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CASE REPORT

Intravitreal triamcinolone acetonide for the management of papillophlebitis and associated macular edema

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Abstract *Background* To investigate the efficacy of intravitreal injection of triamcinolone acetonide in the management of papillophlebitis and associated cystoid macular edema. *Methods* This study was a retrospective medical records review of four eyes of four patients (three males and one female) who had approximately 2–4 months history of papillophlebitis and associated persistent cystoid macular edema. These patients were treated with a single intravitreal injection of 4 mg triamcinolone acetonide. Mean follow-up time was 15 ± 4 months. The outcome measures included best corrected visual acuity (BCVA), intraocular pressure (IOP), and central retinal thickness by optical coherence tomography (OCT). *Results* The BCVA ranged from 20/100 to 20/60 pre-operation. The mean gain in BCVA was 7 ± 1 Snellen lines. All eyes had BCVA of 20/20 at the last visit. The mean baseline central retinal thickness as measured by OCT was 529 ± 53 μm. The mean central retinal thickness by OCT was 235 ± 15 μm at 1-week follow-up examination. At the last visit the mean central retinal thickness by OCT was 161 ± 7 μm. One patient experienced an increase in IOP after the first injection and another patient had IOP elevation after the second injection. Both were well controlled with single topical anti-glaucoma medication. *Conclusion* Intravitreal injection of triamcinolone acetonide appears to be an effective treatment for patients with papillophlebitis and associated cystoid macular edema.

Keywords Cystoid macular edema · Intravitreal injection · Papillophlebitis · Triamcinolone acetonide

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Introduction

Papillophlebitis is an uncommon ophthalmologic condition of obscure etiology. Unlike classic central retinal vein occlusion (CRVO), patients suffering from this disease are usually healthy and younger than 50 years of age [1]. Most patients complain of blurred vision or photopsia. Typical ophthalmologic findings include unilateral optic disc edema, dilatation, and tortuosity of the major retinal veins with a variable amount of retinal hemorrhage [2, 3]. Traditional treatment for papillophlebitis includes systemic and periocular steroid therapy, platelet inhibitors or anticoagulation. However, the effect is controversial [4]. Intravitreal triamcinolone acetonide has increasingly been used for the treatment of diabetic macular

edema [5], neovascular glaucoma [6], retinal vein occlusion [7], chronic uveitis [8], and other clinical situations. The safety and efficacy of intravitreal triamcinolone acetonide have been well studied in animal models [9]. The purpose of this study was to evaluate the efficacy of intravitreal triamcinolone acetonide in the management of papillophlebitis and secondary cystoid macular edema.

Materials and methods

This study was designed as a retrospective medical records review. Between May 2004 and July 2005, patients with papillophlebitis were considered for enrollment in the study. Table 1 summarizes the inclusion criteria. Patients underwent clinical examination including the Snellen visual acuity test, intraocular pressure (IOP) measurement, slitlamp inspection of the anterior segment, dilated fundus examination with indirect ophthalmoscopy, fluorescein angiography (FAG), and optical coherence tomography (OCT-3, Carl Zeiss Meditec, Dublin, CA, USA) prior to the injection of triamcinolone acetonide (40 mg mL^{-1} Kenacort-A, Bristol-Myers Squibb). These four patients also received biochemical examinations for complete blood count (CBC), serum cholesterol, triglyceride, blood sugar, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), venereal disease research laboratory (VDRL), rheumatoid factor (RhF), and antinuclear antibody (ANA). All patients were observed for at least 2 months prior to undergoing this investigative treatment.

All patients gave written informed consent before intravitreal injection. All injections were carried out under sterile conditions in an operation room by a vitreoretinal surgeon. Topical (0.5%) proparacaine hydrochloride (Alcaine; Alcon) was used for anesthesia. Four milligrams (0.1 mL) of crystalline triamcinolone acetonide—without prior removal of the vehicle—was injected into the vitreous cavity by using a 27-gauge needle through the temporal upper pars plana, 4 mm from the corneal limbus. Postoperation, gentamycin eye drops were applied four times daily for one week.

Patients underwent postoperative follow-up with repeated clinical examination including Snellen visual acuity test, IOP measurement, dilated fundus examination, and OCT.

Results

The baseline and follow-up patient data are included in Table 2. There were three males and one female. The mean age of patients was 40 ± 11 years (range: 24–50 years). The biochemical examinations of these four patients were all unremarkable. The mean duration of symptoms before treatment was 3 ± 1 months (range: 2–4 months). The range of pre-operation best corrected visual acuity (BCVA) was 20/100–20/60. All eyes showed significant improvement on BCVA one week after treatment. Three out of four eyes (75%) had BCVA of 20/20 at 1 month post-operation. All four patients were followed up for at least 12 months (range: 12–20 months). Only case 1, with recurrent cystoid macular edema and a decrease in BCVA 6 months after treatment, received a second injection of triamcinolone acetonide, which led to better visual improvement than the first treatment course. During the follow-up period, the increase in visual acuity was stable in all four eyes.

All eyes had a significant reduction in central retinal thickness as demonstrated by OCT (Table 3). The mean central retinal thickness was 529 ± 53 μm pre-operation, and all eyes (3/3) had the thickness back to normal range at one month post-operation. Thereafter, the thickness showed no significant change at each time point. At the last follow-up, the mean central thickness was 161 ± 7 μm (range: 152–168 μm).

Table 1 Inclusion criteria

* Age cannot be older than 50 years
* Without systemic vascular disease or other systemic conditions (hypertension, diabetes, hyperlipidemia, and platelet abnormalities)
* Typical fundus finding of unilateral optic disc edema, dilatation, and tortuosity of the major retinal veins with a variable amount of retinal hemorrhage

Table 2 Summary of baseline and follow-up best-corrected visual acuity for four patients treated with intravitreal injection of triamcinolone acetonide

No/Sex/Age	Duration	Baseline	1 w	1 m	2 m	4 m	6 m	8 m	10 m	12 m	14 m	16 m	18m	Line gain	Time to recurrence	Re-injection
1/M/50 y	2 m	20/100	20/40	20/40	20/30	20/30	20/100	20/20	20/20	20/20	20/20	20/20	20/20	8	6 m	Y
2/M/45 y	3 m	20/100	20/30	20/20	20/25	20/20	20/20	20/20	20/20	20/20	20/20	20/20	N/A	8	N/A	N
3/M/39 y	4 m	20/60	20/30	20/20	20/20	20/20	20/20	20/20	20/20	20/20	N/A	N/A	N/A	6	N/A	N
4/F/24 y	3 m	20/70	20/25	20/20	20/20	20/20	20/20	20/20	20/20	20/20	N/A	N/A	N/A	7	N/A	N

The baseline and follow-up IOP are summarized in Table 4. After the first injection of triamcinolone acetonide, only one eye (case 4) developed IOP values of 22 mmHg or more and responded to single topical anti-glaucoma medication. In this case, the IOP maintained at baseline level after discontinuing anti-glaucoma medication for 4 months. Case 1 received a second injection of triamcinolone acetonide and the IOP increased to 25 mmHg two months after treatment. The IOP was well controlled by single topical anti-glaucoma medication and the medication was able to be discontinued over the course of follow-up. There was no difference between the baseline (15.5 ± 3.8 mmHg) and the last follow-up (16.0 ± 2.4 mmHg) in intraocular pressure ($p = 0.66$).

With the exception of IOP elevation, no other operation-related complications such as endophthalmitis, cataract, or retinal detachment were encountered.

Figure 1 is an illustrative case (case 3) that showed a good anatomical and functional response to treatment. This is a 39-year-old, otherwise healthy man who had sudden onset of blurred vision in his left eye for a duration of 4 months. His medical and ophthalmological history was unremarkable. Fundoscopy of the left eye showed venous tortuous and engorgement, congested optic disc edema, flame-shaped hemorrhages, and nerve fiber layer hemorrhages in the posterior pole (Fig. 1A). No abnormalities were found in the right eye. FAG showed significant disc edema and macular edema. There was no obvious retinal ischemia or neovascularization (Fig. 1B). OCT measured a central macular thickness of 468 μm in the left eye (Fig. 1C). One month after injection, the patient's BCVA in the left eye improved to 20/20. Fundoscopic examination showed a dramatic resolution in disc edema, hemorrhage, venous dilatation, and tortuosity (Fig. 1D). FAG showed almost complete resolution of optic disc edema and cystoid macular edema (Fig. 1E). The central macular measured by OCT also showed a dramatic decrease to 160 μm (Fig. 1F).

Discussion

There is currently no proven effective treatment for papillophlebitis and associated cystoid macular

Table 3 Summary of baseline and follow-up central retinal thickness (μm) from optical coherence tomography

No	Initial	1 w	1 m	2 m	4 m	6 m	8 m	10 m	12 m	14 m	16 m	18 m	20 m
1[a]	N/A	N/A	N/A	N/A	N/A	462	162	170	162	168	170	165	168
2	556	236	160	165	164	163	165	161	164	160	162	N/A	N/A
3	468	220	160	150	152	155	151	156	152	N/A	N/A	N/A	N/A
4	562	250	165	160	165	163	166	162	161	N/A	N/A	N/A	N/A

[a] Case 1 first visited our clinic in May 2004, which was 6 months earlier than the acquisition of OCT in our department

Table 4 Summary of baseline and follow-up intraocular pressure (mmHg)

No	Initial	1 w	1 m	2 m	4 m	6 m	8 m	10 m	12 m	14 m	16 m	18 m	20 m
1	15	16	16	15	16	16	25	17	16	18	15	19	16
2	13	14	18	19	13	14	14	15	14	16	13	N/A	N/A
3	13	18	18	17	17	15	14	14	16	N/A	N/A	N/A	N/A
4	21	23	25	23	21	20	20	20	19	N/A	N/A	N/A	N/A

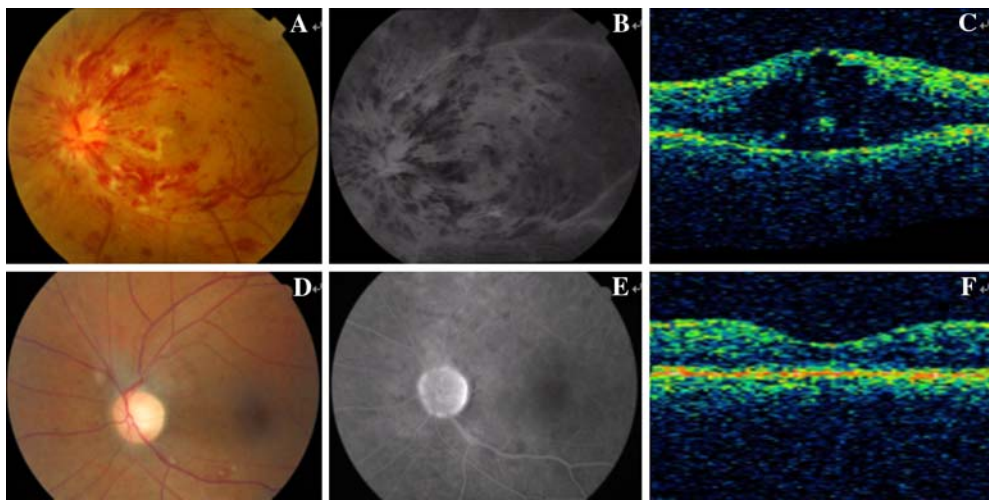

Fig. 1 Patient 3. (**A**) Pre-operation fundus photograph shows prominent congested disc edema, flame-shape hemorrhage in four quadrants, cotton wool spots, and tortuous retinal veins. (**B**) Late phase of fluorescein angiography performed before therapy showed cystoid macular edema. (**C**) Optical coherence tomogram taken before therapy also showed prominent macular edema. (**D**) One month after triamcinolone acetonide injection, there were marked resolution of disc edema and flame-shape hemorrhage. (**E**) In the late phase of fluorescein angiography, no obvious cystoid macular edema was observed. (**F**) Optical coherence tomogram taken 1 month after injection. The visual acuity improved along with resolution of macular edema

edema. Reviewing previous studies, a slow, spontaneous resolution over a 3 to 6 month period in papillophlebitis has been reported [1, 2, 10, 11]. Fong et al. reported that 54% of patients observed for at least 6 months had acuity of 20/40 or better at the time of the final examination [4]. However, some authors have shown some cases to have poor visual outcome, and present visual acuity does not appear to be predictive of visual or anatomic outcome [12]. Recchia et al. found that 40% of patients had final visual acuity of 20/200 or worse [12]. Frucht et al. reported that 55% of patients had visual acuity of counting finger or worse [13].

In this study, intravitreal triamcinolone acetonide was effective in improving visual acuity and reducing the degree of cystoid macular edema in patients with

papillophlebitis. The improvement in visual acuity was very dramatic: All four eyes had BCVA of 20/20 at the last visit. And the improvement in visual acuity was maintained for at least 12 months after treatment. The mean final visual gain was 7 ± 1 Snellen lines, which was very impressive. According to previous reports, patients with incomplete CRVO and good vision (20/200) often do quite well without treatment [1, 2, 10, 11]. However, the associated CME usually takes several months to resolve, and the functional damage is sometimes irreversible. Intravitreal triamcinolone acetonide can markedly improve the inflammation of the retinal vein and rapidly resolve the CME.

In patients with classic CRVO and associated cystoid macular edema, the improvement in visual acuity after injection with triamcinolone acetonide was not as effective as papillophlebitis. Cekic et al reported the mean final visual gain was 1.3 Snellen lines for a mean follow-up of 10 months [14]. Ip et al. found the mean gain in visual acuity was 2.2 Snellen lines at the 6-month follow-up [7].

Recurrent cystoid macular edema with a concomitant reduction in visual acuity only occurred in one of four patients (25%) at the 6-month follow-up examination. In classic CRVO, the rate of recurrent cystoid macular edema was much higher. Williamson et al. reported 67% of patients with CRVO encountered recurrent cystoid macular edema after injection of triamcinolone acetonide [15]. And, disappointingly, even repeated injections did not prevent deterioration in visual acuity at 12 months [15]. Cekic et al. found 10 of 24 eyes had recurrent cystoid macular edema after injection of triamcinolone acetonide [14]. A possible explanation of this finding might be the different etiology and pathogenesis of these two diseases. In papillophlebitis it might result from a phlebitis of major retinal veins surrounding the optic nerve. The inflammation promotes venous thrombosis, which produces papilledema [16]. However, the possible pathogenesis of CVRO might be the obstruction of the scleral outlet, which leads to "compartment syndrome" and thus results in persistent retinal hypoxia [17]. Although the mechanism of triamcinolone acetonide inducing resolution of papillophlebitis and associated cystoid macular edema is not well understood, it is probably due to the potent anti-inflammation character and the ability to reduce the breakdown of the blood-retina barrier [18]. However, in patients with CRVO, intravitreal triamcinolone acetonide can transiently reverse cystoid macular edema, but may need another method to restore blood flow and hypoxic condition. And radial optic neurotomy may be a method for inducing collateral formation to restore blood flow [17, 19].

In conclusion, intravitreal injection of triamcinolone acetonide may be a safe and effective treatment for papillophlebitis and associated cystoid macular edema and achieve rapid improvement in visual acuity. The effect seemed to be long-lasting. However, the main shortcoming of this study was a small sample size. Larger prospective studies are necessary to better ascertain the benefit of intravitreal triamcinolone acetonide in the management of papillophlebitis.

Reference

1. Lonn LI, Hoyt WF (1966) Papillophlebitis: a cause of protracted yet benign optic disc edema. Eye, Ear, Nose Throat Mon 45:62–68
2. Ellenberger C, Messner KH (1978) Papillophlebitis: benign retinopathy resembling papilledema or papillitis. Ann Neurol 3:438–440
3. Sanborn GE, Magargal LE (1988) Papillophlebitis: an update. In: Smith JL (eds) Neurophthalmology Entering the 90's. Masson, New York, pp 47–54
4. Fong ACO, Schatz H, McDonald HR, Burton TC, Maberley AL, Joffe L, Zegarra H, Nadel AJ, Johnson RN (1991) Central retinal vein occlusion in young adults (papillophlebitis). Retina 11:3–11
5. Jonas JB, Sofker A (2001) Intraocular injection of crystalline cortisone as adjunctive treatment of diabetic macular edema. Am J Ophthalmol 132:425–427
6. Jonas JB, Hayler JK, Sofker A, Panda-Jonas (2001) Regression of neovascular iris vessels by intravitreal injection of crystalline cortisone. J Glaucoma 10:284–287
7. Ip MS, Gottlieb JL, Kahana A, Scott IU, Altaweel MM, Blodi BA, Gangnon RE, Puliafito CA (2004) Intravitreal triamcinolone for the treatment of macular edema associated with central retinal vein occlusion. Arch Ophthalmol 122:1131–1136
8. Antcliff RJ, Spalton DJ, Stanford MR, Graham EM, ffytche TJ, Marshall J (2001) Intravitreal triamcinolone for uveitic cystoids macular edema: an optical coherence tomography study. Ophthalmology 108:765–772
9. Tano Y, Chandler BS, Machemer R (1980) Treatment of intraocular proliferation with intravitreal injection of triamcinolone acetonide. Am J Ophtalmol 90:810–816
10. Lyle T, Wybar K (1961) Retinal vasculitis. Br J Ophthalmol 45:778–788
11. Hart CD, Sanders MD, Miller SJH (1971) Benign retinal vasculitis: clinical and fluorescein angiographic study. Br J Ophthalmol 55:721–733

12. Recchia FM, Carvalho-Recchia CA, Hassan TS (2004) Clinical course of younger patients with central retinal vein occlusion. Arch Ophthalmol 122:1545–1549
13. Frucht J, Yanko L, Merin S (1984) Central retinal vein occlusions in young adults. Acta Ophthalmol 62:780–786
14. Cekic O, Chang S, Tseng JJ, Barile GR, Weissman H, Del Priore LV, Schiff WM, Weiss M, Klancnik JM Jr (2005) Intravitreal triamcinolone treatment for macular edema associated with central retinal vein occlusion and hemiretinal vein occlusion. Retina 25:846–850
15. Williamson TH, O'Donnell A (2005) Intravitreal triamcinolone acetonide for cystoid macular edema in nonischemic central retinal vein occlusion. Am J Ophthalmol 139:860–866
16. Hayreh SS (1972) Optic disc vasculitis. Br J Ophthalmol 56:652–676
17. Opremcak EM, Bruce RA, Lomeo MD, Ridenour CD, Letson AD, Rehmar AJ (2001) Radial optic neurotomy for central retinal vein occlusion. Retina 21:408–415
18. Wilson CA, Berkowitz BA, Sato Y, Ando N, Handa JT, de Juan E Jr (1992) Treatment with intravitreal steroid reduces blood-retinal barrier breakdown due to retinal photocoagulation. Arch Ophthalmol 110:1155–1159
19. Williamson TH, Poon W, Whitefield L, Strothidis N, Jaycock P (2003) A pilot study of pars plana vitrectomy, intraocular gas and radial neurotomy in ischemic central vein occlusion. Br J Ophthalmol 87:1126–1129