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CASE REPORT

Intravitreal dexamethasone implant as an option for anti-inflammatory therapy of tuberculosis uveitis

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Abstract

Introduction Tuberculosis-associated uveitis remains a diagnostic and therapeutic challenge. After diagnosis of tuberculosis and initiation of anti-tuberculosis therapy for tuberculosis uveitis, the clinical responses are favorable. However, at 4–6 weeks of the therapy, there commonly occurs paradoxical deterioration due to an increase in inflammation which is often accompanied by cystoid macular edema. Thus, adjuvant administration of anti-inflammatory regimen should be considered. For this purpose, systemic and periocular steroids, systemic and intravitreal immunosuppressive agents have been tested. Nevertheless, there is no report in the literature about intravitreal dexamethasone slow-release implants for the treatment of this inflammatory condition.

Methods Case presentation.

Results We presented a tuberculosis uveitis case whose ocular inflammation is partially modified by systemic and periocular steroid injections and then well controlled by the intravitreal dexamethasone implant.

Conclusion Intravitreal dexamethasone implant injection seems to be a safe and potent option for the treatment of macular edema secondary to tuberculosis uveitis.

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Introduction

Tuberculosis (TB) is still a relatively prevalent infectious disease caused by the pathogen *Mycobacterium* tuberculosis [1, 2]. Extra-pulmonary manifestation of TB can be associated with pulmonary infection or be isolated. Besides the typical systemic manifestations, ocular involvement is a well-known manifestation of extra-pulmonary TB [1, 2]. The most common clinical signs of intraocular TB are retinal vasculitis, multifocal serpiginous choroiditis and choroidal or optic disk granulomas [1, 2]. Although sometimes challenging to diagnose, ocular TB mostly responds to anti-tuberculosis therapy (ATT) favorably [3]. However, a paradoxical response to ATT has been described in some patients with TB uveitis, consisting of progression of the inflammatory component of the disease despite appropriate antimicrobial treatment [4]. This paradoxical worsening is thought to be a hyperacute immunologic reaction occurring against antigen load released after anti-TB therapy [4]. This phenomenon may be suppressed by the addition of systemic corticosteroids or other immunosuppressive agents to the treatment [1–4]. In the literature, there are limited data about the use of intravitreal steroids in

the treatment of posterior infectious uveitis and associated cystoid macular edema [5]. Herein, we report a tuberculosis uveitis case associated with cystoid macular edema, whose inflammation is well controlled by the intravitreal dexamethasone implant.

Case report

A 44-year-old woman consulted our clinic with the complaint of vision loss in her both eyes. Best-corrected visual acuity (BCVA) was found to be counting fingers at 2 m for the right eye and 20/20 for the left eye. Ophthalmic examination revealed bilateral anterior chamber non-granulomatous inflammatory reaction, + 3 cells and + 2 flare in both eyes. Intraocular pressures were 15 mmHg in both eyes. She had no lens opacities in both eyes. Fundus examination showed + 3 vitritis in the right eye. Even though the fundus view was very hazy due to media opacities, presumed subretinal granulomas with overlying vitritis located close to optic disk could be observed (Fig. 1a). In the left eye, + 1 vitritis was observed with multiple tubercle-like lesions in the posterior pole and mid-periphery (Fig. 1b). Consequently, systemic evaluation revealed a lung nodule on the chest X-ray. The lung nodule was biopsied, and pathological analysis of the biopsy material revealed necrotic caseous granuloma. Finally, polymerase chain reaction (PCR) of the biopsy specimen showed mycobacterium, which confirmed the diagnosis as tuberculosis. ATT regimen (isoniazid 5 mg/kg, rifampicin 10 mg/kg, ethambutol 25 mg/kg, pyrazinamide 30 mg/kg) was initiated, which is then followed by the addition of methylprednisolone 1 mg/kg in 2 weeks with a plan to gradual tapering. At the third week, patients BCVA improved to 20/200 in the right eye. Fundus lesions and the vitritis in both eyes started to subside (Fig. 2a, b). Spectral domain optical coherence tomography (SD-OCT) showed normal retinal architecture in both eyes (Fig. 2c, d).

At the sixth week of therapy, the patient complained about decreased vision where examination revealed a slight decrease in BCVA to 20/400 in the right eye. Left eye BCVA was 20/20. Fundus examination showed no evidence of tuberculomas but persistence of + 1 to + 2 vitritis in the right eye (Fig. 3a, b). Additionally, SD-OCT revealed cystoid macular edema (CME) in the right eye (Fig. 3c, d). New onset of inflammatory reaction was assessed as a Jarisch–Herxheimer-like reaction to ATT. Therefore, a subtenon triamcinolone acetonide injection 40 mg/mL was applied to the right eye. A month later, vitritis resolved in the right eye (Fig. 3e) and BCVA improved to 20/50. However, CME persisted (Fig. 3g). Left eye had no vitritis or CME (Fig. 3f, h). Because of the persistent CME, an intravitreal dexamethasone implant (Ozurdex, Allergan, USA) injection is applied for the right eye. A month after the intravitreal dexamethasone implant application,

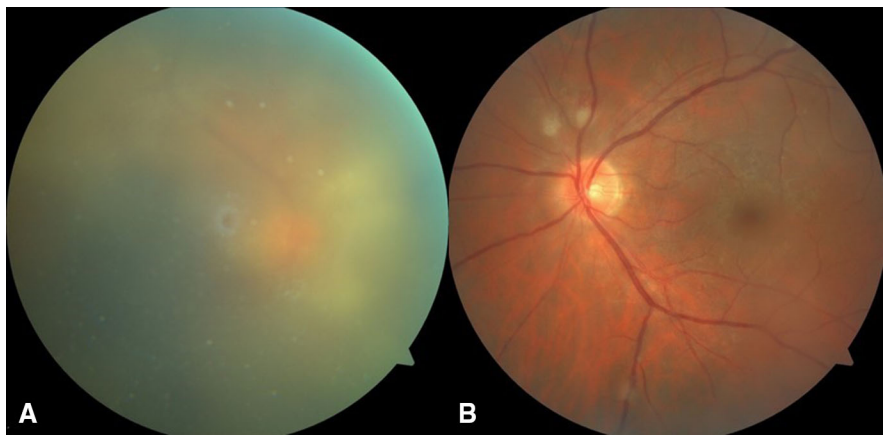

Fig. 1 Color fundus photographs of both eyes at the initial visit. **a** Right eye fundus photograph showing + 3 vitritis causing a hazy fundus view. Subretinal granulomas located close to optic disk with overlying vitritis could be appreciated. **b** Left eye fundus photograph showing round, whitish crème-colored subretinal tubercle lesions scattered mainly around the posterior pole with accompanying + 1 vitritis

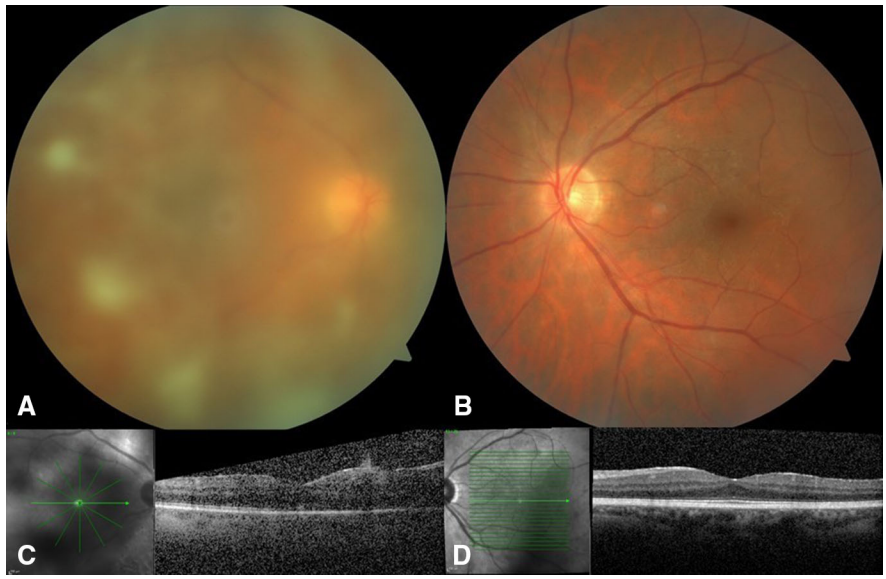

Fig. 2 Color fundus photographs (**a**, **b**) and spectral domain optical coherence tomography (SD-OCT) images 3 weeks after the anti-TB therapy (**c**, **d**). **a** Right eye fundus photograph; + 2 vitritis, subretinal granulomas started to subside. **b** Left eye fundus photograph showing regressing tubercles as greyish white pale spots. **c** SD-OCT of the right eye reveals a lot of optical interference because of vitritis but still normal retinal architecture. There was no evidence of cystoid macular edema. **d** SD-OCT of the left eye reveals normal retinal architecture through a clear vitreous. There was no evidence of cystoid macular edema

BCVA in the right eye improved to 20/32. There was no vitritis in both eyes (Fig. 4a, b). SD-OCT showed an epiretinal membrane in the right eye with only slight thickening of retina without any evidence of CME (Fig. 4c). Left eye was normal on SD-OCT (Fig. 4d). The patient did not experience any relapse for 10 months follow-up period; slight (+ 1) nuclear cataract and (+ 1) posterior subcapsular cataract progression were noted in both eyes. Intraocular pressures were in normal range for both eyes during the treatment and follow-up period.

Discussion

Various studies have addressed the utility of adjunctive anti-inflammatory therapy in the management of TB along with multidrug ATT [1–4]. Systemic corticosteroids which are used for 4–6 weeks especially for ocular TB cases thought to limit damage to ocular tissues caused from delayed-type hypersensitivity [1–4]. Except from the systemic route, intraocular administration of methotrexate and dexamethasone has also been utilized for anti-inflammatory therapy of presumed tuberculous serpiginous-like choroiditis [5–7]. After the Fonollosa and his colleagues' [8] first report about the use of intravitreal dexamethasone implants for tuberculous serpiginous-like choroiditis, we now report a case of granulomatous TB uveitis whose inflammatory component and associated cystoid macular edema were treated successfully with intravitreal dexamethasone implants.

Intravitreal injection of corticosteroids is a common procedure in the management of non-infectious uveitis and associated CME [9]. However, treatment of infectious posterior uveitis with corticosteroids is still under debate because of the risk of worsening of the infectious component of the disease [8, 9]. Therefore, ophthalmologists are rightfully likely to prefer a different approach when treating macular edema in the context of infectious disease. Recently, safety and efficacy of intravitreal dexamethasone implants in the management of infectious posterior uveitis and macular edema were assessed in a retrospective study [5]. The authors concluded that intravitreal dexamethasone implantation was useful and safe option in the treatment of macular edema secondary to infectious uveitis, both in terms of decreasing macular thickness and improving visual acuity [5]. Although the study is a small case series of seven patients, it is valuable as it

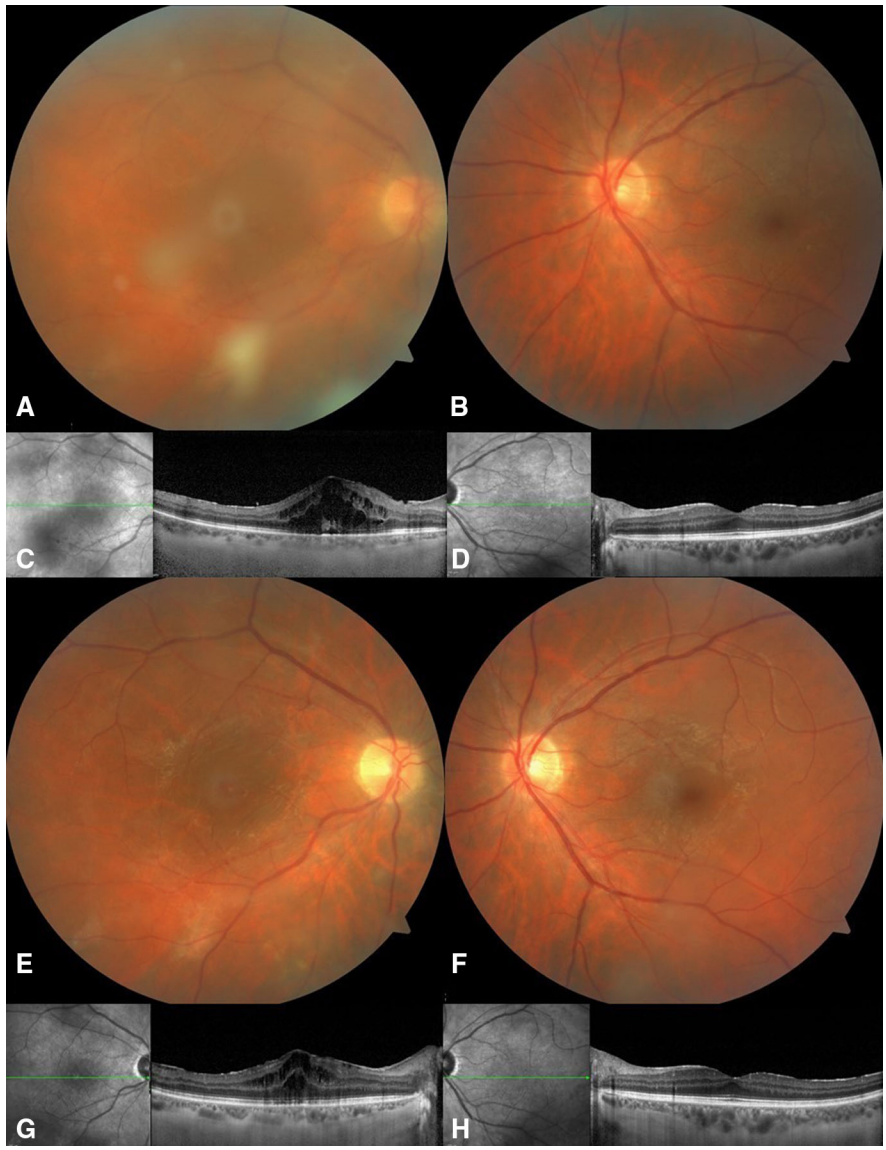

Fig. 3 Color fundus photographs and spectral domain optical coherence tomography (SD-OCT) images at the time of paradoxical inflammatory flare up (**a**, **d**) and 1 month after the subtenon triamcinolone acetonide injection (**e**, **f**). **a** Right eye fundus photograph; persistence of + 1 to + 2 vitritis. There was no retinal or subretinal lesion. Tuberculomas resolved. **b** Left eye fundus photograph showed no vitritis and/or tubercles. **c** SD-OCT of the right eye showed new onset cystoid macular edema. **d** SD-OCT of the left eye reveals normal retinal architecture through a clear vitreous. There was no evidence of cystoid macular edema. **e** Right eye fundus photograph, 1 month after subtenon triamcinolone acetonide injection, showed resolution of vitritis. **f** Left eye fundus photograph showed no vitritis and/or tubercles. **g** SD-OCT of the right eye showed resolution of vitritis but persistence of cystoid macular edema. **h** SD-OCT of the left eye reveals normal retinal architecture through a clear vitreous. There was no evidence of cystoid macular edema

included different types of infectious uveitis such as Herpes simplex virus-type 1, Varicella-Zoster virus, Treponema pallidum, Brucella melitensis, Borrelia burgdorferi, Toxoplasma gondii and cytomegalovirus with a definite diagnosis. Interestingly, the study did not include any case of ocular TB, where the hypersensitivity reaction known to trigger the initiation of the disease and the paradoxical response to ATT may cause clinical worsening of the disease despite appropriate antibiotic treatment [4]. In this

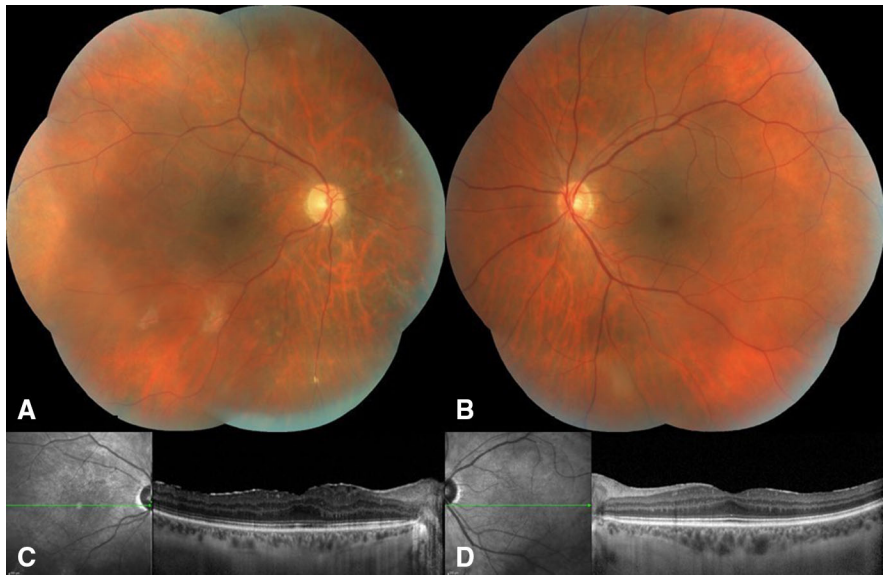

Fig. 4 Color fundus photographs and spectral domain optical coherence tomography (SD-OCT) images after the dexamethasone implant injection at the final visit. **a** Right eye fundus photograph showing only vascular sheathing at the mid-periphery. No vitritis or tuberculomas observed. **b** Left eye fundus photograph showed no vitritis and/or tubercles. **c** SD-OCT image of the right eye showing an epiretinal membrane and only a slight thickening of retina without any evidence of CME. **d** SD-OCT of the left eye reveals normal retinal architecture through a clear vitreous. There was no evidence of cystoid macular edema

current case, after the initiation of ATT and subsequent systemic corticosteroids, the patient developed an inflammatory response which is then only partially controlled with additional subtenon triamcinolone acetonide. This paradoxical response peaked at the sixth weeks of ATT which is in line with previous reports [1–4]. Subtenon TA was only sufficient to control the vitritis, but not CME. CME responded to an IDI injection which allowed a secure tapering of the systemic steroid treatment. We think that local management of this inflammatory response was important as it allowed avoidance of systemic immunosuppression, hence the associated risk of developing active systemic tuberculosis while limiting the ocular damage. Fonollosa et al. reported that more than one injection was needed to control the inflammatory reaction and uveitis. However, our patient did not experience any relapse after the first injection. Our patient did not develop corticosteroid-related ocular hypertension. On the other hand, slight cataract progression was noted during the follow-up, in both eyes.

To summarize, the treatment of TB uveitis may require both ATT for the control and eradication of the bacteria, and anti-inflammatory therapy for the manipulation of the accompanying inflammation. Concomitant treatment with appropriate antimicrobial agents should be initiated to rule out theoretical risk of reactivation or worsening of the ocular inflammatory infectious process before intravitreal steroid administration. IDI injection seems to be a safe and potent option for the treatment of macular edema secondary to TB uveitis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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