Long-term results of intravitreal bevacizumab and dexamethasone for the treatment of punctate inner choroidopathy associated with choroidal neovascularization: A case series

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Abstract

Introduction: To present a case series of three female patients with punctate inner choroidopathy. We report the outcomes after an essentially long follow-up period of up to 14 years and provide evidence of the effectiveness of intravitreal injections of bevacizumab and dexamethasone 0.7 mg in punctate inner choroidopathy patients with choroidal neovascular membrane formation.

Case series presentation: This is a retrospective case series of three female patients with punctate inner choroidopathy who were treated with intravitreal injections anti-vascular endothelial growth factor agent (bevacizumab, 1.25 mg/0.05 mL). Two patients also received intravitreal dexamethasone 0.7 mg. Once a choroidal neovascular membrane developed, the outcome was poor with a best-corrected visual acuity of 6/60 or counting fingers in the affected eyes. The patients were followed up for 5, 14 and 8 years.

Conclusion: The use of dexamethasone 0.7 mg in punctate inner choroidopathy yielded encouraging results and long periods of stability. When choroidal neovascular membrane complicates the primary disease, the prognosis is unfavourable, especially if the macula integrity has already been considerably affected. On the contrary, aggressive early therapy and continued monthly monitoring can prevent severe fibrosis, as showed in previous reports. Further larger-scale studies are needed to evaluate the efficacy of intravitreal dexamethasone 0.7 mg and bevacizumab as an alternative treatment in non-infectious uveitis.

Keywords
Dexamethasone implant, bevacizumab, punctate inner choroidopathy

Introduction

Punctate inner choroidopathy (PIC) is an idiopathic inflammatory disorder of the choroid, and one of the ‘white dot syndromes’. Other white dot syndromes are multiple evanescent white dot syndrome (MEWDS), birdshot retinochoroidopathy, presumed ocular histoplasmosis syndrome (POHS), serpiginous choroiditis, diffuse subretinal fibrosis syndrome (DSF) and acute posterior multifocal placoid pigment epitheliopathy (APMPPE), as well as multifocal choroiditis and panuveitis (MCP). PIC typically affects young myopic patients and is characterized by yellow-grey choroidal lesions progressing to chorioretinal scars and eventually choroidal neovascular membrane (CNVM) formation or subretinal fibrosis. The clinical symptoms include scotomas, photopsias, floaters, photophobia, metamorphopsia and reduced visual acuity.

Therapeutic approaches to PIC incorporate systemic, topical, and periocular steroids, and non-steroidal immunomodulatory agents. Treatments for CNVM include laser photocoagulation, photodynamic treatment, and intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents.

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This study aimed to determine the long-term outcomes of intravitreal anti-VEGF injections and steroid intravitreal implant treatment in PIC patients.

**Case reports**

We retrospectively reviewed the data of three women (mean age, 48.33 ± 16.16 years) treated for PIC in the outpatient department of the University Hospital of Leicester, UK. Collection of data conformed to the tenets of the Declaration of Helsinki and patient’s anonymity was secured. All patients received intravitreal bevacizumab and two additionally received dexamethasone. Their clinical outcomes in terms of the best-corrected visual acuity (BCVA) and presence of retinal exudation are presented below.

**Case 1**

A 54-year-old lady was referred to our hospital with a 4-month history of blurring of vision and flickering in the peripheral field of the left eye. At the time of presentation, she had punched-out lesions in the macula with few cells in the anterior vitreous. The BCVA in both eyes was 6/6. PIC was diagnosed, and her condition remained stable for over 3 years after which she reported a worsening of the distortion in her left eye. The vision in her left eye had deteriorated to 6/36, and optical coherent tomography revealed intraretinal fluid. Since she refused systemic steroids, she was started on oral azathioprine 50mg/day. However, after an initial improvement, her condition recurred again. She was then offered intravitreal dexamethasone (Ozurdex, Allergan Inc., Irvine, CA, USA) and off-label treatment with the anti-VEGF agent bevacizumab (Avastin, Genentech, San Francisco, CA, USA). Subsequently, she received one more intravitreal dexamethasone injection and seven bevacizumab injections to the left eye. However, she developed a disciform scar with a BCVA of counting fingers (CF). The right eye fortunately remained stable (Figure 1).

**Case 2**

A 36-year-old lady presented with a 1-week history of vision deterioration in her left eye. The vision in the right eye had been reduced for over 8 years. The BCVA was 6/12 in both eyes at presentation. Imaging tests confirmed PIC, and the patient was started on prednisolone 60mg/day. Her vision improved rapidly (6/9 right and left), and the steroid was tapered. Over the next 9 years, she had a few recurrences, and each time was treated with oral steroids. Gradually, she developed a disciform scar over the left eye. In 2012 (10 years after the first episode), she presented with reduced vision in the right eye and was started on azathioprine with steroid tapering. She went on to receive seven anti-VEGF injections to the left eye, but the macula continued to scar. The final visual acuity was CF in each eye due to the scar tissue presence (Figure 2).
Case 3

A 22-year-old lady with moderate myopia presented with a 3-week history of blurring of vision in the right eye. The visual acuity was 6/60 in the right eye and 6/6 in the left eye. Fundus fluorescein angiography (FFA) confirmed PIC. The patient received three bevacizumab injections to the right eye, and her vision improved to 6/12. However, she presented 3 months later with distortion of vision in the left eye. She was given three bevacizumab injections, which stabilized her vision to 6/12. However, she presented 3 months later with distortion of vision in the left eye. She was given three bevacizumab injections, which stabilized her vision. Although the right eye has remained stable over the last 8 years, the left eye had recurrences, which were treated with a further eight bevacizumab injections. She was started on azathioprine, which she did not tolerate well. Fortunately, her left eye remains stable after having received eight bevacizumab and two dexamethasone (Ozurdex) injections over 8 years. Her visual acuity is 6/6 in the right eye and 6/9 in the left eye (Figure 3).

Discussion

All treatment modalities for PIC target the inflammatory and neo-angiogenic mechanisms of CNVM formation. The use of dexamethasone 0.7 mg intravitreally demonstrated excellent clinical efficacy in one young PIC patient (Case 3). This patient was in remission for a period of 18 months before experiencing a relapse. When a CNVM formed, the combination of dexamethasone 0.7 mg and bevacizumab 1.25 mg/0.05 mL managed to maintain excellent visual acuity in one patient but failed to prevent total sub-foveal fibrosis in others (Cases 1 and 2). It is possible that during the long follow-up periods, patients developed CNVM and were not treated with anti-VEGF but only with systemic anti-inflammatory therapy because of the unavailability at that time of the anti-VEGF.

The findings of this case series are in accordance with relevant studies that showed that visual loss is frequent in patients with PIC, mostly secondary to late development of CNVM, while treatment with a single dexamethasone intravitreal implant in patients with non-infectious posterior uveitis has been shown to significantly decrease intraocular inflammation and improve BCVA. Furthermore, as previously was demonstrated, combined treatment with steroids or immunosuppressive and anti-VEGF agents (anti-inflammatory and anti-angiogenic effects) is possibly a favourable alternative for the management of PIC-associated recurrent CNV membranes.

In the weaknesses of our case series, include the small number of patient consented for intravitreal dexamethasone implant, the non-randomized nature and lack of post-perspective study design. Also given the longevity of follow-up, it is unclear in some instances if the fall in vision was secondary to the inflammatory or secondary to CNV. In cases where vision drop was due to the inflammation, treatment with steroids resulted to immediate improvement. On the contrary, treatment with immunosuppressants or
anti-VEGF failed to maintain good visual acuity, with the presence of fibrotic tissue. Although, the long follow-up of these patients put forward valuable information regarding the disease’s response to various therapeutic agents.

Further studies with a larger number of PIC patients are needed to investigate the role of intravitreal injections of dexamethasone 0.7 mg and anti-VEGF agents in PIC complicated with CNVM.

**Conclusion**

The study presents a long-term follow-up of female patients with PIC treated with anti-VEGF (bevacizumab) and intravitreal implant of dexamethasone (Ozurdex). The clinical outcome was difficult to be correlated with specific factors since anti-VEGF and dexamethasone intravitreal implant managed to maintain good vision in some instances while failed to others. Also, PIC-associated CNVM exhibited certain characteristics as aggressive fibrosis but minimal exudation.

**Author’s Note**

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**Availability of data and material**

Data sharing not applicable to this article as no datasets were generated or analysed during this study.

**Consent for publication**

Written informed consent was obtained from the patients for publication of this case series and associated images.

**Declaration of conflicting interests**

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**Ethical approval**

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References
1. Watzke RC, Packer AJ, Folk JC, et al. Punctate inner choroidopathy. Am J Ophthalmol 1984; 98: 572–584.
2. Quillen DA, Davis JB, Gottlieb JL, et al. The white dot syndromes. Am J Ophthalmol 2004; 137: 538–550.
3. Raven ML, Ringeisen AL, Yonekawa Y, et al. Multi-modal imaging and anatomic classification of the white dot syndromes. Int J Retina Vitreous 2017; 3: 12.
4. Kedhar SR, Thorne JE, Wittenberg S, et al. Multifocal choroiditis with panuveitis and punctate inner choroidopathy: comparison of clinical characteristics at presentation. Retina 2007; 27: 1174–1179.
5. Gerstenblith AT, Thorne JE, Sobrin L, et al. Punctate inner choroidopathy: a survey analysis of 77 persons. Ophthalmology 2007; 114: 1201–1204.
6. Brown Jr. J, Folk JC, Reddy CV, et al. Visual prognosis of multifocal choroiditis, punctate inner choroidopathy, and the diffuse subretinal fibrosis syndrome. Ophthalmology 1996; 103: 1100–1105.
7. Terelak-Borys B, Zagajewska K, Jankowska-Lech I, et al. Combined treatment in punctate inner choroidopathy. Ther Clin Risk Manag 2016; 12: 1467–1471.
8. Rogers AH, Duker JS, Nichols N, et al. Photodynamic therapy of idiopathic and inflammatory choroidal neovascularization in young adults. Ophthalmology 2003; 110: 1315–1320.
9. Chan WM, Lai TY, Liu DT, et al. Intravitreal bevacizumab (avastin) for choroidal neovascularization secondary to central serous chorioretinopathy, secondary to punctate inner choroidopathy, or of idiopathic origin. Am J Ophthalmol 2007; 143: 977–983.
10. Barth T, Zeman F, Helbig H, et al. Intravitreal anti-VEGF treatment for choroidal neovascularization secondary to punctate inner choroidopathy. Int Ophthalmol. Epub ahead of print 19 April 2017. DOI: 10.1007/s10792-017.
11. Vossmerbaeumer U, Spandau UHV, Baltz S, et al. Intravitreal bevacizumab for choroidal neovascularisation secondary to punctate inner choroidopathy. Clin Exp Ophthalmol 2008; 36: 292–294.
12. Ahnood D, Madhusudhan S, Tsaloumas MD, et al. Punctate inner choroidopathy: a review. Surv Ophthalmol 2017; 62: 113–126.
13. Niederer RL, Gilbert R, Lightman SL, et al. Risk factors for developing choroidal neovascular membrane and visual loss in punctate inner choroidopathy. Ophthalmology 2018; 125: 288–294.
14. Whitcup SM and Robinson MR. Development of a dexamethasone intravitreal implant for the treatment of noninfectious posterior segment uveitis. Ann N Y Acad Sci 2015; 1358: 1–12.
15. Hobberger B, Rudolph M and Bergua A. Choroidal neovascularization associated with punctate inner choroidopathy: combination of intravitreal anti-VEGF and systemic immunosuppressive therapy. Case Rep Ophthalmol 2015; 6: 385–389.