CASE REPORT

Enucleation for haemophthalmus secondary to choroidal neovascularisation in polypoidal choroidal vasculopathy: a therapeutic and diagnostic dilemma

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SUMMARY

We report a case of enucleation for painful blind eye secondary to recurrent bleeding from choroidal neovascularisation in an eye that was irradiated following presumed metastatic breast carcinoma to the choroid. A 58-year-old woman with a history of treated breast malignancy presented with haemophthalmus and intractable glaucoma in the right eye. One year previously she had presented with right vitreous haemorrhage with subretinal mass that had been irradiated given her history of breast carcinoma. Following irradiation, vitrectomy was performed to clear the blood. Intraoperative and postoperative angiography findings suggested a diagnosis of breakthrough bleeding secondary to polypoidal choroidal vasculopathy. At this presentation, however, the intraocular bleeding was recurrent resulting in elevated intraocular pressure and pain. Despite repeat surgery and medical therapy, the eye had to be enucleated. Histopathology showed choroidal neovascularisation.

BACKGROUND

Choroidal neovascularisation (CNV) causes vitreous haemorrhage via breakthrough bleeding (BTB) through the retina into the vitreous. CNV is abnormal growth of blood vessels from the choroidal vessels through a break in the Bruch membrane.¹ Although vitreous haemorrhage is a known sequela of CNV, recurrent episodes of bleeding with hyphaema leading to enucleation have not been previously described. In 1994, MacCumber *et al*² reported a case of enucleation in a 58-year-old man for painful rubeotic glaucoma the histopathological examination of which revealed CNV. It was reported that their patient had dense infiltration of inflammatory plasma cells and lymphocytes which released cytokines causing intraocular neovascularisation and fibrosis. The phenomenon of massive retinal haemorrhage following radiotherapy has been described but not to the extent of haemophthalmus.³ Given the rarity of recurrent haemophthalmus following irradiated CNV in the literature leading to enucleation, we would like to report this case and discuss the possibility of irradiation to the choroid altering the natural history of CNV.

CASE PRESENTATION

A 58-year-old Malay woman with previous history of breast carcinoma presented with acute onset of

right eye blurring of vision for 1-week associated with floaters and photopsia to another hospital. She had a breast lumpectomy 6 years prior to presentation. Histopathology had shown invasive breast carcinoma limited to the breast stage T1N0M0. She was told there was no tumour recurrence up to this point. She was diagnosed with right eye vitreous haemorrhage of unknown cause with no view of the retina and investigations were carried out at the centre. MRI of the brain and orbit was performed which revealed a hyperdense lesion at the posterior globe. This was thought to be choroidal metastasis from the breast carcinoma. She then received a total dose of 30 Gy (5 fractions) of proton beam radiotherapy over 1 week to the right eye.

After a few months, she sought a second opinion at our centre as her vision had not improved. On review, her right eye visual acuity was perception of light in all quadrants with a positive relative afferent pupillary defect. Her intraocular pressure (IOP) was 9 mm Hg and IOP of the fellow eye was 12 mm Hg. There was no fundus view of the right eye. B scan ultrasound revealed dense vitreous haemorrhage with an area of subretinal elevation at the inferior retina, no subretinal fluid or exudative detachment were seen. Ultrasound scan were not suggestive of choroidal melanoma. The fellow eye fundus had no drusen or any similar subretinal lesion. Review by the oncology team did not reveal metastasis to any other organ. Whole body positron emission tomography (PET) scan likewise did not reveal any metastatic disease.

Small gauge diagnostic vitrectomy was performed with lensectomy and sulcus intraocular lens implantation under local anaesthesia. Intraoperatively an area of submacular altered blood and massive subretinal blood at the inferior retina was seen (figure 1). No cancerous-looking solid mass seen. Postoperatively, her vision improved to counting fingers at three feet. The vitreous biopsy and cytology showed no evidence of malignancy.

Optical coherence tomography (OCT) of the macula revealed pigment epithelial detachment with no intraretinal or subretinal fluid (figure 2). Fundus fluorescein and indocyanine green angiography (ICGA) did not reveal polyps or leakage. There was a large area of retinal pigment epithelial damage involving the macula with blinding inferiorly from old subretinal blood (figures 3 and 4). There was no evidence of double circulation or any

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Figure 1 Composite colour fundus photograph of the right eye following the first vitrectomy showing extensive subretinal haemorrhage at the macula with scarring and inferiorly bleached sub-RPE old blood. RPE, retinal pigment epithelium.

active disease. The findings appeared suggestive of massive BTB from CNV, most likely from polypoidal choroidal vasculopathy (PCV). Given the poor vision in the right eye and the absence of further disease activity on OCT scan and angiography, intravitreal antivascular endothelial growth factor treatment was declined by the patient. During this period of postoperative follow-up for 6 months, there was no evidence of disease activity both clinically or on OCT. The patient reported her vision was stable during this period.

A year after the first surgery, she presented with another episode of sudden drop of vision. Her visual acuity was hand motion with generalised injection of the conjunctiva and haemophthalmus (figure 5). IOP was 60 mm Hg and maximum antiglaucoma medications were given. Despite this, she was in severe pain and medical treatment failed to control the IOP. B scan ultrasound revealed the same amount of subretinal lesion and dense vitreous haemorrhage. The patient was not on anti-coagulant or antihypertensive medications.

Anterior chamber and vitreous washout was performed with the injection of intravitreal ranibizumab 0.5 mg/0.05 mL at the end of the surgery. Intraoperatively, the findings were similar with no obvious area of active bleeding. Postoperatively however, recurrent bleeding was seen into the vitreous and anterior chamber resulting in persistent elevation of the IOP. This occurred over the subsequent few weeks. Repeat AC washout with antivascular endothelial growth factor injection was performed. Following the procedure, the fundus view was poor due to blood-stained cornea. After 1 month, the vision had reduced to no perception of light and the patient's pain could not be relieved.

INVESTIGATIONS

- Full blood count, clotting factors including activated partial thromboplastin time, prothrombin time and International Normalised Ratio which were all normal

Figure 2 Postoperative OCT of the right macula showing pigment epithelial detachment with no intraretinal or subretinal fluid. OCT, optical coherence tomography.

Figure 3 Fundus fluorescein angiography showing areas of hyperfluorescence corresponding to RPE damage (blue arrow) which did not leak. RPE, retinal pigment epithelium.

- Repeat PET scan was performed with no evidence of metastases
- Vitreous fluid cytology from the vitreous washout was negative for malignancy

DIFFERENTIAL DIAGNOSIS

Haemophthalmus secondary to:

- Wet age-related macula degeneration
- Polypoidal choroidal vasculopathy
- Ocular metastases

TREATMENT

Given these symptoms, the patient agreed to enucleation of the eye. Enucleation was proposed instead of evisceration or cryotherapy as the possibility of microscopic ocular metastases could not be totally ruled out. Histopathological examination revealed the presence of CNV (figure 6).

OUTCOME AND FOLLOW-UP

The patient is now 4 months postoperative. She is happy as she is no longer symptomatic and relieved to have a tissue diagnosis that indicates no metastasis. She has been fitted with an ocular prosthesis and is happy with the cosmetic result. Her fellow eye shows no evidence of similar lesions and continues to be monitored.

Figure 4 Indocyanine green angiography showing a large area of RPE damage involving the macula with blinding inferiorly from old subretinal blood. RPE, retinal pigment epithelium.

DISCUSSION

CNV describes growth of abnormal vessels originating from the choroid through a break in the Bruch membrane; a condition that disrupts the Bruch membrane aids the growth of CNV beyond the retinal pigment epithelium (RPE).⁴ This includes age-related macular degeneration (AMD), polypoidal choroidal vasculopathy (PCV), trauma, ocular histoplasmosis syndrome and angioid streaks.⁵ PCV is one of the infrequent causes of CNV and 92.2% of CNV are caused by wet ARMD while only 7.8% are caused by PCV. Clinically, CNV appears as subretinal fluid, subretinal or sub-RPE haemorrhage, subretinal or intraretinal lipid or subretinal small vessels. Patients usually have symptom of reduced visual acuity, central metamorphopsia or central scotoma.⁴

PCV is characterised by abnormal branching vascular network arising from the inner choroid with aneurysm-like ends, which appear as reddish-orange nodules on funduscopy. In Asians, PCV is more common in men while among Caucasians, women

Figure 5 Anterior segment photograph of the right eye with diffuse illumination at second presentation prior to anterior chamber and vitreous washout.

Figure 6 Microscopic examination showing abnormal vascular proliferation in the choroid (blue arrows; H&E, ×40).

predominate.⁶ It was found that PCV cases are predominantly male oriented at the mean age of 65 years old and 76% are unilateral.⁷ PCV is frequently seen in patients between the ages of 50–65 years and in Asians the prevalence is between 23.9% and 54.7%.⁸ Clinically, PCV can be classified into exudative (52%), haemorrhagic (35%) and extensive haemorrhagic type involving the fovea (13%). On ICGA, PCV appears as clusters of hyper-fluorescent dots that signify an aneurysmal dilation and polyps. They are commonly located at the macular region (88%), peripapillary region (5%) or both regions (7%).⁷

Diagnosis of PCV is made based on fundus findings of protruded orange-red lesions or via ICGA criteria; abnormal vasculature and recurrent haemorrhage and/or serous detachment of RPE.⁹ Although the diagnosis made is usually based on clinical and angiographic findings, MacCumber *et al* have described findings on histopathological examination (HPE) with samples obtained during vitrectomy. On HPE, multiple fibrovascular proliferations in the subretinal space within the Bruch membrane may be seen.² Up to 20% of PCV results in BTB, whereas in AMD it is about 0.6 to 7%.¹⁰ Given the prevalence of PCV in our population and the tendency of PCV to cause massive BTB, this was considered as the most likely underlying cause for her haemophthalmus prior to the histopathology result.

The visual outcome after vitrectomy for BTB from PCV in the literature depends on the location of the polyps whereby polyps located extrafoveally have the better visual outcome. In this patient there was evidence of macula involvement. Hence the vision was only finger counting after surgery.¹⁰ In a retrospective series of BTB described by Jung *et al*, vitrectomy was helpful for improving vision. Half of the eyes were found to have AMD-related bleeding. Again only half of the eyes had on-going active lesions that required further additional treatments. The visual outcome while better for PCV eyes, was only better than 6/60 in 37.5% of eyes.¹¹

Our patient presented finally with recurrent total hyphaema and dense vitreous haemorrhage that occurred as a result of blood spill over from vitreous haemorrhage seeping through areas of weak zonules. Previous vitrectomy and lensectomy procedure performed a year before could have caused weak zonules. The occurrence of haemophthalmus related to PCV is an uncommon clinical event. Our series on vitrectomy for BTB did not record associated hyphaema.¹² Usage of anticoagulants and hypertension has been identified as possible risk factors for BTB in patients with wet AMD or PCV.¹² However, our patient did not have any of these risk factors. Therefore we were

considering other reasons for her unabated haemorrhaging in this eye.

We would like to postulate that in our patient, the mechanism of recurrent, severe bleeding is due to choroidal new vessels damaged following inadvertent prior radiotherapy (RT) to the right eye. Endothelial cell damage leading to vessel leak and haemorrhage is known to result following RT as blood vessels are not spared during the irradiation.¹³ Vitreous haemorrhage following radiotherapy could also occur following development of radiation-induced neovascularisation.¹⁴ For instance, Spaide *et al*¹⁵ reported a case of CNV in radiation retinopathy due to the ischaemia induced by vascular fragility following RT. In our patient, it is unlikely that the VH and CNV were caused by RT in the first instance as the subretinal lesions had been apparent prior to RT as reported in the MRI. However, it is interesting to consider that RT which is known to result in on-going and relentless blood vessel wall damage, telangiectasia and neovascularisation could have altered the CNV in this patient predisposing to haemophthalmus 2 years later.

Choroidal metastasis was among the differential diagnosis for this patient as the patient had history of breast malignancy. Breast cancer ocular metastasis is very rare. It accounts for only 4.6% of cases.¹⁶ The sensitivity of MRI in detecting small choroidal infiltration (<0.5 mm) is as low as 35%. PET scan can only detect ocular lesions more than 2 mm, hence a negative report does not exclude malignancy.¹⁷ Hence, we were still considering the possibility of choroidal metastasis despite negative findings on imaging.¹⁸ Cytology or biopsy is the only definitive method of diagnosing or excluding malignancy.

Majority of cases of enucleation are due to trauma, painful blind eye secondary to glaucoma followed by ocular tumour.¹⁹ We opted for enucleation instead of evisceration in view of her previous history of breast malignancy. There are reports of unanticipated intraocular malignancies that underwent evisceration that led to seeding of malignancy.²⁰

This brings us back to the hypothesis behind her recurrent and severe intraocular haemorrhage with evidence of CNV on histopathology. We suspect that this could be a rare complication of choroidal neovascularisation, which bled incessantly due to inherent damage to the vasculature from a number of episodes of irradiation to the eye when the working diagnosis was choroidal metastasis, before she presented to our centre.

Learning points

- Choroidal neovascularisation (CNV) may result in recurrent, torrential and recalcitrant intraocular bleeding or haemophthalmus that result in the loss of an eye.
- Patients with CNV should undergo ocular irradiation with caution given the possibility of developing radiation-induced angiopathy that may indirectly result in haemophthalmus subsequently.
- Enucleation provides symptomatic relief and firm tissue diagnosis either for or against metastatic disease in cases of painful blind eye with a possibility of malignancy.

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Contributors MM proposed the study be written up and conducted by all three consultants. M-LCB, MM and AA had operated on the patient and managed the case reporting of the work described. Writing up of the draft and amendments was by NAA. Comments for improvement of the manuscript were provided by all three consultants. Final amendments of the article and submission was performed by M-LCB who is also responsible for the overall content as guarantor(s).

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