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Case report

Topical difluprednate for the treatment of retinal vasculitis associated with birdshot chorioretinitis

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ABSTRACT

Purpose: To report a case of retinal vasculitis associated with birdshot chorioretinitis which was responsive to topical difluprednate alone.
Observations: Two months after initiation of topical difluprednate, fluorescein angiography demonstrated resolution of retinal vasculitis in both treated eyes. Worsening of vasculitis with attempted taper of difluprednate and subsequent control with prior dosing confirmed the response.
Conclusions and importance: Despite potential adverse effects of steroid-induced glaucoma and cataract formation, topical difluprednate in the treatment of retinal vasculitis and other posterior uveitides may have efficacy.

1. Introduction

Topical difluprednate 0.05% is a potent steroid commonly used for the treatment of anterior uveitis. For sight-threatening posterior uveitis, topical steroid therapy is typically considered inadequate and systemic therapy is indicated. There are reports of using topical difluprednate to treat pars planitis and Harada's disease but none describing its use in birdshot chorioretinitis (BCR) [1,2]. Here, we report successful treatment of retinal vasculitis associated with BCR with topical difluprednate alone.

2. Case report

A 59-year old male with a history of HLA-A29 positive BCR diagnosed nine years prior presented for follow-up to the uveitis clinic at the Wilmer Eye Institute. He had been successfully treated with mycophenolate mofetil for two years but stopped the medication in preparation for cardiac bypass surgery six months prior to his clinic visit. After surgery, he had remained off all immunosuppression. He also had a history of mixed-mechanism glaucoma for which he had undergone trabeculectomy OS (oculus sinister, left eye). He was maintained on brimonidine 0.2%-timolol 0.5% BID OD (oculus dexter, right eye).

His visual acuities (VA) measured 20/20 OD and 20/15 OS. His intraocular pressures (IOP) were 13 mmHg OD and 12 mmHg OS. Slit lamp exam revealed trace anterior chamber (AC) cell OD and 1 + AC cell OS with trace vitreous cells and no haze OU (oculus uterque, both eyes). Dilated fundus exam revealed inactive appearing birdshot lesions and absence of cystoid macular edema or perivascular sheathing. The patient commenced topical difluprednate QID OS and continued loteprednol 0.5% BID OD.

Six weeks later, the patient's visual acuity was 20/20 OU, and his IOP was stable at 10 mmHg OD and 14 mmHg OS. He had controlled AC inflammation OU but 1 + vitreous cell without haze OD only. The dilated fundus exam appeared stable compared to prior; however, fluorescein angiogram (FA) was obtained to assess for occult vasculitis. The FA showed diffuse perivascular leakage consistent with retinal vasculitis OD (Fig. 1A). There was no angiographic evidence of vasculitis OS (Fig. 1B). Given the absence of vasculitis OS on topical difluprednate, we changed loteprednol to difluprednate QID OD and continued the same OS. We noted that a differential effect of topical difluprednate on retinal vasculitis may be expected, as he was pseudophakic status post laser capsulotomy OS and still had an early cataract OD.

Two months later, the patient's VA remained stable at 20/20 OU. FA demonstrated resolution of the retinal vasculitis OD (Fig. 1C) and no evidence of vasculitis OS (Fig. 1D). IOP, however, was 28 mmHg

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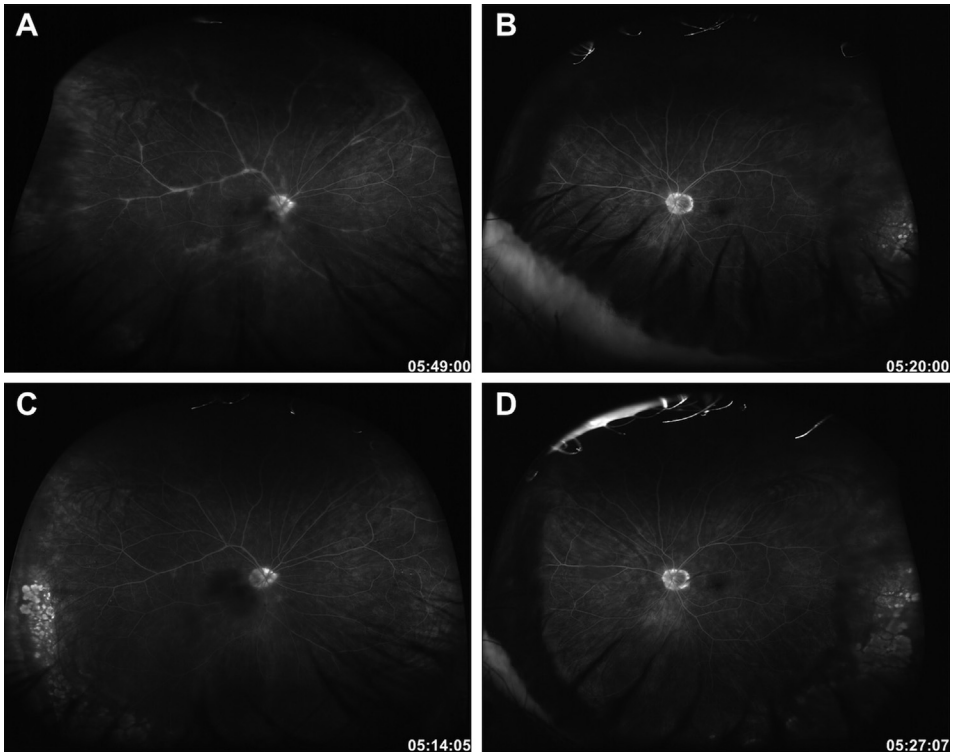

Fig. 1. Initial late phase fluorescein angiography photographs. Late phase fluorescein angiography photographs showing evidence of perivascular leakage OD before treatment with topical difluprednate (A), and resolution after two months of treatment on QID dosing (C). Corresponding late phase angiography photographs show no evidence of perivascular leakage OS (B, D) during continued therapy with topical difluprednate.

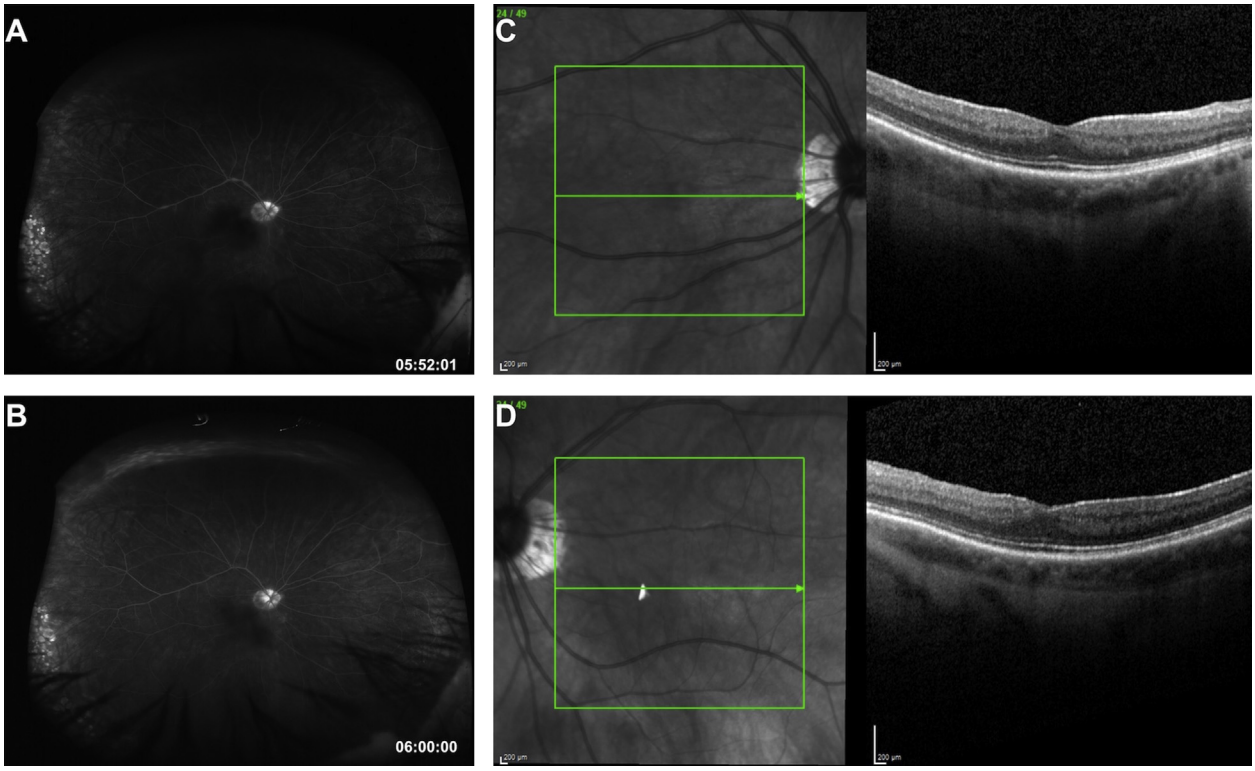

Fig. 2. Follow up late phase fluorescein angiography photographs and optical coherence tomography. Late phase fluorescein angiography photographs showing evidence of mild recurrence of perivascular leakage OD with tapering of topical difluprednate to daily (A), and resolution on subsequent BID dosing (B). Optical coherence tomography of the maculae of both eyes showing healthy ellipsoid zones and foveal contour, and no evidence of atrophy or cystoid macular edema OD (C) and OS (D).

OD and 11 mmHg OS. Latanoprost QHS was initiated OD, and the difluprednate was tapered gradually to daily OD and BID OS.

At the next visit six weeks later, the patient's VA remained at 20/20 OU, and IOPs were 15 mmHg OD and 14 mmHg OS. However, a mild recurrence of retinal vasculitis in the right eye only was noted on FA (Fig. 2A). The difluprednate was increased back to BID OD, and IOP lowering medication continued.

Three months later, having now received difluprednate monotherapy for six months OD and nine months OS, the patient's VA remained stable at 20/20 OU, and FA once again demonstrated no evidence of retinal vasculitis (Fig. 2B). IOP was 26 mmHg OD and 12 mmHg OS. Adequate control of his IOP was achieved with the addition of dorzolamide BID OD and oral acetazolamide 250 mg BID. Optical coherence tomography was obtained at this visit, which demonstrated healthy ellipsoid zones and the absence of atrophy or cystoid macular edema in both eyes (Fig. 2C,D).

3. Discussion

BCR is an uncommon, idiopathic posterior uveitis, for which standard therapy consists of systemic steroids, steroid-sparing immunosuppression including antimetabolites, T-cell inhibitors, and biologic response modifiers, and occasionally the use of intravitreal steroid injections and/or implants. Our case demonstrates resolution of retinal vasculitis associated with BCR with topical difluprednate alone. Our patient had a history of mixed-mechanism glaucoma and did develop steroid-induced ocular hypertension, but this was managed by tapering the difluprednate and initiating additional IOP-lowering medication. Notably, recurrence of retinal vasculitis was observed OD with tapering to daily dosing of topical difluprednate but resolved with resumption of BID dosing, providing additional evidence of a real treatment effect.

According to a recent report, topical difluprednate resolved the serous retinal detachments of three patients with Harada's disease [2]. In each case, hourly dosing was initiated with a variable tapering regimen based on clinical response. A mild steroid response was observed in two out of three patients, which was managed with topical IOP-lowering therapy. In addition, others have previously demonstrated efficacy in treating retinal edema from other causes such as pseudophakic cystoid macular edema and diabetic macular edema with topical difluprednate [3,4]. In a separate case report, twice a day dosing of topical difluprednate was adequate to treat pars planitis in a child for one year [1]. The child subsequently developed an atypical delayed steroid response with ocular hypertension that was refractory to medical management and rapid formation of a posterior subcapsular cataract, which necessitated cessation of the steroid.

Difluprednate is a prodrug that is converted to its active metabolite difluoroprednisolone butyrate by deacetylation after penetration of the corneal epithelium [5]. It is a potent topical corticosteroid owing to its high affinity for glucocorticoid receptors. Furthermore, its preparation as an emulsion may enhance absorption by the cornea [5]. In rabbits, topically applied difluprednate rapidly distributes throughout all ocular tissues, including the retina and choroid, with negligible systemic absorption [5], suggesting that complications and adverse events associated with systemic steroid and steroid-sparing immunosuppression may be obviated.

4. Conclusions

Despite potential adverse effects of steroid-induced glaucoma and cataract formation, our report suggests that topical difluprednate in the treatment of retinal vasculitis and other posterior uveitides may be considered as an adjunct or alternative to conventional immunosuppression, especially when standard therapy is contraindicated or poorly tolerated. We wish to underscore, however, that close IOP monitoring is imperative for any patient maintained on chronic difluprednate.

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