CASE REPORT

Treatment of choroidal neovascularisation secondary to membranoproliferative glomerulonephritis type II with intravitreal ranibizumab

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SUMMARY

Membranoproliferative glomerulonephritis type II (MPGN II) is characterised by electron-dense deposits of complement components in the glomerular basement membrane and retinal pigment epithelium. Approximately, 10% of affected individuals develop serious ocular complications similar to age-related macular degeneration such as choroidal neovascularisation (CNV), which has been managed with photocoagulation or photodynamic therapy; however, these treatments can impact visual acuity. We report the case of a 42-year-old woman with MPGN II presenting with decreased visual acuity and paracentral scotoma in her left eye due to an extrafoveal choroidal neovascular membrane (growth of new vessels under the retina). The patient was successfully treated with intravitreal ranibizumab (Lucentis) with restoration of visual function. This case highlights the successful management of CNV secondary to MPGN II with the antivascular endothelial growth factor agent ranibizumab and emphasises the importance of early referral of patients with MPGN II who are reporting of visual 'distortion'.

BACKGROUND

Membranoproliferative glomerulonephritis type II (MPGN II), also known as dense deposit disease (DDD), is a rare type of glomerulonephritis affecting children and younger adults. It is characterised by electron-dense deposits of complement components in the glomerular basement membrane. Electron-dense material may also be seen in the mesangium, Bowman's capsule and in the tubular basement membrane.¹ MPGN II is the least common form of membranoproliferative glomerulonephritis accounting for less than 20% of cases in children and less than 1% in adults.² All patients with MPGN II have proteinuria +/- haematuria and typically have renal impairment at presentation. A minority also have acquired partial lipodystrophy.³ Most patients have low C3 complement levels.

One of the other extrarenal features of MPGN II involves the formation of drusen-like deposits in the retinal pigment epithelium membrane which can lead to choroidal neovascular membrane formation and in some cases eventually to loss of vision. Until recently photocoagulation was the main therapeutic option, but efficacy is limited in juxtafoveal lesions. Photodynamic therapy (PDT) has been tried for this condition with considerable success, however, with the advent of vascular

endothelial growth factor (VEGF) inhibitors, which are efficacious in the management of choroidal neovascularisation (CNV). There is now a potentially more effective therapy for this ocular complication of MPGN II.^{4 5} We describe successful treatment of a patient with MPGN II-related CNV using the monoclonal antibody ranibizumab (Lucentis).

CASE PRESENTATION

A 42-year-old woman presented with decreased visual acuity and a paracentral scotoma in her left eye for 3 months. She had a medical history of MPGN II confirmed on renal biopsy at the age of 16 years with subsequent progression to end-stage renal disease and renal transplantation by the age of 40 years. The patient was a non-smoker, non-diabetic and was known to have had drusen in both eyes prior to transplantation. She was treated with mycophenolate mofetil, prednisolone, losartan and lansoprazole following transplantation. On examination visual acuity was 6/6 right eye, 6/12+2 eccentrically in the left eye and she reported visual distortion. On slit-lamp biomicroscopy examination the right fundus had multiple drusen (figure 1A), and there was evidence of an area of subretinal fluid with exudates and haemorrhage superonasally to the fovea in the left eye (figure 1B, C).

INVESTIGATIONS

Fundus fluorescein angiography (FFA; figure 1D-F) and optical coherence tomography (OCT) scanning (figure 1G) confirmed a small area of leakage indicative of CNV in the left eye, and no leakage in the right eye.

TREATMENT

The diagnosis was MPGN II retinopathy complicated by extrafoveal CNV in the left eye, and it was decided that due to the proximity of the lesion to the fovea the most beneficial therapy with the least likelihood of secondary reduction in visual acuity would be intravitreal injection of ranibizumab. The patient was treated with two injections of ranibizumab 2 months apart.

OUTCOME AND FOLLOW-UP

Visual acuity in her left eye improved to 6/9 after the first and then 6/6 after the second injection, at which time the patient reported that the distortion of vision had gone. No further injections were

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Figure 1 (A) Colour fundus image of the right eye showing multiple drusen. (B) Colour fundus image of the left eye (pre-treatment) showing multiple drusen, intraretinal exudation superonasal to the fovea indicating the site of choroidal neovascularisation (CNV) (yellow arrowhead). (C) Colour fundus image of the left eye (post-treatment) showing complete resolution of intraretinal exudates and fluid. (D) Early frame fundus fluorescein angiography (FFA) of the right eye showing multiple petaloid areas of hyperfluorescence due to drusen deposits. (E) Early frame FFA of the left eye showing multiple petaloid areas of hyperfluorescence due to drusen deposits and CNV (yellow arrowhead). (F) Late frame FFA of the left eye showing progressive leakage from the CNV. (G) Composite of infrared retinal image and cross-sectional optical coherence tomography (OCT) image of the left retina showing the CNV pretreatment (yellow arrowhead). (H) Post-treatment OCT image of the left retina showing complete resolution of the CNV at 22 months. (I and J) Fundus autofluorescence (FAF) images of the right and left eyes showing the area of decreased autofluorescence around active CNV in the left eye (yellow arrowhead). (K) Post-treatment FAF image of the left eye showing disappearance of exudates and persistence of reduced autofluorescence around the CNV (yellow arrowhead).

needed. On follow-up at 22 months visual acuity was 6/6 in the right eye and 6/5 in the affected left eye. OCT scan confirmed resolution of the neovascular activity that is, a dry,

haemorrhage-free macula with no cysts (figure 1H). FAF demonstrated a return towards normality of the retinal anatomy (figure 1I–K).

DISCUSSION

MPGN II/DDD is a rare condition with an estimated prevalence of 2–3 cases per million of the population.⁶ The retinal changes due to DDD are identical in appearance to those found in age-related macular degeneration (AMD). However, in AMD these changes usually begin to form after the fifth decade of life, while in MPGN II the drusen and CNV changes can be seen in patients in their teens. Impact on visual acuity may be minimal to begin with, although over time abnormalities can be detected in specialised tests of retinal function including electroretinography, electrooculography and dark adaptation. There is a 10% risk of developing symptomatic visual problems with MPGN II, and the severity of disease in the kidney and eye appear to be unrelated.^{1 3}

Laser photocoagulation and PDT have been the mainstay of treatment for CNV caused by AMD. Laser photocoagulation has been an effective treatment modality for CNV, and PDT has been reported to have successfully treated MPGN II-related CNV.⁷ PDT, however, is known to cause atrophy of the surrounding retinal pigment epithelium which may impact on the visual outcome, particularly with lesions close to the fovea. The availability of intravitreal anti-VEGF therapies have revolutionised the treatment of CNV, with the safety and efficacy of ranibizumab demonstrated in various trials.^{4 5} Owing to the rarity of MPGN II and the recent development of anti-VEGF drugs for intravitreal use, an extensive literature search identified just one case of successful treatment of an MPGN II-related subretinal neovascular membrane with bevacizumab, an anti-VEGF monoclonal antibody similar to ranibizumab.

Our previous experience had shown that CNV secondary to MPGN II is difficult to control and the use of laser photocoagulation or PDT can lead to poor visual outcomes, particularly if lesions are located at or near the fovea. This knowledge, and the proven safety and efficacy of anti-VEGF therapies, prompted the use of ranibizumab in this case.

This case report highlights the successful management of CNV secondary to MPGN II with the anti-VEGF agent ranibizumab and highlights to nephrologists in particular, the potential importance of the symptom of visual ‘distortion’ in patients with MPGN II and the need for urgent referral for ophthalmic evaluation. This patient’s visual acuity rapidly improved with two intravitreal injections of ranibizumab and OCT scan 6 weeks post-treatment confirmed a normal, fluid-free macula. MPGN II is a rare condition and serious ocular complications only develop in approximately 10% of such patients. Visual ‘distortion’ will therefore be an uncommon symptom in individuals with MPGN II. Nevertheless we hope that treating clinicians will be aware that there is effective therapy available for CNV secondary to MPGN II, and to promptly refer those who develop visual problems to ophthalmologists for assessment and possible treatment with an anti-VEGF agent such as ranibizumab.

Learning points

- ▶ Membranoproliferative glomerulonephritis type II is a rare condition with clinical and biochemical features including proteinuria or haematuria, renal impairment, partial lipodystrophy and low C3 complement levels.
- ▶ Approximately 10% of these patients will develop serious ocular complications due to drusen-like deposits within the retinal pigment epithelium and choroidal neovascularisation. This will present as visual distortion or blurring, with or without visual field defects/scotomas, and should prompt urgent ophthalmology input.
- ▶ The ocular complications have been demonstrated to be treatable, previously with laser photocoagulation and photodynamic therapy, and now with antivascular endothelial growth factor agents such as ranibizumab.
- ▶ Caution must be exhibited in the choice of treatment for choroidal neovascular or other lesions at the fovea or macula as the risk of damage to these structures and deleterious effects on vision must be considered.

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