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SHORT COMMUNICATION

Incomplete posterior hyaloid detachment after intravitreal pegaptanib injection in diabetic macular edema

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PURPOSE. *Posterior hyaloid adherences play a role in the pathogenesis of diabetic macular edema (DME). Intravitreal antivascular endothelial growth factor (VEGF) drugs are presently being used to treat DME. The authors report one case of incomplete posterior hyaloid detachment (PHD) following intravitreal pegaptanib to treat DME. This case shows a combined mechanism of DME resolution by anti VEGF and PHD.*
METHODS. *Prospective, interventional, single case report. One male patient with bilateral DME was treated by intravitreal pegaptanib in his right eye every 6 weeks for 6 months (five injections) and followed for 42 months.*
RESULTS. *Central macular thickness decreased from 511 to 376 µm at month 4 in the treated eye and remained within 10% of this value during follow-up. The posterior hyaloid became taut and partially detached after the third injection and was almost completely detached 1 year later. Visual acuity remained unchanged in both eyes during follow-up.*
CONCLUSIONS. *PHD may play an important role in cases where macular thickness is successfully reduced or better acuity is achieved after intravitreal injections. (Eur J Ophthalmol 2008; 18: 469-72)*

KEY WORDS. *Diabetic macular edema, Pegaptanib, Posterior hyaloid detachment*

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INTRODUCTION

Vascular endothelial growth factor (VEGF) is known to play a role in increased vascular permeability occurring in diffuse diabetic macular edema (DME) (1). This idea has prompted the use of intravitreal steroids and antiangiogenic drugs such as pegaptanib, bevacizumab, and ranibizumab to treat this condition and its efficacy has been proved by clinical trials and series reports. However, intravitreal injections may be associated with side effects such as endophthalmitis, uveitis, cataracts, and changes in intraocular pressure, among others.

We describe the appearance of incomplete posterior hyaloid detachment (PHD) in one patient with DME treated by repeated intravitreal injections of pegaptanib.

METHODS

A 67-year-old male diabetic patient with bilateral diffuse DME not respondent to grid laser photocoagulation was treated by intravitreal pegaptanib every 6 weeks during 6 months (five injections) in the left eye. Best-corrected visual acuity (BCVA), optical coherence tomography (OCT), anterior segment and fundus examination were performed every 6 weeks during the first 6 months and then every 12 months.

The injection of pegaptanib took place within one multicenter clinical trial on the use of pegaptanib to treat DME. Written informed consent was obtained and the treatment and follow-up were performed in accordance with the ethical standards of the 1964 Declaration of Helsinki.

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RESULTS

Follow-up was 42 months. BCVA did not change in either eye (right eye 20/80 at baseline and at month 42; left eye 20/80 at baseline and at month 42). Central macular thickness (CMT) measured by OCT changed from 511 µm to 376 µm at month 4, 376 µm at month 9, and 396 µm at month 19 in the treated eye. Initial OCT showed DME (Fig. 1A) which did not decrease after the second injection (Fig. 1B). Posterior hyaloid became partially detached after the third injection associated with decreased macular thickness (Fig. 1C), and 1 year later it was almost completely detached and macular edema was solved (Fig. 1D). No changes in posterior hyaloid or DME appeared in the untreated fellow eye during the follow-up period (Fig. 2).

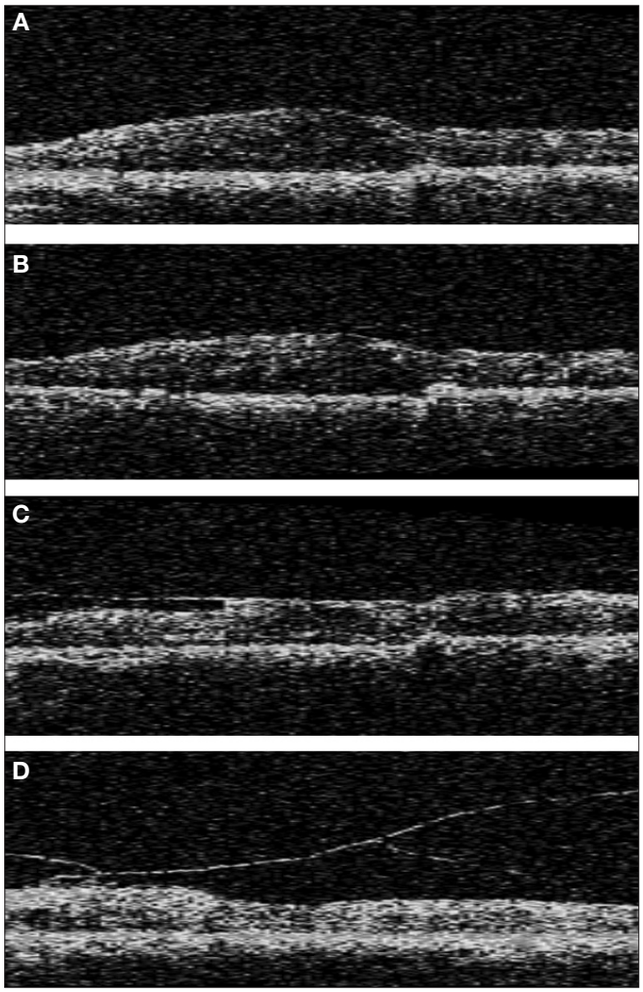

Fig. 1 - *Left eye (treated eye) optical coherence tomography (OCT, vertical scans).* **(A)** *Basal OCT before intravitreous injection shows diffuse macular edema and retinal hard exudates. Posterior hyaloid is not thickened and no retinal traction can be observed.* **(B)** *OCT after the second injection shows little change compared with (A). Posterior hyaloid is slightly thickened.* **(C)** *OCT after the third injection shows partially detached posterior hyaloid and decreased macular thickness.* **(D)** *OCT 1 year after the first injection shows almost complete hyaloid detachment with reduction in macular edema, and focal vitreoretinal adherences.*

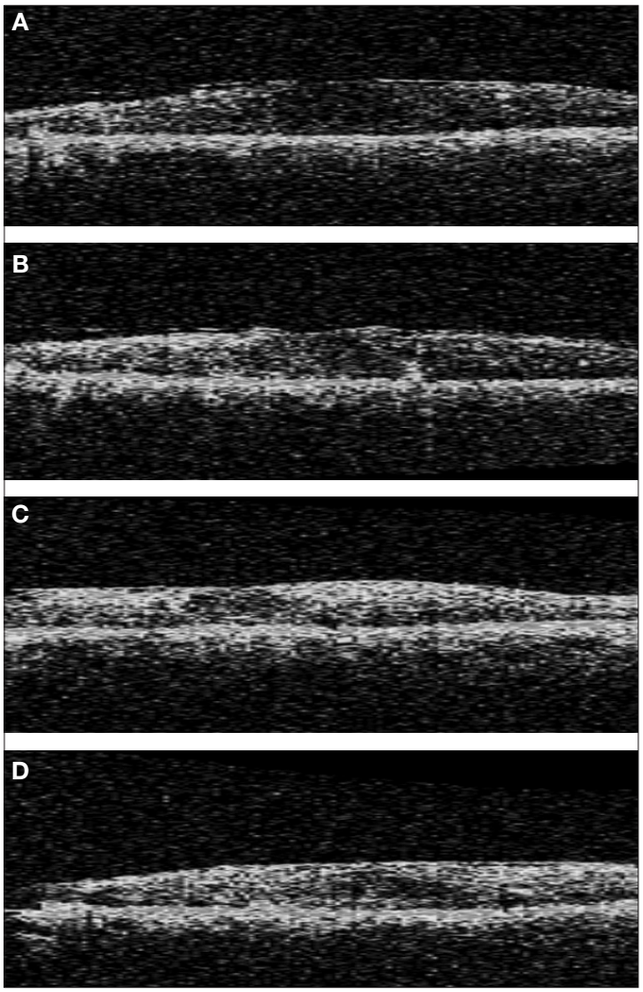

Fig. 2 - *Right eye (fellow eye) optical coherence tomography (OCT) at the same timing as in Figure 1 (vertical scans).* **(A)** *Basal OCT;* **(B)** *OCT at week 12;* **(C)** *OCT at week 18;* **(D)** *OCT at week 54. No significant changes can be observed on macular edema or posterior hyaloid during follow-up.*

DISCUSSION

Anti VEGF drugs have been used to treat DME. One clinical trial demonstrated an average 68 µm decrease in CMT and BCVA gain of more than 10 letters in 34% of the eyes injected with pegaptanib (2). More recently, Avery et al reported improvement in DME and diabetic proliferative retinopathy in eyes injected with bevacizumab (3). This effect was more remarkable in the treated eyes, and to a lesser degree it was also noticeable in the fellow eyes. A more extensive multicenter study was reported by Arevalo et al describing 78 eyes treated by intravitreal 1.25 or 2.5 mg bevacizumab repeated every 4 to 28 weeks. This study showed an improvement in BCVA in 55% of the eyes and a significant reduction of CMT was observed (4).

The findings described in this case report suggest that physical mechanisms may be involved in the resolution of DME in certain cases, and may help stabilizing the presumed pharmacologic effect of the drug.

Posterior hyaloid adherences seem to play a role in the pathogenesis of DME. PHD has been described associated with the injection of intravitreal plasmin, gas, and bevacizumab, among others. Autologous plasmin has been used associated with vitrectomy to produce PHD and reduce macular thickness in patients with DME. PHD is probably not caused by the specific pharmacologic action of these drugs but by the inflammation and vitreous syneresis induced by the injection procedure. This hypothesis is consistent with what has been described for intravitreal bevacizumab (5). However, none of the previously mentioned studies on the use of intravitreal anti VEGF to treat DME reports any changes on the posterior hyaloid. Nevertheless, spontaneous PHD is common, and in the reported case there is no clear evidence that the intravitreal injection was responsible of the vitreous detachment.

On the other hand, in the previously reported clinical trial (2) the average reduction in CMT at week 36 was significant only for the 0.3 mg pegaptanib concentration and not for the 1 and 3 mg ($p=0.02$, $p=0.44$, and $p=0.8$, respectively, analysis of covariance model). Mean changes in retinal thickness from baseline to week 36 as determined at the center point were –68.0, –22.7, –5.3 µm, and +3.7 µm in the 0.3 mg, 1 mg, 3 mg, and sham groups, respectively. It is not reported whether changes in macular thickness occurred in the period between the last injection and the end of follow-up, though it seems reasonable that DME would reappear after cessation of the pharmacologic effect of pegaptanib. In the case we report, no significant changes were observed during the period between month 4 and month 19. This fact may be related to the reduction of posterior pole traction secondary to PHD. DME persisted throughout the follow-up period. The persistence of DME has been previously reported (5). In that article, only 6 to 12% of the eyes had a reduction of more than 200 µm from baseline at week 36. This may be secondary to the multifactorial etiology of DME (posterior pole traction and increased vascular permeability) and the selective inhibition of pegaptanib on $VEGF_{165}$.

It is likely that with the trend toward increasing and frequent use of intravitreal injections in DME, clinicians will begin to gain a feel for whether the induction of PHD is a frequent occurrence, and whether clinical improvement is mediated as much by this change as by any presumed pharmacologic effect of the drug administered.

We encourage clinicians to pay attention to the role of the posterior hyaloid in cases where macular thickness is successfully reduced after intravitreal injections.

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