CASE REPORT

Ziv-aflibercept: a novel option for the treatment of polypoidal choroidal vasculopathy

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Accepted 28 November 2015

SUMMARY

Polypoidal choroidal vasculopathy (PCV) is an exudative maculopathy usually treated using photodynamic therapy (PDT) and antivascular endothelial growth factor agents. However, these cases may sometimes be refractory to both PDT and ranibizumab or bevacizumab, and may have persistent intra-retinal fluid. Recently, studies have reported that aflibercept may be effective in such resistant cases. However, high cost and limited availability has restricted its use to only a few countries. Ziv-aflibercept (Zaltrap), a systemic analogue of aflibercept, has been tried recently and it has been effective in macular oedema. We report a case of PCV resistant to PDT and ranibizumab, which responded well to intravitreal ziv-aflibercept.

BACKGROUND

Polypoidal choroidal vasculopathy (PCV) is an exudative maculopathy with features similar to neovascular AMD with subretinal haemorrhage, pigment epithelial detachment (PED) and neurosensory detachment.[1] Available treatment options are laser photocoagulation or photodynamic therapy (PDT) along with anti-vascular endothelial growth factor (VEGF) agents.[2] The exudative maculopathy in PCV may be refractory to anti-VEGF treatment with monthly injections. Ziv-aflibercept has been recently shown to be safe and effective in macular diseases such as age-related macular degeneration and macular oedema.[3] In the present case, the fluid was persistent in spite of multiple prior ranibizumab injections. However, after a single Zaltrap injection, the fluid disappeared completely.

CASE PRESENTATION

A 79-year-old man presented with symptoms of blurring of vision in both eyes for 3 weeks. Best-corrected visual acuity (BCVA) was 20/400 in the right eye and 20/60 in the left eye. Intraocular pressure measured with Goldmann applanation tonometry was 14 and 12, respectively, in the right and left eye. The anterior segment examination was within normal limits in both eyes except for early nuclear sclerosis of the lens. Fundus examination was normal in the left eye. However, the right eye showed haemorrhagic PED and subretinal haemorrhage, and corresponding indocyanine green angiography (ICG) showed a single polyp (figure 1). The patient was advised PDT and intravitreal ranibizumab injection in the right eye. One month after PDT and injection, the BCVA in the right eye was 20/120. The fundus showed hard exudates at the macula, and subretinal haemorrhage. Optical coherence tomography (OCT) at this presentation showed altered foveal contour but no subretinal fluid. However, the retinal pigment epithelium (RPE) was thick and elevated. The patient was advised one more injection of ranibizumab and, 2 months after injection, the macula showed resolution of the haemorrhage with formation of a scar (figure 2A).

INVESTIGATIONS

Fluorescein angiography (FA), CG and OCT were performed. FA in the right eye revealed blocked fluorescence with an area of hyperfluorescence, which increased in size and intensity in later phases (figure 2B), whereas the FA in the left eye did not reveal any abnormal fluorescence. ICG showed a hot spot corresponding to the hyperfluorescence seen on FA (figure 2C). The OCT showed fluid in the inner retina, with subretinal fluid and PED (figure 2D).

TREATMENT

As there was recurrence of subretinal fluid on OCT, the patient underwent two more injections of ranibizumab at monthly intervals, but the sub-retinal fluid (SRF) was persistent and the BCVA was 20/200 (figure 1E). As the macular oedema was persistent even after PDT, and was resistant to repeated injections of ranibizumab, the patient was advised intravitreal injection of ziv-aflibercept (Zaltrap). Informed consent, after explaining the off-label use of ziv-aflibercept, was taken from the patient. Ethics committee approval from our Local Institutional Review Board was granted.

OUTCOME AND FOLLOW-UP

One month after ziv-aflibercept injection, OCT showed that the SRF had completely disappeared (figure 1F), but the vision was maintained at 20/200 even after 3 months of follow-up.

DISCUSSION

The exudative maculopathy in PCV may be refractory to anti-VEGF or may recur after stopping the treatment with monthly injections. Aflibercept has also been used to treat resistant cases of PCV, and it has been shown to improve and maintain BCVA and central macular thickness.[4]

However, because of the problems of high cost and non-availability in some countries, ziv-aflibercept may be considered as a useful cost-effective option. Initially, some concerns were raised about the osmolarity of Zaltrap. However, studies have shown that intravitreal injections of

To cite: Videkar C, Kapoor A, Chhablani J, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2015-212988

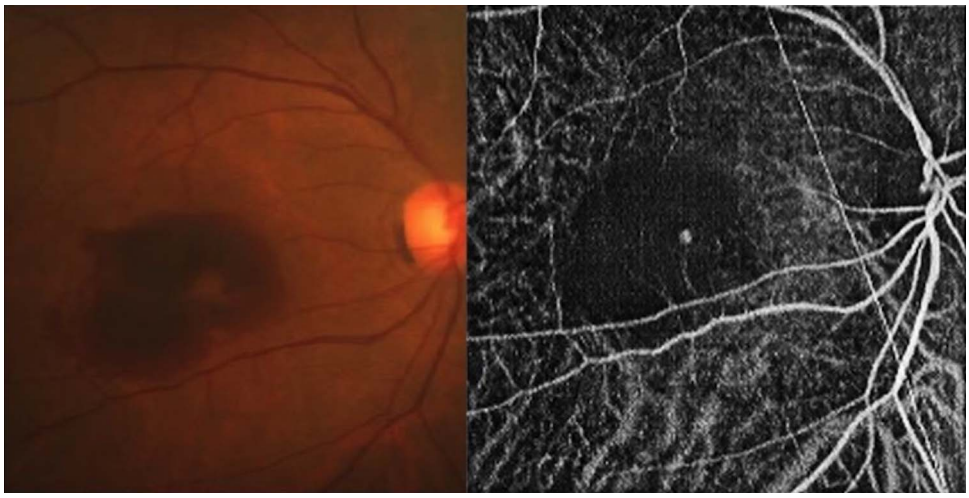

Figure 1 Left: colour fundus photograph shows large subretinal haemorrhage; right: indocyanine green angiography shows a hot spot corresponding with the polyp, and surrounding hypofluorescence due to subretinal haemorrhage.

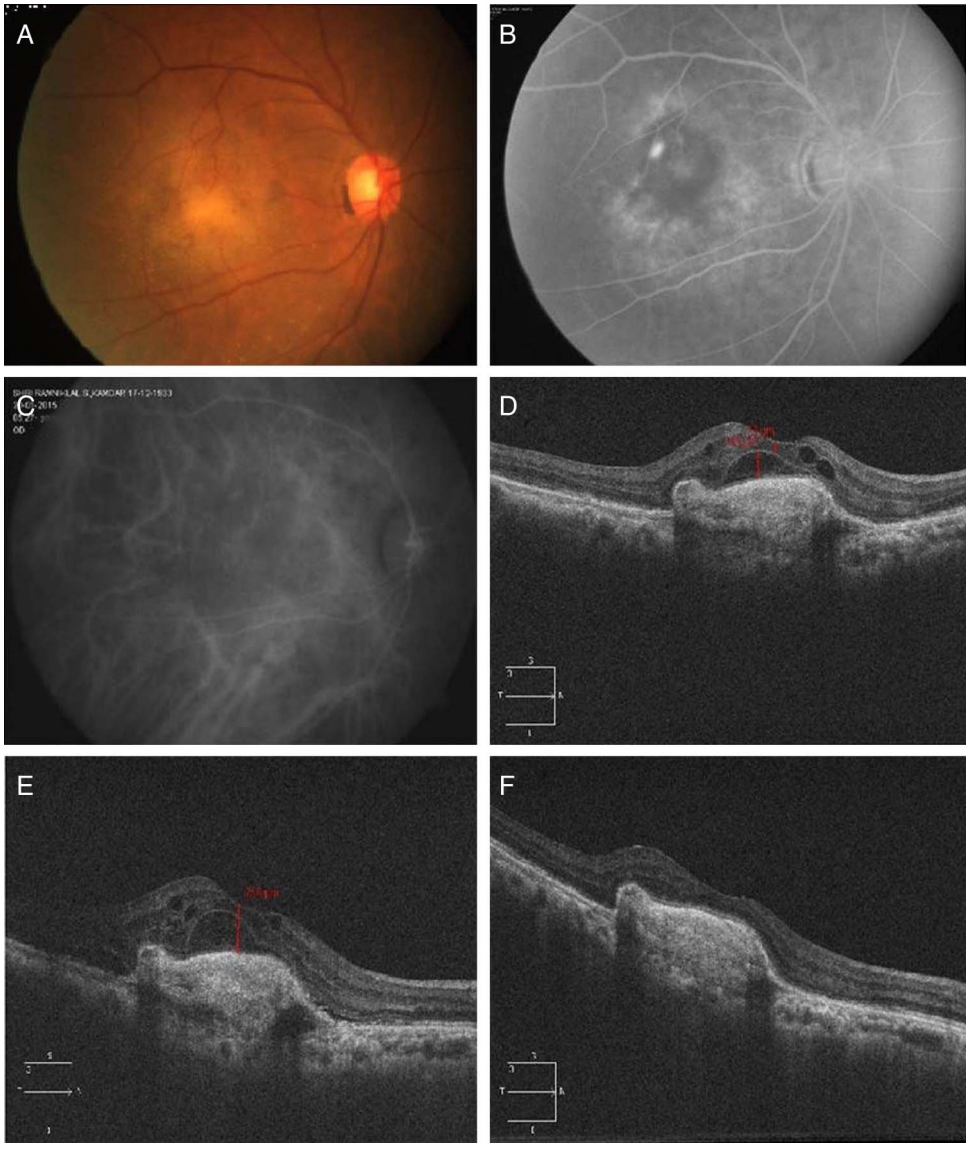

Figure 2 (A) Colour fundus photo, (B) FA (C) ICG and (D) OCT of right eye showing persistent SRF after PDT and two ranibizumab injections; (E) SRF still persisting before Zaltrap injection; (F) SRF completely resolved after Zaltrap injection. FA, fluorescein angiography; ICG, indocyanine green angiography; OCT, optical coherence tomography; PDT, photodynamic therapy.

osmolarity <500 mOsm does not cause any RPE damage.[5] Hence, even when 0.05 mL of ziv-aflibercept of 1000 mOSm concentration is injected into 4 mL of vitreous, the final osmolarity is of around 312 mOsm, which is in the safe physiological range. A safety profile has been established in animal studies and in humans with age-related macular degeneration.[6 7] On funduscopy, OCT and ERG, median baseline serum, vitreous and aqueous osmolarity were shown to be within normal limits 30 days after the procedure.[6 7]

Patient's perspective

I was very satisfied with the treatment because I was worried that I might lose further vision if the fluid on optical coherence tomography did not resolve.

Learning points

- Resistance can be encountered to ranibizumab and bevacizumab in polypoidal choroidal vasculopathy (PCV).
- Ziv-aflibercept could be effective in PCV-resistant to ranibizumab and bevacizumab.
- Ziv-aflibercept may be a good cost effective option with acceptable safety profile.

In our present case, the fluid was recurring in spite of multiple prior ranibizumab injections. However, after Zaltrap injection, the fluid disappeared completely. We conclude that ziv-aflibercept could be a less expensive and effective option for management of cases of PCV refractory to other anti-VEGF agents. However, dosing needs to be ascertained with larger studies and longer follow-up.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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