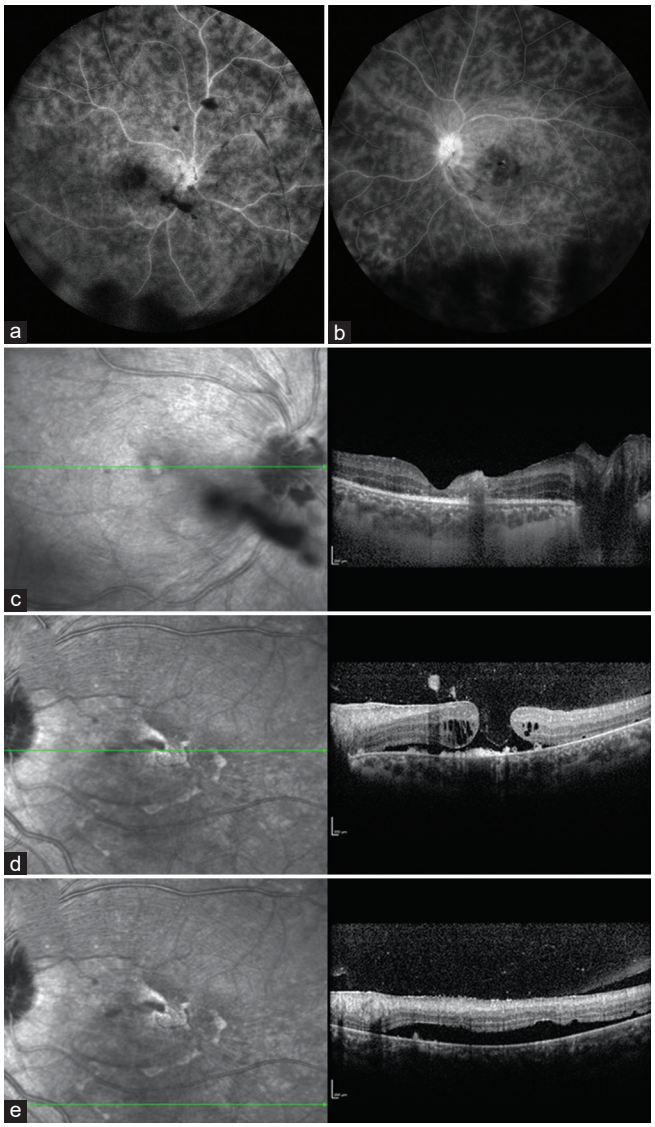

Figure 2: Wide-field FA of the right (a) The left eye (b) At presentation shows optic disc staining and diffuse fern-like retinal capillary leakage. OCT scan of the right eye (c) Foveal atrophy and juxtafoveal inner retinal thickening, hyperreflectivity causing shadowing and juxtapapillary subretinal fluid in the right eye; macular hole (d) Retinal detachment in the left eye (e). FA: Fluorescein angiography, OCT: Optical coherence tomography

dose. Every 2-week dose interval of certolizumab pegol was changed to weekly injections due to uncontrolled inflammation. At the final visit (33rd month of follow-up), the patient was in clinical remission; however, there was still persistent angiographic inflammation [Figure 5] under certolizumab pegol 200 mg/week, CsA 200 mg/day, mycophenolate mofetil 2 g/day, and prednisolone 7.5 mg/day treatment. The left eye was phthisical and his VA was 0.4 in OD and hand movement in OS.

Discussion

Timely diagnosis and prompt institution of immunomodulatory agents and monitoring side effects are crucial for optimal and

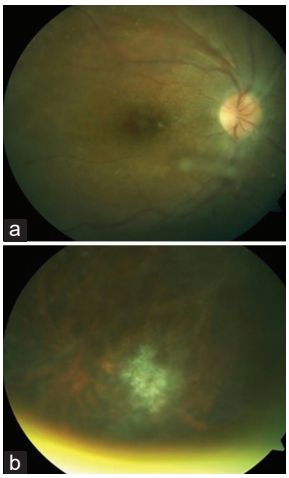

Figure 3: Color fundus photograph of the right eye shows vitreous opacities and juxtafoveal scar at the posterior pole (a) Granular type cytomegalovirus retinitis at the inferior periphery (b)

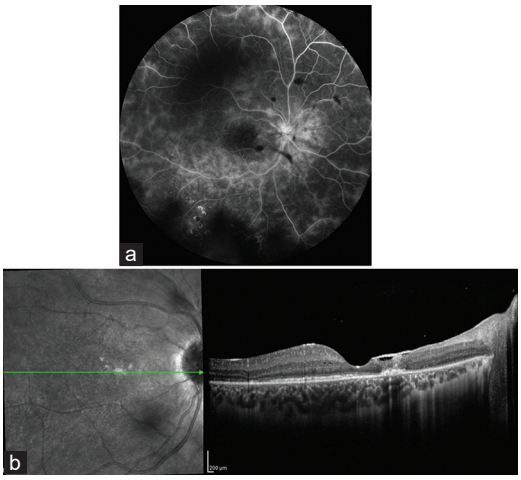

Figure 5: FA of the right eye (a) At the final visit shows blockage due to cataract, vitreous opacities, optic disc hyperfluorescence, and vascular and capillary leakage. OCT of the right eye shows epiretinal membrane and juxtafoveal scar (b). FA: Fluorescein angiography, OCT: Optical coherence tomography

early control of ocular inflammation in BU.[2-8] CS monotherapy may cause severe visual loss as it fails to prevent recurrent uveitis attacks. Serious adverse events may develop in the course of aggressive immunomodulatory treatment such as hepatotoxicity, infusion reaction, and opportunistic infections as in the present case. Prompt recognition and appropriate management of adverse events are essential.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

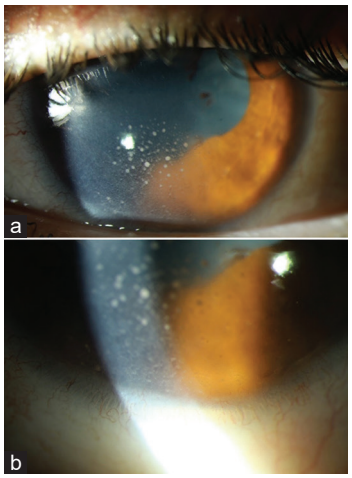

Figure 4: Anterior segment photograph (a and b) shows granulomatous keratic precipitates and hypopyon in the left eye

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Conflicts of interest

There are no conflicts of interest.

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