CASE REPORT

Radiation retinopathy treated successfully with aflibercept

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SUMMARY

Aflibercept (aflibercept) is a novel anti-vascular endothelial growth factor drug indicated for wet age-related macular degeneration and macular oedema secondary to retinal vein occlusion and diabetic macular oedema. While only newly introduced on the market, it is growing in popularity and over 5.5 million doses have been prescribed worldwide. Due to its versatile mechanism, it is indicated for numerous eye pathologies, and in particular, has been adapted to treat various types of retinopathy. To our knowledge, this is the first case report of solely using aflibercept to treat cystoid macular oedema in radiation retinopathy.

BACKGROUND

Radiation retinopathy, a complication of radiotherapy treatment, is an occlusive microangiopathy secondary to endothelial cell loss and capillary closure. Macular oedema after exposure to radiation is a documented complication. Also possible are microaneurysms, telangiectasis, neovascularisation, rubeosis, neovascularisation of the retina, vitreous haemorrhage and tractional retinal detachment.¹

It is a slowly progressive condition with a delayed onset of months to years after radiation, it is dose, daily fraction size and fraction interval dependent. The usual threshold dose for retinal damage varies at 30–35 Gy. Patients with vascular diseases such as diabetes, hypertension or previous chemotherapy have been reported to develop radiation retinopathy at lower doses of radiation.¹

Patients initially report blurred vision or floaters and present with radiation vasculopathy seen as microaneurysms and telangiectasis. Consequently, retinal hard exudates and haemorrhages, macular oedema, neovascularisation and tractional retinal detachment may result.²

Due to the clinical and histopathological similarity between radiation retinopathy and diabetic retinopathy, similar treatment methods are indicated.¹ Current treatments for radiation retinopathy-associated macular oedema and choroidal neovascularisation include laser photocoagulation, intravitreal Bevacizumab, a humanised monoclonal anti-vascular endothelial growth factor (VEGF) antibody as well as photodynamic therapy and hyperbaric oxygen treatment, all of which present inconclusive and unsatisfactory results.³

CASE PRESENTATION

A 22-year-old woman was referred to the University Hospital of Wales after her radiotherapy for a WHO Grade 2 Meningioma in 2006 and has developed a recurrence in the right temporalis muscle in 2012. She had no other medical history or relevant family history. Shortly postradiation, she developed from right eye radiation related keratopathy and early lens opacity. This episode settled well with intensive lubrication with vision maintained at 6/12 and a normal optical coherence tomography (OCT) scan. In early 2016, her vision dropped and was noted to have right eye radiation cystoid macular oedema (CME) and a drop in visual acuity to 6/18. Her left eye was normal with a visual acuity of 6/4 (figure 1A). Treatment was started on 18 January 2016, with her first intravitreal injection of aflibercept 2 mg/0.05 (Bayer Pharmaceuticals) (figure 1A). There was an improvement in OCT appearance and vision on her subsequent follow-up. Although we planned a loading phase for her at 4 weeks, the patient opted to not attend her follow-up due to personal circumstances and was seen after 5 months when she contacted the department to report a drop in vision. She was noted to have cystoid macular edema (CMO) again in June 2016 with V/A of 6/38 OD (figure 1B). Her response to treatment was excellent with improvement in both OCT anatomical appearance and vision in August 2016 (V/A 6/15) (figure 1C) and September 2016 (V/A 6/15) (figure 1D) and progressive improvements up to December 2016 (figure 2). As a result, a total of three injections were given. As seen in figure 2, the fundus showed minimal blot haemorrhages in less than two quadrants with no new vessels detectable.

OUTCOME AND FOLLOW-UP

The OCT scans follow-up during the regimen also showed improvement in her condition (please see attached figures in the separate figure files).

DISCUSSION

Summary of results and diagnosis

This case report explores the novel and unprecedented application of aflibercept to treat and improve CME induced by radiation treatment. The patient was managed with a prn regimen of intravitreal aflibercept injection which lead to significant improvements in OCT macular thickness and an improved right eye visual acuity.

Current conventional treatments for radiation retinopathy remain limited and include

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Figure 1 (A) Before first treatment in January 2016. (B) Before second treatment in June 2016. (C) After second intravitreal Eylea in August 2016. (D) After third intravitreal Eylea in September 2016.

photodynamic therapy, laser photocoagulation, oral pentoxifylline and hyperbaric oxygen, all with inconclusive results. More recently, intravitreal injections of anti-VEGFs such as bevacizumab, ranibizumab and pegaptanib sodium have been used with variable effectiveness.² This is the first case report in the English literature describing Eylea as a successful primary and only treatment for CME after radiation. There is a case report where Eylea was used after the use of Avastin and was shown to yield successful therapeutic results.⁴ As such, this is the first case report exploring the application of solely using aflibercept as a primary treatment for CME secondary to radiation treatment. Further, another prospective trial is currently recruiting patients with retinopathy to be treated with aflibercept.⁵

VEGF is an important growth factor for angiogenesis and is secreted during hypoxic episodes, acting as a mediator in retinal ischaemic-associated neovascularisation. Anti-VEGF agents vary and can come in the form of humanised monoclonal antibody, which binds and neutralise VEGF, or as aptamers, which are small RNA-like molecules that bind exclusively to VEGF.⁶

Anti-VEGF aflibercept is the first fully human intravitreal fusion protein and binds to VEGF-A and placental growth factor dimers thereby preventing endothelial growth and angiogenesis.⁷ The recommended dose in age-related macular degeneration is 2mg every 4 weeks for the first 12 weeks followed by 2mg dose every 2 months. In contrast to previous anti-VEGF agents, aflibercept requires less frequent injections and no monitoring

requirements, reducing cost and time for patients, potentially increasing compliance.⁸ Further, literature shows that aflibercept outperforms Avastin for Diabetic Macular Oedema for those with 20/50 or worse vision. At 2 years follow-up, aflibercept participants were able to read 3.5 additional on an eye chart, compared with baseline visual acuity, whereas Lucentis participants showed an improvement in 3 additional lines, and Avastin participants, 2.5 lines. Furthermore, laser treatments were given to participants with unresolved diabetic macular edema (DME) after 6 months of assigned drug injections. The need for laser treatment also varied between the treatment groups, with 41% of aflibercept participants receiving laser treatment to treat DME, compared with 64% of the Avastin and 52% of the Lucentis group. Moreover, the risk of heart attack, stroke or death from a cardiovascular condition by the end of trial was higher among the Lucentis group, with 12% in the group having at least one event compared with only 5% in aflibercept.⁹

These promising results, along with the positive results obtained in this case study encourages further exploration in the use of aflibercept to treat radiation retinopathy. Potential adverse effects of aflibercept include endophthalmitis, retinal detachment, potential risk of nonfatal stroke, nonfatal myocardial infarction or vascular death and traumatic cataracts.⁶

Learning points

- Radiation retinopathy is a serious complication of radiotherapy treatment and must be addressed.
- The use of aflibercept injection is a promising treatment for radiation retinopathy and has been shown to yield positive results.
- Current conventional treatments for radiation retinopathy are inconclusive and relatively unsatisfactory.

Contributors TY-Z and AA-b were responsible for collecting patient information and results while PP was responsible for writing the case report.

Competing interests None declared.

Patient consent Obtained.

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Figure 2 (A) Fundus photograph of the right eye. (B) OCT of right eye in December 2016 after the third intravitreal Eylea.

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