Graefes Arch Clin Exp Ophthalmol (2009) 247:1427–1430
DOI 10.1007/s00417-009-1143-1

CASE REPORT

Early neovascular bridging of choroidal neovascularization after ranibizumab treatment

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Received: 13 April 2009 / Accepted: 27 June 2009 / Published online: 21 July 2009

Abstract
Background To report three cases of early choroidal neovascularization (CNV) bridging after ranibizumab treatment.
Methods Three patients with two separated foci of CNV secondary to age-related macular degeneration (ARMD), pathologic myopia and multifocal choroiditis were treated with monthly injections of ranibizumab por a period of 3 months.
Results All three cases showed early coalescence across the fovea of the two neovascular foci, already 1 month after the first ranibizumab injection. Best-corrected visual acuity (BCVA) decreased in the three cases more than 20 letters due to early foveal involvement.
Conclusions Two different foci of CNV show a great tendency to decrease patients' vision because of neovascular bridging with foveal implication.

Keywords Choroidal neovascularization · Ranibizumab · Optical coherence tomography · Neovascular bridging

Introduction

Choroidal neovascularization (CNV) secondary to age-related macular degeneration (ARMD) and pathologic myopia (PM) is a major cause of visual loss [1, 2]. CNV appears to be a unique lesion, but on rare occasions the CNV complex is formed by two separated foci. The bridging of these different foci may occur across the fovea, thus involving visual impairment secondary to central damage.

In recent years, Ranibizumab® (Lucentis, Novartis, Basel, Switzerland), an anti-vascular endothelial growth factor (anti-VEGF) agent, has achieved promising results in the treatment of CNV secondary to ARMD [3].

In this case series, we report three cases of early CNV bridging secondary to ARMD, PM and multifocal choroiditis after ranibizumab treatment.

Case reports

Case 1

A 74-year-old man with a history of disciform scar secondary to ARMD in his right eye was examined due to a metamorphopsia in his left eye. Best-corrected visual acuity (BCVA) was counting fingers at 1 meter in the right eye and 63 ETDRS letters in the left eye. Fluorescein angiography (FA) showed two small juxtafoveal classic CNV in the left eye. The patient received one intravitreal ranibizumab injection monthly for a period of 3 months. Fundus ophthalmoscopy 1 month after the first ranibizumab injection showed progression and initial bridging of both foci. FA 1 month after the dosing charge revealed a complete bridging of the CNVs across the fovea, without any angiographic leakage (Fig. 1). BCVA decreased to 45 letters. After 12 months follow-up, the patient has received three more injections with a mild enlargement of the lesion. Final BCVA decreased to 41 letters.

This study has been done without any financial support. It is in conformance with the declaration of Helsinki. None of the authors has any financial interest.

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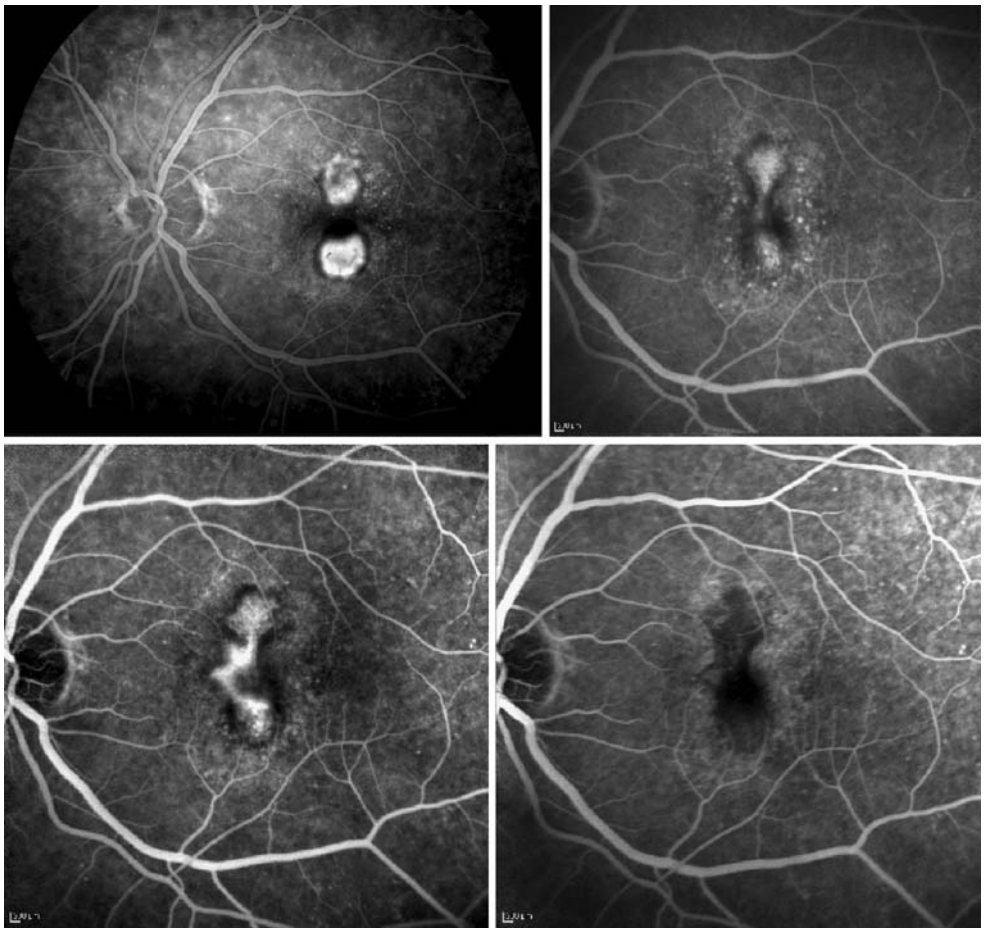

Fig. 1 Case 1. *Top left*; baseline FA showed two juxtafoveal CNV separated by normal retina in the fovea. *Top right*; FA 1 month after the third ranibizumab injection showed early coalescence of the two foci without fluorescein leakage. *Bottom left*; a mild enlargement of the lesion with leakage of the lesion at the 11-month visit. *Bottom right*; FA at 12 months showed no leakage

Case 2

A 42-year-old man with a history of a single extrafoveal CNV secondary to multifocal choroiditis in the left eye, treated with one single PDT 8 months before, referred decreased vision. Baseline BCVA was 59 letters; FA showed leakage from the initial extrafoveal lesion (inferior to fovea) and from a new CNV complex on the temporal side of the fovea. Monthly injections of ranibizumab were performed for 3 months. At the 3-month visit, FA showed a complete neovascular bridge between the two lesions across the fovea. BCVA was 52 letters. After 18 months follow-up, the patient received six more ranibizumab injections; BCVA was 27 letters and FA revealed a great fibrotic reaction (Fig. 2).

Case 3

A 70-year-old woman with a clinical history of a single juxtafoveal myopic CNV treated successfully with PDT 1 year before in the right eye was referred for visual loss in the same eye. BCVA was 52 letters in the right eye. FA confirmed the presence of leakage in the initial CNV and showed a new CNV completely separated from the other CNV. Initial FA also showed several lacquer cracks corresponding to the site of the CNV. The patient received a ranibizumab dosing charge. Biomicroscopy carried out 1 month after the first injection revealed an initial coalescence of the two CNV, confirmed by FA performed at 3 months. BCVA at that point decreased to 39 letters. After the 16-month follow-up, the patient needed four more ranibizumab injections, with a great enlargement of the lesion and a reduction of BCVA to 31 letters (Fig. 2).

Discussion

The presence of two simultaneous separated foci in a CNV complex is really infrequent. The bridging of these two foci across the fovea has already been described in literature, not only a spontaneous bridging such in multifocal choroiditis [4], but also secondary to PTD in high myopia [5].

Independent of neovascular origin, this case series reports the early bridging of two CNV foci, with the development of a neovascular bridge across the fovea.

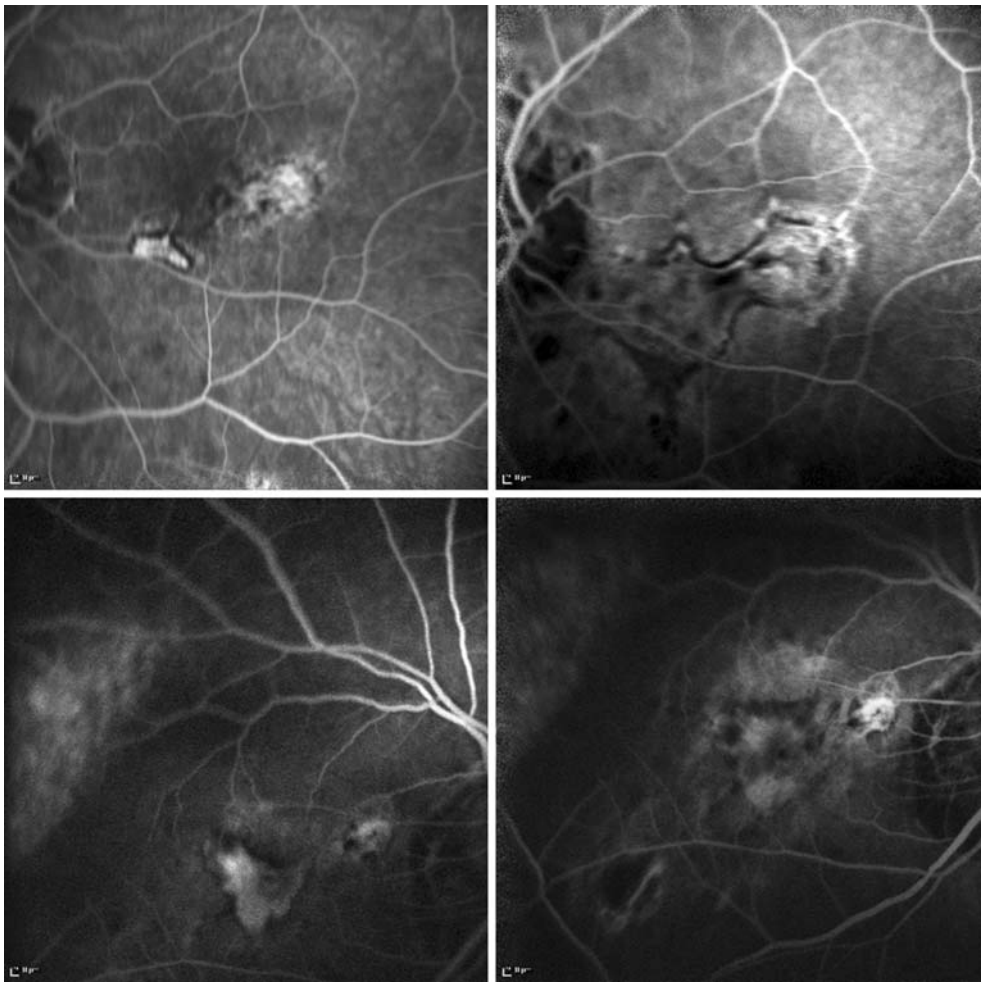

Fig. 2 Case 2. *Top left*; baseline FA showed an extrafoveal CNV inferior to fovea, previously treated with PDT and a juntafoveal CNV on the temporal side of the fovea. *Top right*; after 18 months follow-up, FA showed a neovascular bridge with a great fibrotic reaction. Case 3. *Bottom left*; FA showed at baseline two myopic CNV, separated by normal retina. *Bottom right*; FA at 16-month visit showed a CNV bridging between the two lesions

Anatomic reasons may justify this behaviour. All three cases were eyes with predominantly classic CNV, with an innate trend to injure Bruch's membrane [6] and rapidly expand into the subretinal compartment. In addition, these were non-subfoveal foci, with a natural tendency to affect the fovea [7]. The existence of lacquer cracks could enhance the junction of the two foci by guiding the formation of the CNV bridge (case 3). Inflammatory conditions could also benefit this behaviour, as CNV coalescence is a typical feature of multifocal choroiditis [4] (case 2).

Bevacizumab, a non-selective anti-VEGF agent, has obtained promising results in non-subfoveal CNV, preventing foveal implications, although the number of cases is low [8]. On the contrary, we describe an early coalescence of the foci despite ranibizumab treatment. Lanzetta et al. [5] also published this bridging in myopic CNV soon after PTD treatment. Proangiogenic stimuli secondary to choroidal hypoperfusion were produced after PTD, and the treatment of the two foci with an unique spot could represent the pathogenetic origin of the CNV bridging. In our series, case 1 did not receive any PDT. Cases 2 and 3 were treated with PTD more than 6 months before the formation of the second CNV. These facts lead us to suggest that anatomic features may play an important role in bridging pathogenesis.

After ranibizumab dosing charge, all three eyes had subfoveal extension, with a significantl decrease in their visual acuity. No additional intravitreal injections were needed at 3 months, due to the absence of leakage in FA, nor were intrarretinal edema shown by optical coherence tomography (OCT).

The three eyes have received several ranibizumab injections justified by angiographic or tomographic activity in the follow-up. Case 2 developped an extense fibrotic reaction, probably associated to inflammatory factors and the disruption of the blood–retinal barrier.

On conclusion, premature bridging of two foci in a CNV complex is a common situation, despite the origin of the neovascular foci and the treatment with ranibizumab. More studies are necessary to conclude the reasons for this behaviour.

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