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Research Article

BEVACIZUMAB IN THE TREATMENT OF MACULAR EDEMA IN ACUTE CENTRAL RETINAL VEIN OCCLUSIONS

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A B S T R A C T

Even if bevacizumab is unlicensed, a majority of retina specialists still currently recommends it in retinal vein occlusion-related macular edema. For the first time, the results of our studies showed evidence suggesting that an early treatment administered immediately after the onset of venous occlusion, provided a significant and sustained improvement in visual acuity and foveal thickness, with inactive disease (dry retina and stable visual acuity for at least 6 months after the last injection) in most phakic patients with acute central/ hemicentral retinal vein occlusions, making this treatment option a rational and viable therapeutic strategy. Central/ hemicentral retinal vein occlusion has to be considered an ophthalmic emergency. The highlighting of the ocular conditions most frequently associated with central/ hemicentral retinal vein occlusion (ocular hypertension, primary open angle glaucoma, primary angle closure suspect, primary angle closure, and primary angle closure glaucoma) is mandatory. Regardless of the anti-vascular endothelial growth factor agents used (bevacizumab/ ranibizumab / aflibercept/), and regardless of the treatment approaches chosen (treat-and-extend/ pro re nata algorithm), the efficacy of therapy depends primarily on the precociousness of the therapy after the diagnosis of central/ hemicentral retinal vein occlusion. Any delay in the treatment will adversely influence the restoration of visual functions, which are difficult to correct even with subsequent treatment.

INTRODUCTION

Even if bevacizumab is unlicensed, a majority of retina specialists still currently recommends it in retinal vein occlusion-related macular edema. For the first time, the results of our studies showed evidence suggesting that an early treatment administered immediately after the onset of venous occlusion, provided a significant and sustained improvement in visual acuity and foveal thickness, with inactive disease (dry retina and stable visual acuity for at least 6 months after the last injection) in most phakic patients with acute central/ hemicentral retinal vein occlusions, making this treatment option a rational and viable therapeutic strategy. The aim of our work is to evaluate the efficacy of intravitreal injection of bevacizumab in the treatment of macular edema complicating RVO.

PATIENTS AND METHODS

His is a retrospective study of 30 eyes of 30 patients with macular edema complicating RVO. All our patients had undergone complete ophthalmologic examination, retinal fluorescein angiography, and retinal optically coherent tomography (OCT). Intravitreal injection of 1.25 mg bevacizumab was performed for all our patients in the operating room under local anesthesia with strict asepsis. Postoperative monitoring included visual acuity, TO, and a fundus microscopy performed on day 1, day 7, 3 months, 6 months, and one OCT every 3 months. Reinjection of bevacizumab was performed in case of recurrence of OM after an average of 2.6 months. The average follow-up was 6.8 months.

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RESULTS

The age of the patients ranged from 26 to 69 with an average of 53.2 years. Ten patients were female and 20 male patients. Central retinal vein occlusion (CRVO) was noted in 19 eyes, retinal vein occlusion (RVO) was noted in 11 eyes. Initial visual acuity ranged from 1/50 to 5/10, with an average of 1.25 / 10. The mean macular thickness before injection was 746 µm, with extremes ranging from 364 µm to 1222 µm. An improvement in visual acuity was noted in 20 eyes, stabilization in 5 eyes [Figure 1] and worsening in 5 eyes. The average final visual acuity was 2.5 / 10 (1/50 -10/10).

A reduction in macular thickness with OCT was noted with a final macular thickness ranging from 150 µm to 950 µm with an average of 412.6 µm [Figure 2]. Recurrence of macular edema was noted in 12 eyes [Figure 3].

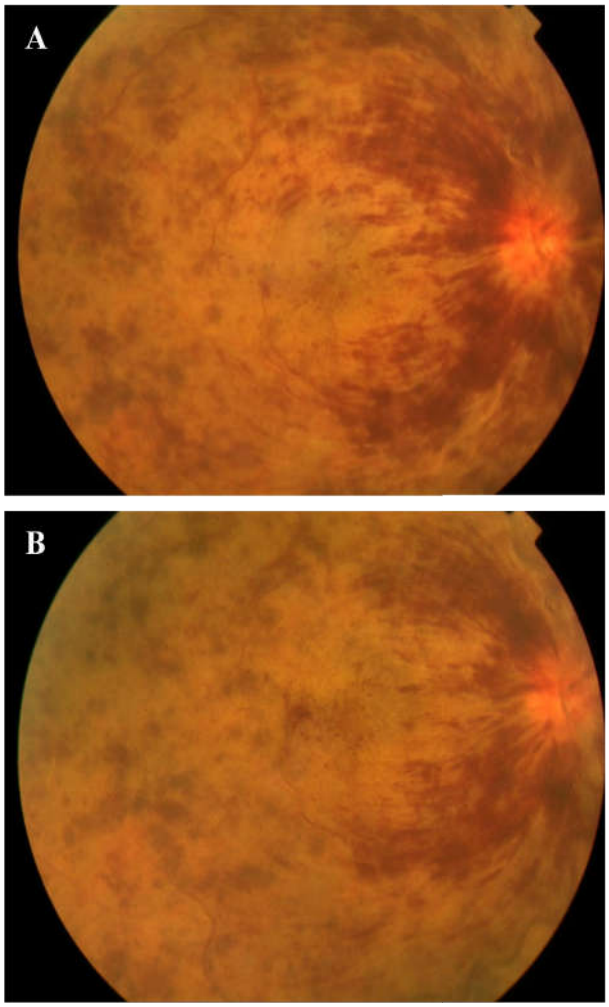

Fig 1 [A] fundus photo preoperatively showing CRVO with macular edema; [B] fundus photo 1 month after intravitreal injection of bevacizumab: decreased hemorrhages with persistence of cystoid macular edema.

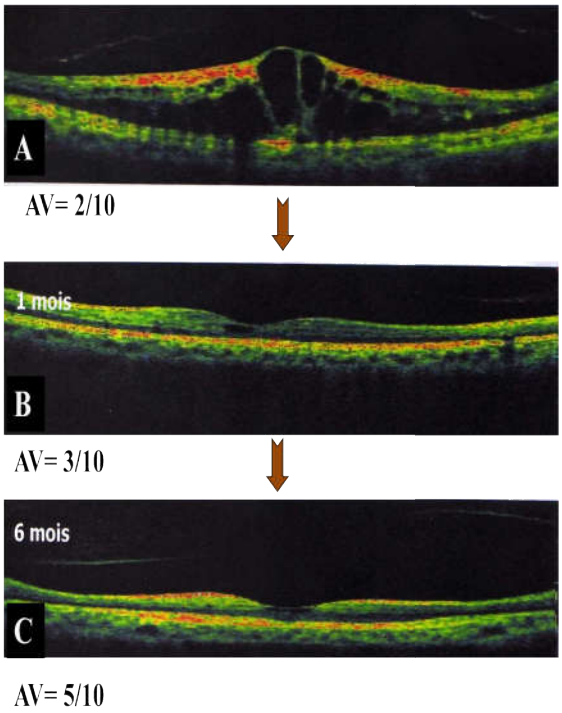

Fig 2 [A] OCT appearance of macular edema complicating OBVR preoperatively; [B] decrease in edema after 1 month of avastin IIV; [C] Complete regression of macular edema at 6 months.

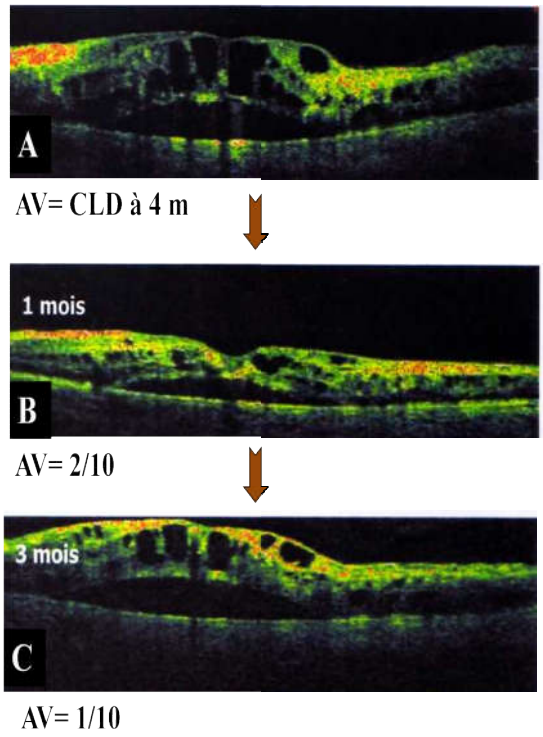

Fig 3 [A] OCT appearance of macular edema with retinal serous delamination (RSD) complicating an RCVO preoperatively; [B] slight improvement in edema after 1 month of avastin IIV; [C] recurrence of macular edema and RSD after 3 months.

DISCUSSION

Retinal vein occlusion (RVO) is a second most common retinal vascular disorder following diabetic retinopathy and is often associated with visual loss. RVOs have an estimated prevalence of 0.5% in individuals over 40 years old [1]. A recent population-based study estimated the 15-years cumulative incidence of RVOs to be 2.3% [2]. The most common age range is from the 6th to the 7th decade. RVOs are relatively uncommon in individuals under age 40. Central retinal vein occlusion (CRVO) is generally reckoned as one of the major threats to vision because many patients suffer irreversible visual loss even in the face of several therapeutic alternatives. Main causes of visual impairment include macular edema (ME), retinal neovascularization with secondary neovascular glaucoma, epiretinal membrane formation, rubeosis iridis, retinal hemorrhages, vitreous hemorrhage, and retinal tissue destruction due to the retinal ischemia [3-5]. Various treatments for CRVO have been advocated over the last decade. These include medical therapy with anticoagulants, fibrinolytics, corticosteroids, acetazolamide, and isovolemic hemodilution. Panretinal or sectorial retinal laser photocoagulation should only be considered for the treatment of neovascularization [3,6]. Surgical options, including pars plana vitrectomy, surgically induced retinochoroidal anastomoses, direct venous cannulation, and radial optic neurotomy, may provide a potential benefit in RVO related ME. The evidence for the justification of these modalities has remained unproven or at least unclear for most of them. More recently, the intravitreal anti-vascular endothelial growth factor (VEGF) injections with bevacizumab (Avastin; Genentech Inc., San Francisco, CA, USA), ranibizumab (Lucentis; Genentech, Inc.,) and aflibercept (Eylea; Regeneron Pharmaceuticals, Inc, Tarrytown, New York, USA) quickly became incorporated into the clinical

management of CRVO representing its front-line therapy [7-10].

The rationale for administering early intravitreal bevacizumab treatment [7] to patients with acute occlusions included the following: initial abrogation of the increased VEGF levels in the acute phase, which are responsible for the main symptoms and complications, most of which occur in the natural clinical course during the first 7-8 months of the disease (ME, retinal capillary nonperfusion, neovascularization and neovascular glaucoma); binding of the bevacizumab to all VEGF-A isoforms, preventing their attachment to receptors situated on the endothelial cell surface; rapid, effective, and direct blocking of the neovascular process and its complications; reversal of increased vascular permeability mediated by VEGF, ensuring the stability and integrity of the inner blood retinal barrier; maintenance of a relatively normal or almost normal foveal anatomy during the acute phase of occlusion, when the VEGF levels are increased, until improvement of the draining circulation; prevention of acute functional curable retinal capillaropathy, that is present immediately after the onset of occlusion, to develop into a permanent capillaropathy, with limited reversal; and normalization of the long term physiological VEGF expression, which is essential for vascular endothelial homeostasis, blood pressure homeostasis, and neuroprotection of the retinal ganglion cells.

CONCLUSIONS

Central/ hemicentral RVO has to be considered an ophthalmic emergency. The highlighting of the ocular conditions most frequently associated with central/ hemicentral RVOs (OH, POAG, PACS, PAC, and PACG) is mandatory. Therapy with anti-VEGF agents has to be promptly applied as soon as possible after RVO onset. The sooner the treatment is started after the RVO onset, the sooner the patient is likely to have gains in visual and FT. Every delay of therapy adversely influences the delayed deterioration of visual functions, which are difficult to restore even with subsequent treatment. Regardless of the anti-VEGF agents used (bevacizumab/ranibizumab/aflibercept), and of the treatment approaches chosen (treat-and-extend/ PRN algorithm), the efficacy of therapy depends primarily on the precociousness of the therapy after RVO diagnosis.

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