CASE REPORT

Intravitreal bevacizumab for postviral fever retinitis: a novel approach for early resolution of macular oedema

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SUMMARY

Severe macular oedema causing marked loss of vision is seen in cases of retinitis developing postviral fever. The use of antivascular endothelial growth factor agents for macular oedema and submacular fluid secondary to viral retinitis has not been studied or well established in the past. We report a case series of two patients of postviral retinitis with severe macular oedema resistant to steroid therapy, treated with intravitreal bevacizumab. The patients showed significant symptomatic improvement in the visual acuity. The retinitis lesions resolved slowly and macular oedema regressed. Bevacizumab appears to be a safe and useful agent to manage macular oedema subsequent to postviral retinitis. An early resolution of macular oedema helps in the preservation of visual acuity which left untreated can cause severe visual loss.

BACKGROUND

Macular oedema is a major cause of vision loss in patients with viral retinitis.¹ Literature signifies the role of bevacizumab (Avastin, Genentech) a humanised monoclonal antibody to vascular endothelial growth factor (VEGF) in treating uveitic cystoid macular oedema.^{2–4} Bevacizumab probably

reduces the effect of the elevated vitreous levels of VEGF seen in patients of uveitis.⁵ According to our knowledge, the use of anti-VEGF agents for macular oedema and neurosensory detachment secondary to viral retinitis has not been well established in the past. Here, we report two similar case scenarios explaining the benefits of this novel approach in the treatment of macular oedema post-viral retinitis.

CASE PRESENTATION

Case 1

A 19-year-old apparently healthy male came to our centre with complaints of bilateral sudden painless loss of vision following an episode of fever. The best corrected visual acuity (BCVA) was finger counting close to face in the right eye (OD) and 1/60 in the left eye (OS). The anterior segment showed cellular reaction 3+ with no evidence of keratitis and fundus showed ill-defined whitish patches with intraretinal haemorrhages localised to the posterior pole with macular oedema (figure 1A,B).

Case 2

A 45-year-old non-diabetic, non-hypertensive healthy male presented to us with complaints similar to case 1 having BCVA of 3/60 OD and 1/60 OS. The ocular features resembled case 1 (figure 3A,B).

In both the patients, the visual symptoms were preceded by an episode of fever which lasted for around 5–7 days. There was no history of any associated rash, sore throat, respiratory symptoms, gastrointestinal disturbance, lymphadenopathy, joint pain or nephropathy. There was no history of recent immunisation, travel or any drug therapy. The fever was non-specific, treated only by antipyretics and subsided in 5–7 days. The visual symptoms started around 10–14 days following the fever. There was no history of any ocular disease such as central serous retinopathy or any chorioretinitis.

Figure 1 Ultrawide field fundus imaging on presentation of right eye (OD) and left eye (OS), respectively, (A and B) showing multiple ill-defined whitish patches at the posterior pole with intraretinal haemorrhage; (C and D) showing an increase in the size of retinitis lesions (red circle) after 10 days of empirical therapy with oral valacyclovir and oral steroids; (E and F) after 6 weeks of intravitreal bevacizumab showing resolution of the retinitis lesions and macular oedema.

INVESTIGATIONS

A clinical diagnosis of infectious/hypersensitivity retinitis was considered. In both the patients, investigations for tuberculosis, rickettsia, typhoid, cat scratch fever, HIV, Lyme's disease and syphilis were negative. Serology for dengue, West Nile fever, Rift Valley fever and chikungunya was negative. PCR of vitreous tap sent for Herpes simplex and cytomegalovirus infection was also negative.

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Figure 2 (A and B) Spectral domain optical coherence tomography (SD-OCT) on presentation of right eye (OD) and left eye (OS), respectively, showing intraretinal oedema with neurosensory detachment. (C and D) SD-OCT of OD and OS, respectively, 6 weeks postintraocular injection showing complete resolution of macular oedema.

Case 1

Spectral domain optical coherence tomography (SD-OCT) showed marked intraretinal oedema with neurosensory detachment. The central macular thickness (CMT) was 1292 μm OD and 853 μm OS (figure 2A,B).

Case 2

Swept source OCT showed intraretinal thickening with neurosensory detachment. The CMT was 504 μm OD and 1052 μm OS (figure 3C,D).

DIFFERENTIAL DIAGNOSIS

Viral/hypersensitivity retinitis.

TREATMENT

Case 1—this patient was seen by us prior to case 2. He was started empirically on oral valacyclovir 900 mg twice a day and

Figure 3 (A and B) Fundus imaging on presentation of right eye (OD) and left eye (OS), respectively, showing multiple ill-defined whitish patches at the posterior pole with intraretinal haemorrhage. (C and D) Swept source optical coherence tomography on presentation of OD and OS, respectively, showing intraretinal oedema with neurosensory detachment.

Figure 4 (A and B) Fundus imaging of right eye (OD) and left eye (OS), respectively, after 6 weeks of intraocular bevacizumab showing resolution of the retinitis lesions and macular oedema. (C and D) Swept source optical coherence tomography of OD and OS, respectively, 6 weeks postintraocular injection showing complete resolution of macular oedema.

oral steroids (tab prednisolone 1 mg/kg/day) suspecting a diagnosis of viral/hypersensitivity retinitis. On follow-up at 10 days, the patient did not show significant improvement, rather there was change in configuration of the retinitis patches with development of a few fresh retinitis lesions with persistence of macular oedema (figure 1C,D). The patient was then treated with an intraocular injection of bevacizumab (1.25 mg in 0.05 mL) in one eye, followed by an intraocular injection in the fellow eye 2 days later.

Based on our experience with case 1, the second patient (case 2) was directly treated with intraocular bevacizumab.

OUTCOME AND FOLLOW-UP

Within 48 hours following treatment with bevacizumab, both the patients started showing improvement. The patients showed significant improvement in the visual acuity. The retinitis lesions resolved slowly and macular oedema regressed (figure 1E,F). After 6 weeks, the first patient's BCVA improved to 6/36 OD and 6/9 OS. The CMT reduced to 153 μm OD and 215 μm OS (figure 2C,D).

The second patient improved to 6/12 OD and 6/9 OS (figure 4A,B) with CMT of 224 μm OD and 184 μm OS (figure 4C,D).

The visual acuity was maintained at the end of 6 months with no episodes of recurrence.

DISCUSSION

The clinical manifestation of posterior uveitis is variable based on the aetiology and the involvement of structures adjacent to the retina such as the choroid, vitreous, optic nerve head and the retinal blood vessels. Retinitis, in particular, evokes a suspicion towards a viral infection. Herpes simplex and varicella zoster are the most common causes in immunocompetent individuals, whereas rare entities like chikungunya and influenza also contribute in some cases.⁶

Bilateral neuroretinitis has also been described in viral infections caused by measles, influenza, Epstein-Barr virus, dengue virus, Rift Valley fever and West Nile fever.^{7,8} The exact cause

Patient's perspective

- Case 1: I was blessed by god to have come to this hospital and get treated by Dr Rohan and Dr Prasad. I am currently doing my graduation all thanks to him I can continue my further studies.
- Case 2: I had stopped going to work after this illness. I went to many doctors in my village for cure but nothing worked. I came over here as the last resort and thankfully got treated well. God bless Dr Rohan and his team.

Learning points

- Bevacizumab appears to be a safe and useful agent to manage macular oedema in cases of postviral fever retinitis.
- These cases are rare and if left untreated can cause severe loss of vision.
- Rapid resolution of macular oedema helps to achieve good visual recovery in such cases.

of retinitis can be due to an immune reaction secondary to the viral infection or directly by the virus itself.⁷ Although lack of evidence prevails, the treatment in such conditions preferably involves an antiviral agent with or followed by systemic steroids according to certain published reports.¹⁷⁹

But, both our cases did not show improvement to oral steroids and antiviral agents. After the use of anti-VEGF in both the cases, we noticed a dramatic improvement in the macular oedema. We infer that the early improvement of BCVA in both the cases was due to the reduction in the height of the macular detachment. The retinitis lesions might have resolved on its own as these patients were immunocompetent. We also feel that adding steroids without appropriate anti-infective agents in cases of infectious retinitis can lead to rapid centrifugal spreading and worsening of the retinitis as discussed in some studies.¹⁰ Three different patterns of fluid distribution have been reported in eyes with uveitic macular oedema based on OCT findings. The diffuse and cystoid varieties involve intraretinal fluid accumulation, whereas the third pattern is a neurosensory detachment.¹¹ Both our patients had large neurosensory detachments. A number of measures for treating macular oedema secondary to uveitis have been described which include non-steroidal anti-inflammatory agents, corticosteroids, carbonic anhydrase inhibitors, interferons, mycophenolate mofetil and somatostatin analogues.⁵ The role of anti-VEGFs has been described in cases of inflammatory choroidal neovascular membranes and cystoid macular oedema.¹² However, there are limited reports regarding its role

as a first-line treatment in treating macular detachment following viral retinitis. The suggested mechanism of development of a neurosensory detachment in cases of uveitis is the breakdown of the blood–retinal barrier secondary to inflammation. However, the exact mechanism of how anti-VEGF agents help in amelioration of macular oedema and neurosensory detachment in cases of inflammation warrants further research. It is postulated that the retinal pigment epithelium damage secondary to ischaemia also contributes to the pump failure and thereby serous retinal detachment.¹³ Afshar *et al* have previously mentioned the use of bevacizumab to treat a case of West Nile chorioretinitis with macular oedema. They witnessed prompt resolution of macular oedema with improvement in visual acuity.⁸

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