CASE REPORT

Inflammatory optic disc neovascularisation managed with oral steroids/immunosuppressants and intravitreal ranibizumab

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SUMMARY

Inflammatory optic disc neovascularisation (NVD) has been treated with periocular or systemic steroids, immunosuppressants, panretinal photocoagulation and bevacizumab. However, the role of intravitreal ranibizumab in inflammatory NVD has not been explored in the peer-reviewed indexed literature. In case 1, NVD and associated subhyaloid haemorrhage showed rapid and dramatic regression after intravitreal ranibizumab. Recurrence was noted 8 weeks after injection which was managed by oral steroids. In case 2, intravitreal ranibizumab led to partial resolution of NVD. The addition of steroids, azathioprine and panretinal photocoagulation led to further fibrosis of the neovascularisation. Ranibizumab may be an important adjunct to anti-inflammatory therapy in the management of inflammatory NVD.

BACKGROUND

Inflammation-induced optic disc neovascularisation (NVD) is characterised by diffuse capillary leakage during fundus fluorescein angiogram (FFA) in the absence of 'extensive' (at least one quadrant) retinal capillary non-perfusion (CNP).¹ Several treatment options including steroids, immunosuppressants, panretinal photocoagulation, and intravitreal bevacizumab have been tried successfully for the management of inflammatory NVD.¹⁻³ We describe the management of two cases of inflammatory NVD with a combination of intravitreal ranibizumab, steroids and immunosuppressants.

CASE PRESENTATION (CASE 1)

A 14-year-old girl presented with right eye acute granulomatous anterior uveitis with NVD surrounded by subhyaloid haemorrhage ([figure 1A](#)) and mild vasculitis along the inferotemporal vein. There were no signs of vitritis, chorioretinitis or snow-banking in the right eye. The best-corrected visual acuity (BCVA) was 6/12 in the right eye and 6/6 in the left eye. No signs of anterior or posterior segment inflammation were seen in the left eye.

INVESTIGATIONS

FFA showed early hyperfluorescence of the right optic disc with an intense leak in late phase suggestive of neovascularisation ([figure 1B](#)) with no retinal CNP areas ([figure 1C](#)) in either eye. Mild staining was evident along the inferotemporal vein. History

of systemic illness and general physical examination was unremarkable. Chest X-ray showed hilar lymphadenopathy. Fasting blood sugar, glycated hemoglobin (HbA1c) and blood pressure were normal. High-resolution computed tomography revealed right and left upper lobe fibronodular opacification with enlarged calcified hilar lymph nodes. Pulmonary function tests showed mild restrictive pulmonary disease (FEV1/FVC-97, forced expiratory volume at 1 second or FEV1%-68% and forced vital capacity or FVC-60%). Mantoux test was negative. The serum angiotensin converting enzyme (ACE) level of the patient (59 units/L) was slightly elevated (normally less than 40 units/L). The haematological evaluation showed raised erythrocyte sedimentation rate (ESR, 25 mm) with no other abnormality. Serological tests for syphilis and HIV were non-reactive. As the patient did not have any systemic symptoms, she did not give consent for hilar lymph node biopsy. A diagnosis of presumed ocular sarcoidosis ('Biopsy not done; presence of bilateral hilar lymphadenopathy (BHL) with a compatible uveitis')⁴ was made based on International Criteria for the Diagnosis of Ocular Sarcoidosis.

TREATMENT

Intravitreal ranibizumab was given in the right eye with informed written consent from the guardian explaining the off-label use of the drug. Simultaneously, the patient was started on topical steroids and cycloplegic drops. Systemic steroids were not started as significant vasculitis or posterior uveitis was not evident. By 2 weeks, significant regression of NVD was noted with near total regression by 4 weeks. The BCVA improved to 6/6. However at 8 weeks after injection, the NVD started reappearing. Considering this to be inflammatory in nature, the patient was started on oral prednisolone at a dose of 1 mg/kg body weight. Again a dramatic complete regression of NVD was seen in the next 4 weeks ([figure 1D](#)). Oral steroids were tapered to a maintenance dose of 5 mg per day, which is being continued.

OUTCOME AND FOLLOW-UP

We have a 1-year follow-up of the patient and there has been no recurrence of NVD. The patient maintains a BCVA of 6/6 in either eye.

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Figure 1 (A) Right fundus of case 1 at presentation, showed disc neovascularisation with associated subhyaloid haemorrhage. (B) Fluorescein angiography image of the same eye showed intense leakage at the disc due to the neovascularisation. (C) The peripheral retina did not reveal retinal capillary non-perfusion. (D) Fundus photograph of right eye demonstrated dramatic resolution of the disc neovascularisation after intravitreal ranibizumab and steroid therapy.

CASE PRESENTATION (CASE 2)

A 22-year-old young man presented with mild non-granulomatous anterior uveitis in both eyes with no vitritis, chorioretinitis or periphlebitis. BCVA was 6/9 in either eye. Both the eyes showed significant NVD. Mild vitreous haemorrhage was evident in the right eye. FFA did not reveal any active retinal vasculitis, chorioretinitis or CNP areas. Systemic examination was unremarkable. The haemogram with ESR, Mantoux, chest X-ray and serum ACE were normal. Plasma glucose value, HbA1c and blood pressure were within normal limits. The serology was negative for HIV and VDRL (venereal disease research laboratory test for syphilis). Intravitreal ranibizumab was given sequentially in both eyes after obtaining informed consent. The anterior uveitis was treated with topical steroids. Though the vitreous haemorrhage cleared, there was only a partial regression of NVD of both eyes. Lack of CNP areas pointed against an ischaemic cause of NVD.

Figure 2 Post-treatment fundus image of both eyes of case 2 showed fibrotic neovascular fronds at the optic disc. The absence of macular oedema and lack of inflammation of vessels at posterior pole is evident.

TREATMENT

The presence of anterior uveitis was suggestive of inflammation and thus considering this NVD to be inflammatory in origin, the patient was started on oral steroids (1 mg/kg body weight which was slowly tapered to 5 mg). Though the fibrous component of NVD seemed to increase it did not regress fully. However, as the vitreous haemorrhage had absorbed and the patient was asymptomatic, no further intervention was done. BCVA at this time was 6/6 in either eye. The patient returned after 2 months with a fresh episode of vitreous haemorrhage in both eyes and BCVA of 6/12 in the right eye and 6/9 in the left eye. Intravitreal ranibizumab was again repeated in both eyes. In view of the aggressive NVD and lack of full response to oral steroids and ranibizumab, this time, we also performed panretinal photocoagulation in both eyes. The vitreous haemorrhage slowly absorbed and there was evidence of further fibrosis of the neovascularisation (figure 2). Since the neovascularisation was primarily presumed to be due to inflammation, the patient was also started on 1.5 mg/kg body weight azathioprine along with oral steroid.

OUTCOME AND FOLLOW-UP

We have a further 12-month follow-up of the patient during which the patient has not had any fresh episode of vitreous haemorrhage. BCVA at last follow-up was 6/9 in either eye.

DISCUSSION

Vitreous concentrations of vascular endothelial growth factor (VEGF) have been shown to rise significantly in uveitis,⁵ and in Eales^{6,7} disease. Intravitreal anti-VEGF agents seem to be potential adjuncts to steroids and immunosuppressives for managing complications of intraocular inflammation like cystoid macular oedema⁵ and inflammatory NVD.³ Anti-VEGF agents may also help in retinal neovascularisation and NVD related to retinal ischaemia as in proliferative diabetic retinopathy. Recently, ranibizumab⁸ and aflibercept⁹ have been shown to be non-inferior to panretinal photocoagulation with regard to visual acuity outcomes in proliferative diabetic retinopathy. Though the results of success using intravitreal bevacizumab for inflammatory NVD have been reported,^{2,3} we could not find any prior reports using intravitreal ranibizumab for the same indication. It may be noted that multiple studies worldwide have proven similar efficacy and safety profile of intraocular use of bevacizumab and ranibizumab in various ocular indications.¹⁰ However, intraocular use of bevacizumab is still not approved by drug approval authorities (off-label use).¹⁰ Mansour AM and colleagues³ studied the role of one intravitreal injection of bevacizumab in 11 eyes with inflammation induced NVD or neovascularisation elsewhere (NVE) in the retina. Complete regression of NVD/NVE was seen in seven eyes and partial regression was seen in four eyes at 3 months follow-up.³ Eighty-two per cent patients had active uveitis, 91% patients were on oral corticosteroids and the rest were on systemic immunosuppression.³ In our cases, we found that intravitreal ranibizumab causes an early, total or partial resolution of the optic disc neovascularisation which may be inflammatory in origin. This helped in the early clearing of associated vitreous haemorrhage as the active bleed stopped.

We noted that the neovascularisation tends to recur as the effect of ranibizumab wanes. Thus, long-term oral immunosuppressive therapy in the form of steroids or immunosuppressive agents must be added along with treatment with ranibizumab. Systemic steroid and immunosuppressant constitute the most important therapy for inflammatory NVD even in the absence of

cystoid macular oedema or extensive vasculitis at the posterior pole.

In fact, early institution of oral steroid or immunosuppressive agents along with intravitreal ranibizumab in such cases of an inflammatory NVD may have resulted in earlier regression of NVD with fewer rebleeds. Anterior segment inflammation with an area of active vasculitis in case 1 was suggestive of an inflammatory aetiology of NVD. Systemic anti-inflammatory therapy should have been started from the beginning along with ranibizumab in this case, and this was a learning experience for us.

The aggressive nature of NVD in the left eye of case 2 prompted us to do panretinal photocoagulation and also add steroids and immunosuppressives along with intravitreal ranibizumab. In conclusion, anti-VEGF agents may have a role in rapid suppression of NVD in ocular inflammatory disorders. However, this effect is temporary and it should be augmented by systemic immunosuppression. Larger randomised control trials are needed to evaluate and compare the efficacy of various anti-VEGF agents for this indication.

Learning points

- Inflammatory optic disc neovascularisation (NVD) is diagnosed in cases with NVD where fundus fluorescein angiogram does not reveal extensive retinal capillary non-perfusion and there is evidence of intraocular inflammation.
- Primary therapy for inflammatory neovascularisation of disc is systemic steroid or immunosuppression.
- Intravitreal antivascular endothelial growth factors such as ranibizumab may be an important adjunct therapy for inflammatory NVD.

Contributors BLK and RC had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. KT

and BLK were responsible for acquisition of data. RC and PV provided administrative, technical and material support, and supervised the study. All the authors were involved in study concept and design, analysis and interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content.

Competing interests None declared.

Patient consent Obtained.

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