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Short-term anatomic effect of ranibizumab for polypoidal choroidal vasculopathy

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PURPOSE. *To assess the short-term anatomic effect of intravitreal ranibizumab for polypoidal choroidal vasculopathy.*
METHODS. *All patients had undergone a full ophthalmic examination. A monthly injection of ranibizumab was performed for 3 months. Indocyanine angiography (ICG) and optical coherence tomography (OCT) were performed 1 month after the third-month ranibizumab injection.*
RESULTS. *Polyps disappeared on ICG angiography in 9 out of 13 lesions (69.2%). Retinal thickness diminished significantly on OCT (p=0.02). In our series we noticed a significant reduction of the percentage of patients presenting with subretinal fluid (p=0.02) and pigment epithelium detachment between the initial and final visits (0.016). In addition, we noticed that BCVA increased significantly (p 0.02).*
CONCLUSIONS. *Monthly intravitreal injection of ranibizumab for 3 months has a short-term beneficial anatomic effect. (Eur J Ophthalmol 2008; 18: 645-8)*

KEY WORDS. *Polypoidal choroidal vasculopathy, Ranibizumab, Optical coherence tomography, Indocyanine green angiography*

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INTRODUCTION

Whether polypoidal choroidal vasculopathy (PCV) represents abnormal vessels from the choroidal circulation or neovascularization from choriocapillaris is debated (1). Various studies corroborated the fact that vascular endothelial growth factor (VEGF) could be an etiologic agent in the pathogenesis of this disease (2, 3).
Recently, Gomi et al (4) published the results of a series of 11 patients with PCV treated with bevacizumab, in which only a single polypoid lesion was obliterated at 3 months following the injection, in addition to increased frequency of reappearance of subretinal fluid (SRF) and pigment epithelium detachment (PED) on OCT.
The aim of this study is to evaluate the short-term efficacy and safety of ranibizumab in treating PCV.

METHODS

This retrospective study included patients with symptomatic PCV not treated previously who had macular involvement defined as the presence of SRF or intraretinal edema on OCT. Patients with demonstrated areas of leakage on fluorescein angiography (FA) not corresponding with the presence of polyps in these areas on indocyanine green angiography (ICG) were excluded owing to suspicion of choroidal neovascularization (CNV).
Patients received a monthly injection of 0.05 mL ranibizumab for 3 months. Patients have been followed up monthly. All follow-up visits included determination of best-corrected visual acuity (BCVA) and examination to measure the central thickness of the neurosensory retina on OCT.

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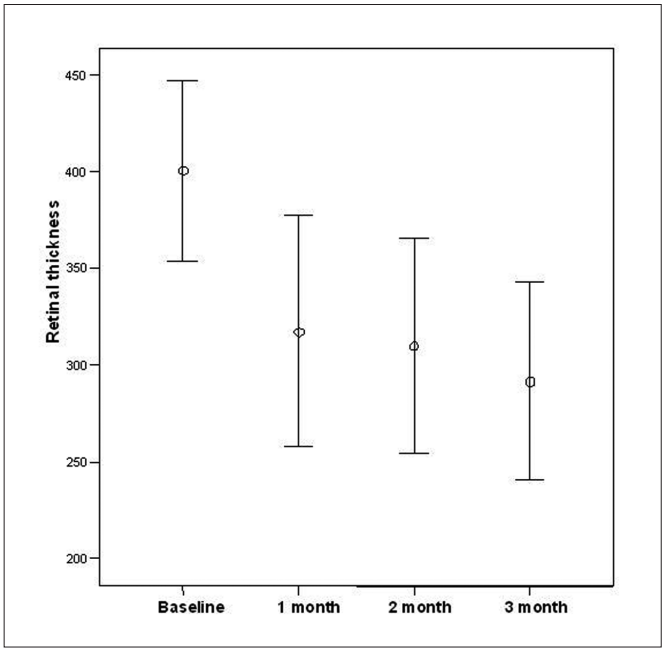

Fig. 1 - *A statistically significant (p=0.03 at 1 month, 0.02 at 2 months, and 0.02 at 3 months) reduction of maximum thickness of the neurosensory retina was demonstrated by optical coherence tomography.*

In addition, ICG angiography was repeated on the final visit, 1 month following the third injection of ranibizumab.
The main outcome measure of the study is to determine the percentage of polypoidal lesions obliterated on ICG angiography done 1 month after administering a ranibizumab load (monthly injection for 3 months).

RESULTS

Thirteen eyes of 13 patients were included (9 women and 4 men), mean age 70.92 years (range 61–80). Table I summarizes the baseline characteristics.
Three months after the initial visit, polypoidal lesions disappeared on ICG angiography in 9 patients (69.2%). A statistically significant (p=0.02) reduction of maximum thickness of the neurosensory retina was demonstrated by OCT (Fig. 1), from an initial mean value of 400.85 µm (range, 310–548) to a final mean value of 292.00 µm (range, 207–491).
On the initial visit, OCT examination of 11 patients (84.6%) showed neurosensory retinal detachment. At 3 months, OCT of only one patient (7.7%) showed persis-

TABLE I - CLINICAL CHARACTERISTICS IN PATIENTS WITH PCV TREATED WITH RANIBIZUMAB

Pat N.	Age (yrs)	Gn	No polyp	Foveal Height (µm) baseline	Foveal Height (µm) 3m	PED baseline	PED 3m	SRF baseline	SRF 3m	BCVA Baselin (letters)	BCVA 3m (letters)	ICGA PCV closure
1	74	M	3	464	491	No	No	No	No	73	77	No
2	80	M	2	432	240	Ser	No	Yes	No	51	60	Yes
3	71	F	6	548	448	SH	No	Yes	No	60	65	Yes
4	80	F	3	356	207	Ser	No	Yes	No	44	55	Yes
5	69	F	4	323	265	SH	SH	No	No	65	75	Yes
6	64	F	2	489	265	Ser	No	Yes	No	34	44	Yes
7	69	M	5	348	224	No	No	Yes	No	51	71	Yes
8	77	M	5	310	232	Ser	No	Yes	No	64	69	Yes
9	72	F	3	506	315	SH	SH	Yes	No	63	68	No
10	62	F	6	352	284	Ser	No	Yes	No	53	75	No
11	79	F	4	346	285	SH	No	Yes	No	36	46	Yes
12	61	F	5	381	273	Ser	Ser	Yes	Yes	70	73	No
13	64	F	4	356	267	SH	SH	Yes	No	65	75	Yes

Gn = Gender; F = Female; M = Male; RPE = Retinal Pigment Epithelium; PED = Pigment Epithelium Detachment; SRF = Subretinal Fluid; BCVA = Best Corrected Visual Acuity; ICGA = Indocyanine Green Angiography; PCV = Polypoidal Choroidal Vasculopathy. Ser = Serous PED; SH = Sero

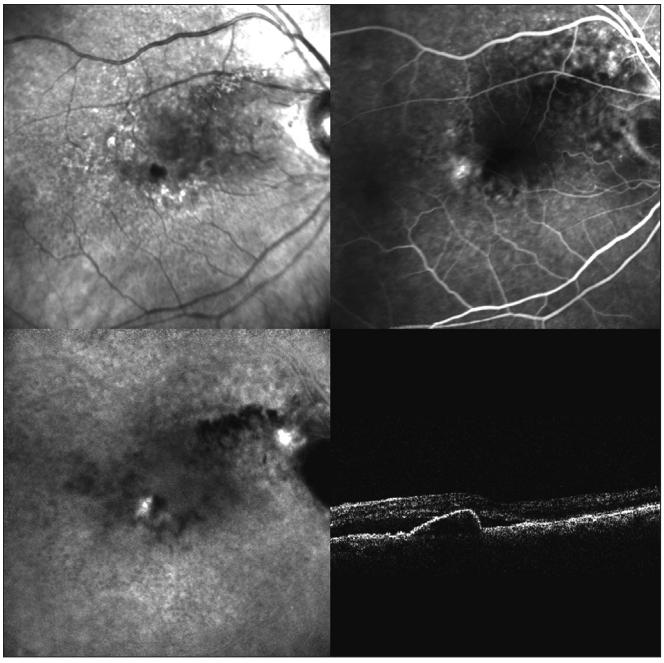

Fig. 2 - (Top left) *Case 8, a 77-year-old man. Fundus photograph showing a mild juxtafoveal hemorrhage.* (Top right) *Fluorescein angiography at baseline with juxtafoveal and peripapillary leakage.* (Bottom left) *Baseline indocyanine green angiography with two areas of polyps, one juxtafoveal and other peripapillary.* (Bottom right) *Baseline optical coherence tomography showing a juxtafoveal pigment epithelium detachment and subretinal fluid.*

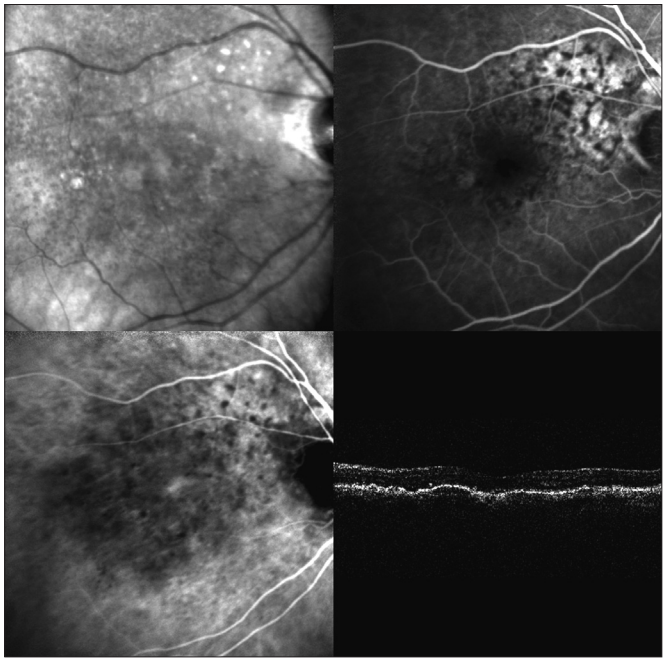

Fig. 3 - (Top left) *Case 8, 1 month after the third-month ranibizumab injection fundus photograph shows disappearance of the hemorrhage.* (Top right) *Fluorescein angiography at the end of the study, showing a mild retinal pigment epithelium mottling without leakage.* (Bottom left) *Disappearance of the polyps on indocyanine green angiography in both areas.* (Bottom right) *Resolution of subretinal fluid and flattening of pigment epithelium detachment on optical coherence tomography.*

tent subretinal fluid (p=0.02). The percentage of patients who presented with PED was reduced from a baseline value of 84.6% to 30.8% at the end of the study (p=0.016).

Statistically significant improvement of BCVA has been noticed throughout the study (p=0.02), where BCVA improved from a mean initial value of 0.59 logMar (range 0.3–1) to a final mean value of 0.4 logMar (range 0.2–0.8).

In addition, we did not detect, in any case, side effects such as subretinal hemorrhage, retinal pigment epithelium tears, or increased retinal pigment epithelium atrophy.

DISCUSSION

The results of our series demonstrate short-term efficacy of ranibizumab with almost 70% of polypoidal lesions obliterated 1 month after the third-month ranibizumab injection (Figs. 2 and 3). This percentage is slightly less than that observed with PDT (5), with similar visual results though with much shorter follow-up period in our series. Nevertheless, none of our patients developed subretinal hemorrhage, which is relatively frequent in patients treated with PDT (5).

Similarly, significant improvement of OCT scans has been noticed, with decrease of mean neurosensory retinal thickness and significant reduction of the percentage of lesions that showed PED and SRF on OCT.

It is noteworthy that more than half of the patients included in Gomi et al's series (4) had their intraretinal edema reduced following bevacizumab injection, only to worsen over the following weeks after stopping treatment, which indicates that bevacizumab could be effective in reducing exudative activity associated with PCV, albeit insufficient dosage in that series.

Another possible hypothesis is that bevacizumab has less capacity than ranibizumab to penetrate through the retinal thickness and the retinal pigment epithelium. This is because ranibizumab theoretically possesses greater penetration capacity (6). This penetrability could be especially

important in PCV, as the lesion is located beneath the retinal pigment epithelium.

In conclusion, our study shows the efficacy, at least in the short term, of ranibizumab in obliteration of polypoidal lesions and reduction of exudative phenomena. Nevertheless, this series presents numerous limitations including retrospective design, limited study sample, and absence of treatment-free follow-up period of patients included in the study. Therefore, more studies are needed to evaluate the role of ranibizumab in PCV.

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