Intravitreal ranibizumab for the management of serous maculopathy secondary to optic disc coloboma-associated choroidal neovascularisation

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SUMMARY

We report the case of a 19-year-old patient with symptomatic unilateral serous maculopathy associated with an optic nerve coloboma. Fluorescein angiography detected a focal late leak at the temporal edge of the coloboma which was later found to correspond with an area of choroidal neovascularisation on optical coherence tomography angiography. A course of intravitreal ranibizumab achieved good clinical and structural response. This report contributes to the evidence that maculopathies associated with cavitary optic nerve anomalies may in some instances result from choroidal neovascularisation. It also highlights the importance of angiography to identify potential choroidal neovascular membranes, particularly in the absence of haemorrhages and neovascular membranes on fundus examination and conventional optical coherence tomography.

BACKGROUND

Maculopathies resulting from anomalous optic discs present significant management challenges. Previous case reports[1 2] have suggested the use of intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents in the management of this condition in children with a demonstrable choroidal neovascular membrane (CNVM). To our best knowledge, intravitreal ranibizumab monotherapy has not previously been described in the treatment of serous maculopathy associated with optic disc coloboma in an adult patient. We report the clinical course and serial optical coherence tomography (OCT) images of such a patient.

CASE PRESENTATION

A 19-year-old female student presented with gradual deterioration of vision in her right eye over 3 months. Ophthalmic history was significant for non-syndromic bilateral optic disc colobomata. The refraction was plano/−2.75×100 right,+0.25/–4.00 x 40 left. She had a medical history of asthma and vitamin B_{12} deficiency. At presentation, best-corrected visual acuity (BCVA) was 6/18 right and 6/6 left. Dilated fundus examination showed bilateral optic disc colobomata (figure 1A,B) and a right serous maculopathy with no retinal haemorrhages or visible CNVM. OCT demonstrated subretinal fluid (SRF) extending from the optic disc to the fovea with a central macular thickness of 279 µm (figure 1C). Pars plana vitrectomy with tamponade and focal laser treatment were deemed high risk due to the proximity of the fovea to the anomalous optic disc margin. The right BCVA progressively deteriorated to 6/48 over 6 months.

INVESTIGATIONS

The patient was referred for further assessment to Moorfields Eye Hospital where fundus fluorescein angiography (FFA) demonstrated a late focal leak from the right temporal coloboma margin with (figure 2A,B) associated SRF and intraretinal fluid cysts. A focal hyperreflective subretinal lesion at the temporal coloboma margin in keeping with a peripapillary subretinal scar in the left eye was also noted (figure 2C). OCT angiography at this stage did not reveal a definitive CNVM.

TREATMENT

A trial of intravitreal ranibizumab (0.5 mg/0.05 mL; Novartis Pharma AG, Basel, Switzerland) was offered in an attempt to halt progression and assess reversibility of the SRF. Ranibizumab was chosen due to its availability and its effectiveness in similar conditions such as myopic choroidal neovascularisation. Following three doses of 4-weekly intravitreal ranibizumab, there was gradual resolution of the SRF (figure 3A–C). However, the right BCVA remained largely unchanged at 6/30.

OUTCOME AND FOLLOW-UP

Four months after the last intravitreal ranibizumab injection, BCVA had improved to 6/18 in the right eye and OCT did not show any recurrence of SRF (figure 3D). At her latest review 6 months after the last treatment, BCVA and OCT appearance (figure 3E) remained stable and follow-up OCT angiography demonstrated an area of choroidal neovascularisation corresponding to the area of late leakage on FFA (figure 3F).

DISCUSSION

Optic disc colobomata result from incomplete closure of the embryonic fissure and may be unilateral or, as in this case, bilateral.[3] As with other congenital disc anomalies such as optic disc pits, serous retinal detachments and maculopathies are rare but potentially sight-threatening complications. The pathogenesis of these conditions remains controversial. Proposed mechanisms include vitreous fluid entering the subretinal space through a break or hole in the retina, vitreous traction at the optic disc margin, or late leakage from neovascular tissue at the anomalous optic disc margins.[4]

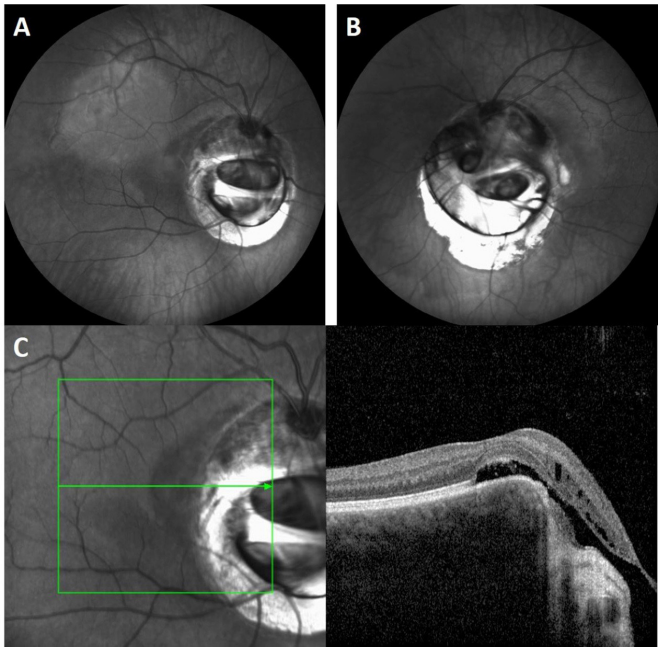

Figure 1 Fundus autofluorescence of the right (A) and left (B) eyes showing prominent optic disc colobomata. Optical coherence tomography of the right eye (C) showing subretinal fluid tracking centrally under the fovea.

Late hyperfluorescence on FFA at the margin of an optic nerve pit was first described by Gass.[5] These findings have since been replicated by other authors[1 2 6] and are consistent with the FFA results in this case (figure 2). Localised defects in Bruch's membrane at the coloboma margins may facilitate the proliferation of choroidal vessels with a similar pathogenesis seen in myopic CNV.[1 7]

Coloboma-associated CNVM may spontaneously resolve or progress to cause permanent visual impairment. The management of serous maculopathies associated with cavitary optic nerve anomalies remains challenging with no current treatment guidelines. Small case series describe good clinical response to laser photocoagulation and photodynamic therapy (PDT) with and without adjuvant intravitreal anti-VEGF agents.[1 8 9] However, these treatment modalities are less suitable for lesions located in close proximity to the fovea as in this described case.

Surgical management options in adults are often based on the assumption that vitreous traction may be partially responsible for the SRF accumulation.[4 10 11] Pars plana vitrectomy with gas tamponade has been shown to achieve a postoperative BCVA of 6/18 with a worse visual prognosis in patients with SRF as opposed to intraretinal fluid.[10] However, vitrectomy carries a risk of retinal breaks and detachment, particularly in young patients without a posterior vitreous detachment.

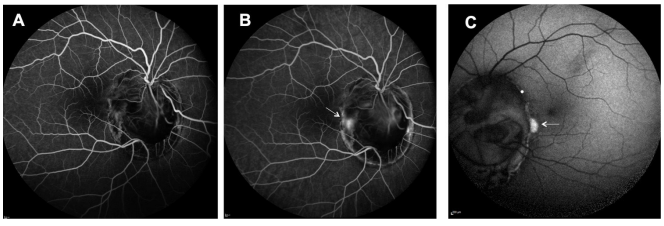

Figure 2 Fundus fluorescein angiography images of the right eye at 0:40 min (A) and 5:26 min (B) showing late leak at the colobomatous disc margin (arrow). Fundus autofluorescence of the left eye (C) showing a focal peripapillary hyperreflective lesion (arrow).

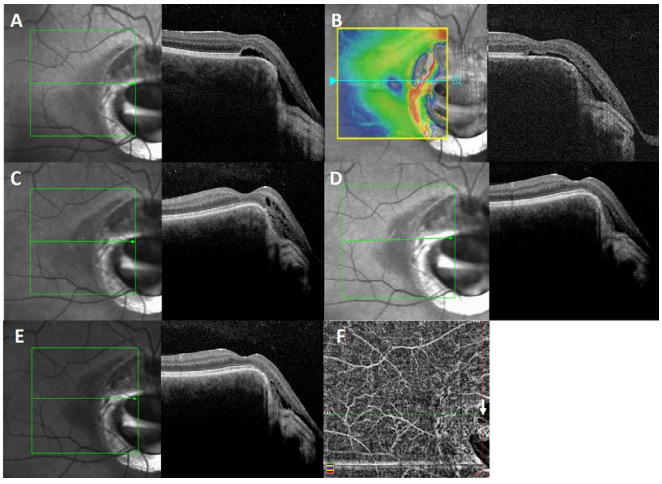

Figure 3 Serial optical coherence tomography taken prior to the first intravitreal ranibizumab injection (A), prior to the second ranibizumab injection (B), prior to the third ranibizumab injection (C), at 4 months (D) and 6 months (E) after the final treatment showing a gradual reduction in subretinal fluid. Optical coherence tomography angiography (F) taken 6 months after the final treatment displaying an area of choroidal neovascularisation (arrow).

To our best knowledge, intravitreal ranibizumab monotherapy for serous maculopathy due to presumed CNV associated with optic disc colobomata in adults has not previously been described in the literature. Rajendran *et al*[12] demonstrated resolution of CNV related to an inferior retinochoroidal coloboma without optic nerve involvement in an adult patient treated with intravitreal bevacizumab, while Bhende *et al*[9] showed good clinical and angiographic response to intravitreal bevacizumab in combination with PDT. Anti-VEGF agents, often alongside PDT, have also been used to successfully treat CNVM in children with optic disc and retinochoroidal colobomata.[1 2 6] In contrast to our case, all of the previously described cases presented with subretinal haemorrhages on fundus examination and CNVM on OCT.

In summary, our case highlights that some patients with coloboma-associated maculopathy may have subclinical CNV responsive to anti-VEGF treatment. It is, therefore, important to perform FFA to potentially identify active neovascular tissue associated with the anomalous optic disc that is not necessarily visible on dilated fundus examination or routine OCT imaging. Late fluorescein leakage associated with intraretinal fluid and SRF in the context of an optic nerve coloboma may represent an underlying CNVM. OCT angiography may aid in identifying

Learning points

- In a subset of patients, coloboma-associated maculopathy may be a result of choroidal neovascularisation at the anomalous optic disc margin.
- Fluorescein or optical coherence tomography angiography should be used early to identify choroidal neovascular membranes in patients with maculopathies related to cavitary optic nerve anomalies.
- If choroidal neovascularisation is detected, the condition may respond well to intravitreal anti-vascular endothelial growth factor agents.

neovascular tissue but as a relatively recent technology, reliable image acquisition may be difficult to obtain. If FFA demonstrates late leakage in the presence of intraretinal fluid or SRF and reduced visual acuity, intravitreal anti-VEGF agents should be considered as a management option, particularly in cases where surgical intervention or laser treatment are unsuitable.

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