Eye (2012) 26, 882–885
© 2012 Macmillan Publishers Limited All rights reserved 0950-222X/12
www.nature.com/eye

Fast Track Paper

CASE SERIES

High-dose ranibizumab therapy for vascularized pigment epithelial detachment

CK Chan[1,2], P Abraham[3] and D Sarraf[4,5]

[1]Southern California Desert Retina Consultants, Medical Group, Palm Desert, CA, USA

[2]Department of Ophthalmology, Loma Linda University, Loma Linda, CA, USA

[3]Black Hills Regional Eye Institute, Rapid City, SD, USA

[4]Retinal Disorders and Ophthalmic Genetics Division, Jules Stein Eye Institute, University of California, Los Angeles, CA, USA

[5]Greater LA VA Healthcare System, Los Angeles, CA, USA

Correspondence:
CK Chan, Southern California Desert Retina Consultants, Medical Group, PO Box 2467, Palm Springs, CA 92263, USA
Tel: +1 760 340 2394;
Fax: +1 760 340 2369.
E-mail: Pschan@aol.com

Received: 12 March 2012
Accepted in revised form: 29 March 2012
Published online: 11 May 2012

These cases were presented in part at the 43rd annual scientific meeting of The Retina Society, 23 September 2010, San Francisco, CA, USA.

Abstract

Purpose **The conventional dose of anti-vascular endothelial growth factor treatment may slowly reduce the subretinal fluid and height of a vascularized pigment epithelial detachment (vPED), but rarely leads to its complete resolution. We report a dramatic outcome involving a high dose (2 mg) of ranibizumab for treating vPED.**

Methods **This report describes three eyes with vPED that received 2 mg in 0.05 ml of ranibizumab injections on a monthly basis and were followed prospectively. Each patient received a complete ocular examination, including best-corrected standardized ETDRS testing, fundus photography (FP), fluorescein angiography (FA), optical coherent tomography (OCT), and indocyanine-green angiography at baseline. ETDRS and OCT testing were repeated monthly, while FP and FA were performed every 3 months.**

Results **Following a single intravitreal injection of 2 mg ranibizumab, there was rapid resolution of the subretinal fluid, haemorrhage, exudates, and flattening of the vPED within 10 days for Case 1, and within 1 month for Case 2 and Case 3.**

Conclusion **Rapid and dramatic decrease in the exudative changes and collapse of the vPED may develop after a single injection of high-dose (2 mg) ranibizumab in certain eyes with a vPED. The improvement was maintained with additional monthly injections to 12 months.**

Eye (2012) **26,** 882–885; doi:10.1038/eye.2012.90; published online 11 May 2012

Keywords: age-related macular degeneration; anti-vascular endothelial growth factor therapy; high-dose ranibizumab; 2 mg ranibizumab; retinal pigment epithelial detachment; vascularized pigment epithelial detachment

Introduction

Although multiple studies[1–6] and the pivotal ANCHOR and MARINA trials[7,8] have shown high efficacy in the treatment of choroidal neovascularization (CNV) due to age-related macular degeneration (ARMD) with anti-vascular endothelial growth factor (anti-VEGF) therapy, analysis of the responses based on specific lesion subtypes (ie, pigment epithelial detachments (PEDs)) was not performed. Previous studies have shown suboptimal and inconsistent outcome for the treatment of vascularized pigment epithelial detachment (vPED).[7–10] Although conventional doses of anti-VEGF therapy may reduce associated haemorrhage and intraretinal or subretinal fluid, the vPED does not typically resolve[10] and residual visual disturbance may persist. Herein, we report three cases of rapid resolution of the vPED after only a single high dose (2 mg/0.05 ml) of ranibizumab. Approval by the respective institutional boards for this study and a full informed consent from all patients were obtained.

Case reports

Case 1

An 86-year-old man reported a 6-month history of metamorphopsia affecting the left eye (LE). Best-corrected VA was 20/30 in the right eye (RE) and 20/100 in the LE. Fundus examination showed nonexudative ARMD in the RE, and a large PED with a neovascular focus, consistent with vPED, in the LE, which was confirmed by

fluorescein angiography (FA) and optical coherent tomography (OCT) imaging (Figures 1a–c). Baseline indocyanine-green (ICG) angiography showed no evidence of polypoidal choroidal vasculopathy (PCV) in the LE. Following a single injection of high-dose (2 mg) ranibizumab (Genentech Inc., San Francisco, CA, USA), resolution of subretinal fluid and collapse of the vPED were noted by day 10 post treatment visit (Figures 1d–f). Repeat high-dose injections were performed for the LE on a monthly basis. The vPED remained flat with improved vision (RE: 20/30, LE: 20/30) at the 12-month follow-up examination.

Case 2

A 60-year-old woman reported vision loss in both eyes for 3 months. The best-corrected VA was 20/30 in the RE and 20/100 in the LE. Macular atrophy was noted in the LE and subfoveal vPED in the RE, confirmed by FA and OCT (Figures 2a–c). Baseline ICG angiography showed absence of PCV in the RE. After a single injection of 2 mg ranibizumab, there was resolution of most of the subretinal fluid, hard exudates, and collapse of the vPED 1 month after the injection (Figures 2d–f). Injections were repeated for the RE on a monthly basis. Twelve months later, the vPED remained flat without leakage and associated with stable vision (RE: 20/20, LE: 20/100).

Case 3

An 85-year-old man presented with a 7-month history of progressive metamorphopsia affecting both eyes. Best-corrected VA was 20/60 in the RE and 20/400 in the LE. The posterior-segment examination showed a subfoveal vPED with hard exudates in the RE. There was an irregular vPED associated with diffuse subretinal fluid in the LE. FA showed CNV associated with a retinochoroidal anastomosis at the margin of the vPED in the RE (Figures 3a–c), and occult CNV associated with the vPED in the LE. Baseline ICG angiography did not show PCV in both eyes. He received 2 mg of ranibizumab, RE, initially, which was repeated on a monthly basis. His LE received 0.5 mg ranibizumab monthly. After a single injection, there was resolution of the subretinal fluid and exudates and flattening of the vPED in the RE 1 month after the injection (Figures 3d–f). After a follow-up of 12 months, there was no recurrent leakage, and the VA was 20/40 in the RE and 20/100 in the LE.

Discussion

The highly favourable outcomes on treatment of combined subtypes of neovascular AMD with conventional doses of ranibizumab shown by the pivotal clinical trials (ie, ANCHOR, MARINA, FOCUS, and SAILOR)[5,6,11,12] are not consistently achieved for vPED, a difficult-to-treat subtype of neovascular AMD. The aetiology of the slow and inconsistent response of vPED to conventional doses of anti-VEGF therapy is unknown.[10] Rapid flattening of the PED with high-dose therapy may be explained by the greater concentration of ranibizumab that penetrates the RPE barrier and suppresses CNV and resolves the associated fluid and haemorrhage.

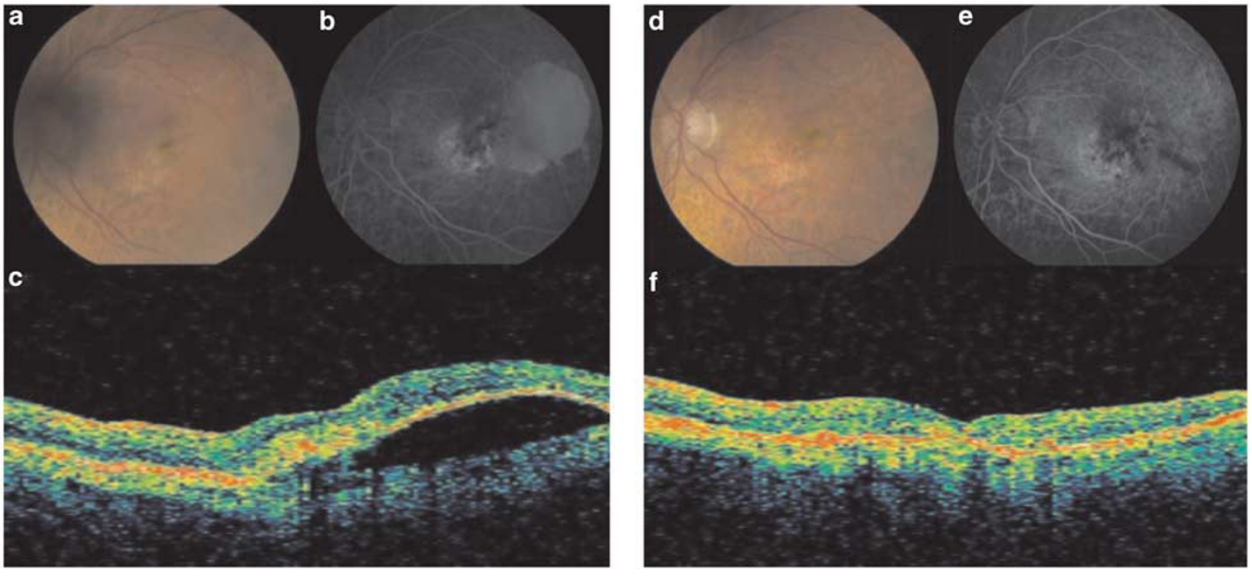

Figure 1 (a) Pre-treatment FP, (b) FA, and (c) OCT show a large vPED with a subfoveal choroidal neovascular focus. (d) FP, (e) FA, and (f) OCT 10 days after a single injection of 2 mg ranibizumab show collapse of the vPED.

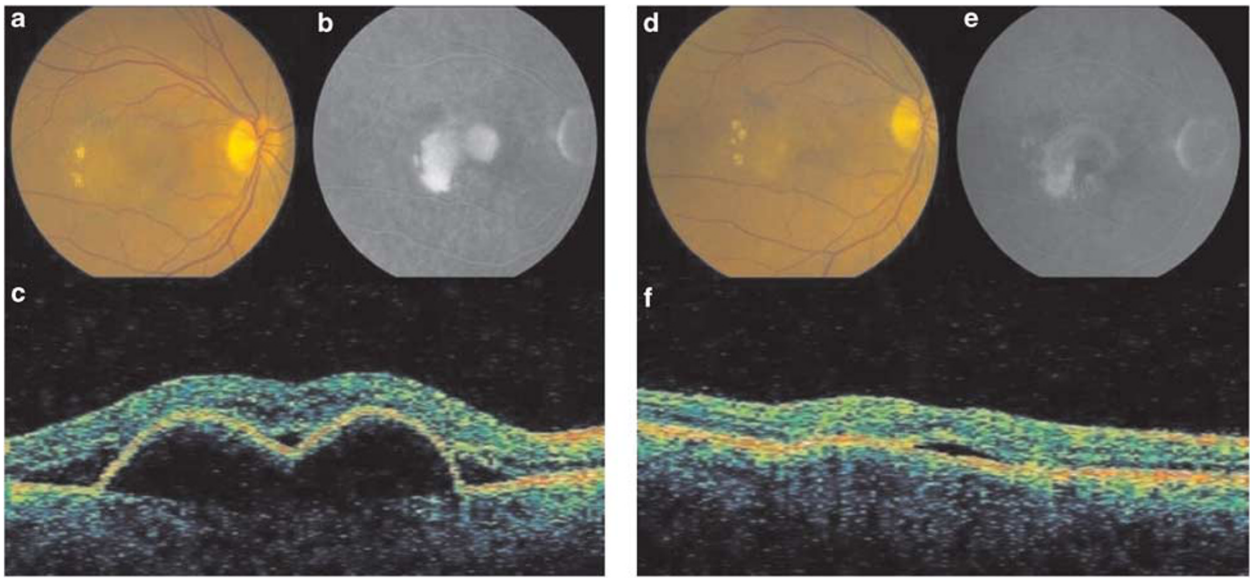

Figure 2 (a) A subfoveal vPED was noted in the RE on pre-treatment FP, (b) FA, and (c) OCT. (d) Resolution of most of the subretinal fluid and the vPED was noted on FP, (e) FA, and (f) OCT 1 month after a single intravitreal injection of 2-mg ranibizumab.

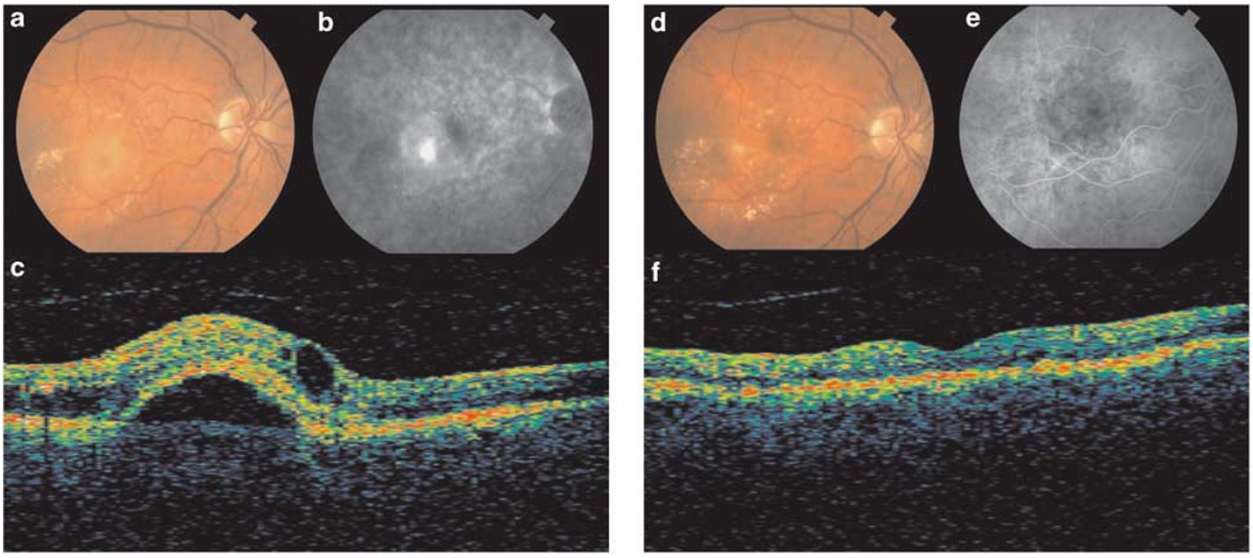

Figure 3 (a) Baseline FP and (b) FA of the RE showed a retinochoroidal anastomosis within a vPED. (c) Baseline OCT also confirmed the diagnosis of PED in the RE. His RE received 2 mg ranibizumab, and the LE also received conventional 0.5 mg ranibizumab injections. (d) After a single 2mg ranibizumab injection, there was resolution of the subretinal fluid and flattening of the vPED in the RE, as shown on follow-up FP, (e) FA, and (f) OCT 1 month later.

For our 3 cases, monthly maintenance injections were performed for 12 months. Patients were monitored on a prospective basis for ocular and systemic adverse events, and none of them developed any cardiovascular, neurological, or thromboembolic complications. However, further monitoring is needed to analyse potential ocular adverse events, such as RPE tears. The preliminary 1-year results of HARBOR, a large multicenter randomized trial, showed no dose–response safety signals relating to ocular or systemic adverse events (A Ho, unpublished data, AAO subspecialty day presentation, Orlando, October 2011).

In conclusion, this case series shows that high-dose ranibizumab may rapidly resolve vPED without complications. Further prospective analysis of a larger cohort of eyes is necessary to validate these outcomes.

Summary

What was known before

- Vascularized pigment epithelial detachments (PEDs) associated with AMD are difficult to treat. Conventional therapies frequently yield inconsistent and suboptimal responses for eyes with vascularized PED.

What this study adds

- Rapid resolution of the vascularized PED following intravitreal injection of high-dose (2 mg) ranibizumab is possible for certain eyes.

Conflict of interest

The authors declare no conflict of interest. This report constitutes the clinical application of a non-FDA-approved dosage of an FDA-approved medication.

Acknowledgements

This work was supported by Genentech Inc. (CKC, PA, DS), Owen Locke Foundation (CKC), and Karl Kirchgessner Foundation (DS). This study was approved by the Western Institutional Review Board and the UCLA Institutional Review Board, and conformed to the standards of the 1964 Declaration of Helsinki. All study subjects gave full informed consent.

References

1 Avery RL, Pieramici DJ, Rabena MD, Castellarin AA, Nasir MA, Giust MJ *et al*. Intravitreal bevacizumab (Avastin) for neovascular age-related macular degeneration. *Ophthalmol* 2006; **113**: 363–372.
2 Fung AE, Lalwani GA, Rosenfeld PJ, Dubovy SR, Michels S, Feuer WJ *et al*. An optical coherence tomography-guided, variable dosing regimen with intravitreal ranibizumab (Lucentis) for neovascular age-related macular degeneration. *Am J Ophthalmol* 2007; **143**: 566–583.
3 Chan CK, Meyer CH, Gross JG, Abraham P, Nuthi ASD, Kokame GT *et al*. Retinal pigment epithelial tears after intravitreal bevacizumab injection for neovascular age-related macular degeneration. *Retina* 2007; **27**: 541–551.
4 CATT Research Group, Martin DF, Maguire MG, Ying GS, Grunwald JE, Fine SL, Jaffe GJ *et al*. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med* 2011; **364**: 1897–1908.
5 Brown DM, Kaiser PK, Michels M, Soubrane G, Heier JS, Kim RY *et al*, for the ANCHOR Study Group. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355**: 1432–1440.
6 Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY *et al*, for the MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355**: 1419–1431.
7 Chuang EL, Bird AC. The pathogenesis of tears of the retinal pigment epithelium. *Am J Ophthalmol* 1988; **105**: 285–290.
8 Pauleikoff D, Löffert D, Spital G, Radermacher M, Dohrmann J, Lommatzsch A *et al*. Pigment epithelial detachment in the elderly. Clinical differentiation, natural course and pathogenetic implications. *Graefes Arch Clin Exp Ophthalmol* 2002; **240**: 533–538.
9 The Moorfields Macular Study Group. Retinal pigment epithelial detachments in the elderly: a controlled trial of argon laser photocoagulation. *Br J Ophthalmol* 1982; **66**: 1–16.
10 Chen E, Kaiser RS, Vander JF. Intravitreal bevacizumab for refractory pigment epithelial detachment with occult choroidal neovascularization in age-related macular degeneration. *Retina* 2007; **27**: 445–450.
11 Antoszyk AN, Tuomi L, Chung CY, Singh A, for the FOCUS Study Group. Ranibizumab combined with verteporfin photodynamic therapy in neovascular age-related macular degeneration (FOCUS): Year 2 results. *Am J Ophthalmol* 2008; **145**: 862–874.
12 Boyer DS, Heier JS, Brown D, Francom SF, Ianchulev T, Rubio RG *et al*, for the SAILOR Study Group. A Phase IIIb Study to evaluate the safety of ranibizumab in subjects with neovascular age-related macular degeneration. *Ophthalmol* 2009; **116**: 1731–1739.