Effectiveness of combined laser photocoagulation therapy with intravitreal anti - VEGF in *Retinal arterial macroaneurysms*: case report

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Abstract

Background: *Retinal arterial macroaneurysms (RAM) is a pathological dilatation of retinal arterial vessel.*
Argon laser photocoagulation has been for a long time the gold standard of many vascular diseases of the retina such as macroaneurysm. From this work emerges how the introduction of intravitreal anti-VEGF therapies have enhanced the 'effectiveness of the combination of argon laser photocoagulation in cases of persistent retinal edema, we present the case of a retinal macroaneurysm with macular hemorrhage focus and oedema in a patient with a history of systemic arterial hypertension.
Methods: *A 77 year-old woman patient reported sudden decline in visual acuity in the left eye; the best corrected visual acuity (BCVA)was 1/10 in left eye. Fluorescein angiography (FAG) resulted in diagnosis of Macroaneurysm at the posterior pole with macular hemorrhage focus and oedema. The patient was treated with laser treatment in the left eye; after 30 days, the visual acuity was 1/50 and at optical coherence tomography (OCT) the retinal profile was significantly altered. After 30 days, a single intravitreal ranibizumab injection was performed and, after 7 days, visual acuity was 1/10. After 24 months from ranibizumab-based therapy the final visual acuity was 10/10 and OCT examination revealed a normal retinal profile.*
Conclusion: *In this case report the association of argon laser photocoagulation with intravitreal anti-VEGF injection has been proven to be effective and safe in case of persistent retinal oedema.*

Keywords: *Retinal arterial macroaneurysms (RAM), laser photocoagulation, anti-VEGF intravitreal injection*

Introduction

Retinal arterial macroaneurysms (RAM) represent a distinct clinical entity [1]. It is an acquired retinal vascular dilation that has developed from retinal arteriole [2]. It is prevalent in the elderly and in women and is associated with systemic hypertension, atherosclerosis, hyperlipidemia, polycythemia and cardiovascular disease [3].

The classic presentation allows easy diagnosis, however different presentations can make diagnosis difficult, as the subretinal hemorrhage, macular exudate and epiretinal membranes [4]. Therefore differential diagnosis includes retinal and systemic diseases that require further investigation, such as retinal telangiectasia, angiomatosis retinae, venous macroaneurysms, background diabetic retinopathy,

cavernous hemangioma and cancer [5].

Retinal macroaneurysm may have subretinal exudation secondary to bleeding, often asymptomatic, but when it involves the macular region causes severe reduction of BCVA.

The loss of BCVA is the result of bleeding of macroaneurysm; hemorrhage may occur forward or behind the retina, or in some cases, in both directions and is often associated with an exudative retinal detachment [6]. Progression can be spontaneously favourable depending on the severity and the location of the haemorrhage. A poor visual prognosis is usually reported in subretinal haemorrhage [7].

Figure 1. Fluorescein angiography (FAG) revealed in the initial phases a fluorescent formation, circular in shape, whose perfusion seems to be rooted in a further subdivision of the afferent artery, with which it is linked.

Currently, it is preferred to perform before the laser therapy, intravitreal anti-VEGF with the aim of reducing retinal areas by photocoagulate and complications.

In support of the validity of these new treatment protocols, we report our clinical experience.

Photocoagulation is now considered the gold standard treatment; it may accelerate visual recovery, but it is not always feasible especially in those forms involving the macular region [8].

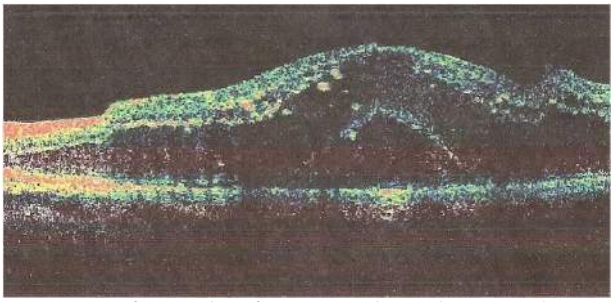


Figure 2. : After 30 days from Argon laser photocoagulation in OS, optical coherence tomography (OCT) revealed altered retinal profile with the disappearance of physiological foveal depression, intraretinal oedema widespread, foveal detachment of the neuroepithelium.

If central vision is reduced, photocoagulation directly applied either to the macroaneurysm, or indirectly by surrounding the macroaneurysm, or to both these areas, determines further impairment of central vision secondary to atrophic scar laser treatment [9].

Figure 3. After 30 days from laser therapy in OS, FAG showed the as an area of intense focal coloration at the posterior pole, with perifoveal exudative oedema with retinal detachment headed toward the macula.

For this reason, to reduce edematous exudation areas arising also from the laser treatment, we decided to associate laser therapy with anti-VEGF antibody (ranibizumab) prior informed consent.

Case presentation

A 77-years-old woman reported sudden decline in visual acuity in the left eye came to our attention. In general anamnesis, the patient presented pharmacologically-treated hypertension.

The woman had a history of ocular severe myopia and reported previous operation for retinal detachment in the right eye (cerclage and vitrectomy). Biomicroscopic slit-lamp examination revealed in the right eye postsurgical aphakia; BCVA was 2/50 (1.39 LogMAR) in right eye (with Early Treatment Diabetic Retinopathy Study - ETDRS- table placed at a distance of 4 m). In the left eye were not appreciated major alterations at biomicroscopic examination; BCVA was 1/10 (1 LogMAR).

Intraocular pressure (IOP) resulted 10 mmHg in right eyes and 16 mmHg in left eye.

At fundus examination, outcomes of a retinal detachment ab internal and ab external were appreciated in the right eye, whereas in the left eye was evident a macroaneurysm in the posterior pole, along the vascular course of an arterial formation on the superior temporal arch surrounded by a halo with yellowish subretinal hemorrhage, exudative retinal detachment directed toward the macula and lipoidal alterations barely noticeable. The presence of macroaneurysm was confirmed by Fluorescein angiography (FAG) (Fig. 1).

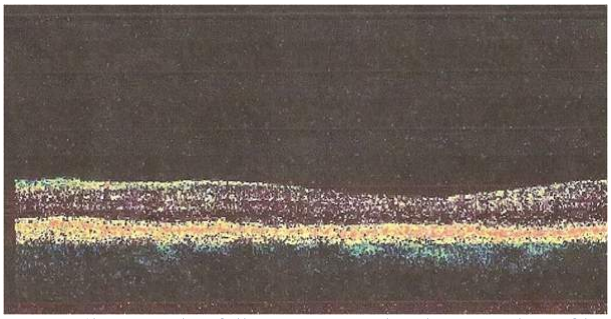


Figure 4b. : In the following controls, the retinal profile appeared normal at OCT at 24 months after treatment laser photocoagulation with association i.v. anti-VEGF.

Once submitted the informed consent, the patient was treated with Argon laser photocoagulation in OS, with spots with a diameter of 300 µm, 80 mw and 120 ms, outside the macroaneurysm, mainly at the upper margin of the aneurysmatic dilatation. After 30 days BCVA markedly reduced (1/50, 1.69 LogMAR).

Figure 5a: Atrophic scar: result after treatment laser photocoagulation with association i.v. anti-VEGF at 24 months.

At optical coherence tomography (OCT), performed using Spectralis HRA-OCT Heidelberg Engineering, the retinal profile was significantly altered with the disappearance of physiological foveal depression, intraretinal oedema widespread, foveal detachment of the neuroepithelium (Fig. 2).

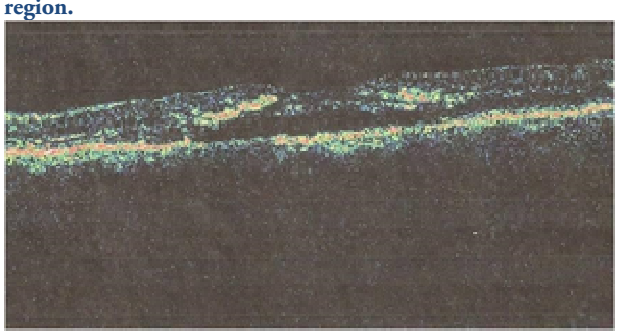
At FAG the macroaneurysm is outlined as an area of intense focal coloration at the posterior pole, with a hemorrhagic component shielding and perifoveal exudative oedema with retinal detachment headed toward the macula.

It showed also a possible exudative local spread of the dye (Fig. 3).

After 30 days from the laser therapy, OCT revealed residual retinal oedema thata no improvement the BCVA; then, after obtaining informed consent, a single intravitreal (IV) anti-VEGF injection (ranibizumab) was performed. The treatment was performed after approval by the local ethics committee.

After 7 days, BCVA was 1/10 (1 LogMAR) and improved gradually to 8/10 (0.09 LogMAR) after 14 days and to 10/10 after 30 days from the intravitreal injection (Fig. 4a).

Figure 4a. After 14 days from the intravitreal (i.v.) injection ranibizumab, the OCT revealed an improvement: it showed marked reduction in the lifting of the foveal region and in the detachment of the neuroepithelium in juxtafoveal region.



The improvement in visual acuity was following by the reduction of CMT. Indeed, the OCT showed a marked reduction in the lifting of the foveal region, as well as intraretinal oedema and in the detachment of the neuroepithelium in juxtafoveal region (Fig. 4a-4b).

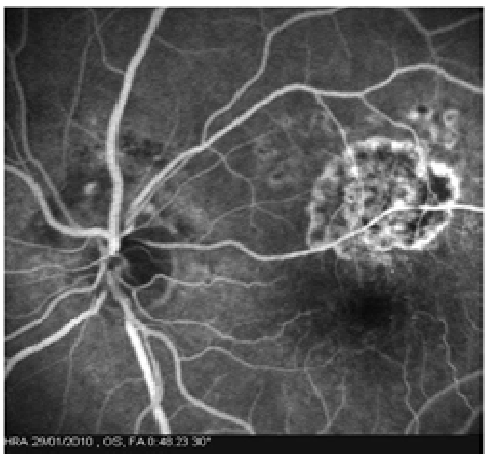


Figure 5b: FAG: shows the result of the previous focal laser treatment with the combination of IV anti-VEGF at 24 months: chorioretinal local shielding, the perifoveal area with superior maintenance of physiological model of the foveal region.

In the following controls after 3, 6,12 and 24 months, the BCVA remained stable, equal to 10/10. Fundus examination revealed adherent retina, absence of oedema and outcomes of previous laser treatment along the superior-temporal arch. At OCT (Fig.4b) the retinal profile appeared normal, with no edematous areas.

Discussion

The literature [10] reports a case of spontaneous resorption of a sub-retinal hemorrhage [11]. In cases of pre-retinal hemorrhage, the therapeutic indication is laser

photocoagulation. In most cases, serous component of the exudative reaction tends to resolve, by direct spread to the retinal vascular circle, within a few weeks, while the lipid exudation, dissolving by a cell-mediated process, requires several weeks or months [6-12].

The persistent lipid concentration may cause irreversible structural changes of the retinal pigment epithelium and the neurosensory retina and thereby adversely affect the recovery of visual acuity [13-14].

In our case, after the treatment, there is currently an atrophic scar and narrowing of the affected vessel; FAG detects a change in local tissue chorioretinal shielding as the outcome of previous focal laser treatment to the upper perifoveal sector with maintenance of the physiological pattern of the foveal region (Fig. 5b).

Conclusion

The results emerging in our work indicate that photocoagulation is definitely the effective treatment of RAM.

In some cases of subretinal oedema persistent, the association with I.V. anti-VEGF, results in a more rapid resolution as documented by OCT and from the results of BCVA. In particular, in the case reported by us it was sufficient to associate with laser photocoagulation a single injection of anti-VEGF for the resolution, also clinical-symptom (BCVA).

In the case reports were not present none of the complications described in the literature the laser photocoagulation therapy combined Intravitreal injection 16-18 .

For this reason, in accordance with the literature, we believe that the combination of laser photocoagulation Intravitreal Thetapy with anti -VEGF in RAM is effective and safe 19,20.

However, further follow-up and case studies will be useful to confirm the results obtained.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors participated in the design, drafting the manuscript and have read and approved the final manuscript.

References

1. Rabb M F, Gagliano D A, Teske M P: Retinal arterial macroaneurysms. Surv Ophthalmol 33(2):73-96, 1988.
2. Cleary, PE, Kohner, EM, Hamilton, AM, and Bird, AC: Retinal macroaneurysms. Br J OphthalmoI 59:355-361, 1975.
3. Green, WR: Retinal ischemia: vascular and circulatory conditions and diseases. In Spencer, ed: Ophthalmic pathology, PhiladeIphia, 1985, WB Saunders.
4. Zghal-Mokni I, Nacef L, Yazidi B, Malek I, Bouguila H, Ayed S: Clinical and progressive features of macular hemorrhage secondary to retinal artery macroaneurysms. J Fr Ophtalmol 30:150-4, 2007.
5. Perry, HD, Zimmerman, LE, and Benson, WE: Hemorrhage from isolated aneurysm of a retinal artery: report of two cases simulating malignant melanoma. Arch OphthaImoI 95:281, 1977.
6. Abdel-Khalek, MN, and Richardson, J: Retinal macroaneurysm: natural history and guidelines for treatment. Br J Ophthalmol 70:2-11, 1986.
7. Gurwood AS, Nicholson CR: Retinal arterial macroaneurysm: a case report. J Am Optom Assoc Jan 69:41-8, 1998.
8. Palestine AG, Robertson DM, Goldstein BG: Macroaneurysms of the retinal arteries. Am J Ophthalmol 93: 164-171, 1982.

9. Russell SR,Folk JC: Branch retinal artery occlusion after dye yellow photocoagulation of an arterial macroaneurysm. Am J Ophthalmol 104:186-7, 1987.
10. Kim J, Kim SJ, Chang YS, Park WS.: Combined intravitreal bevacizumab injection and zone I sparing laserphotocoagulation in patients with zone I retinopathy of prematurity. Retina. 2014 Jan;34(1):77-82.
11. Zghal-Mokni I, Nacef L, Yazidi B, Malek I, Bouguila H, Ayed S: Clinical and progressive features of macular hemorrhage secondary to retinal artery macroaneurysms. J Fr Ophtalmol 30:150-4, 2007.
12. Joondeph, BC, Joondeph, HC, and Blair, NP: Retinal macroaneurysms treated with the yellow dye laser. Retina 9:187-192,1989.
13. Panton RW, Goldberg MF, Farber MD: Retinal arterial macroaneurysms: risk factors and natural history. Br J Ophthalmol 74:595-600, 1990.
14. Pacella E, Pacella F, La Torre G, et al.:Testing the effectiveness of intravitreal Ranibizumab during 12 months of follow-up in venous occlusion treatment. Clin Ter. 2012 Nov;163(6):e413-22.
15. Lewis, RA, Norton, EWD, and Gass, JDM: Acquired arterial macroaneurysms of the retina. Br J OphthalmoI 60:21-30, 1976.
The effect of photocoagulation in ischemic areas to
16. Takamura Y, Tomomatsu T, Matsumura T, et al.: prevent recurrence of diabetic macular edema after intravitreal bevacizumab injection. Invest Ophthalmol Vis Sci. 2014 Jul 15;55(8):4741-6. doi: 10.1167/iovs.14-14682.
17. Shikari H, Silva PS, Sun JK. Complications of intravitreal injections in patients with diabetes. Semin Ophthalmol. 2014 Nov;29(5-6):276-89.
18. Haddock LJ, Ramsey DJ, Young LH. Complications of subspecialty ophthalmic care: endophthalmitis after intravitreal injections of anti-vascular endothelial growth factor medications. Semin Ophthalmol. 2014 Nov;29(5-6):257-62.
19. [BRAVO and CRUISE: ranibizumab for the treatment of macular edema secondary to retinal vein occlusion]. Arch Soc Esp Oftalmol. 2012 Dec;87 Suppl 1:46-53.
20. Ho AC, Busbee BG, Regillo CD, et all.;for the HARBOR Study Group. Twenty-four-Month Efficacy and Safety of 0.5 mg or 2.0 mg Ranibizumab in Patients with Subfoveal Neovascular Age-Related Macular Degeneration. Ophthalmology. 2014 Jul 9. pii: S0161-6420(14)00429-1