Bevacizumab (Avastin): Off-label Use in Ophthalmology

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Introduction

Off-label (unlabelled or unapproved) use of approved product refers to the use of an approved product in a scenario that is not included or is disclaimed in the product information. Examples include use for a different indication, in a different patient age range-group, different dose or different route of administration to that which is approved by regulatory authorities.

Genetech (San Francisco, CA) developed a monoclonal antibody against vascular endothelial growth factor (VEGF) that was as a cancer therapy with the idea that reducing the vascular supply to a tumor may inhibit growth of the cancer.

VEGF is a protein and is the most important growth factor for neovascularization in a variety of tissues including the eye.

VEGF plays a pivotal role in the development of pathologic angiogenesis in ischemic and inflammatory diseases such as proliferative diabetic retinopathy, central retinal vein occlusion and retinopathy of prematurity. Bevacizumab (avastin Genetech Inc, San Francisco, CA) is a full-length, humanized monoclonal antibody against VEGF. It is currently approved as an intravenous treatment for metastatic colorectal cancer.

There is anecdotal evidence that off-label use intravitreal bevacizumab improves short-term visual outcomes in patient with neovascular age-related macular degeneration age-related macular degeneration AMD[3]. Intravitreal administration of bevacizumab has recently been reported to be of benefit in choroidal neovascular membrane[1-2], retinal neovascularization in proliferative diabetic retinopathy and iris neovascularization [4-5].

Key words: neovascularization, choroidal, macular, telangectasia.

Case Report – 1

A 35- year- old woman presented with deterioration of vision in her left eye. Visual acuity in the left eye was 6/60 and 6/6 in the right eye. The right eye was normal (Figure 1)

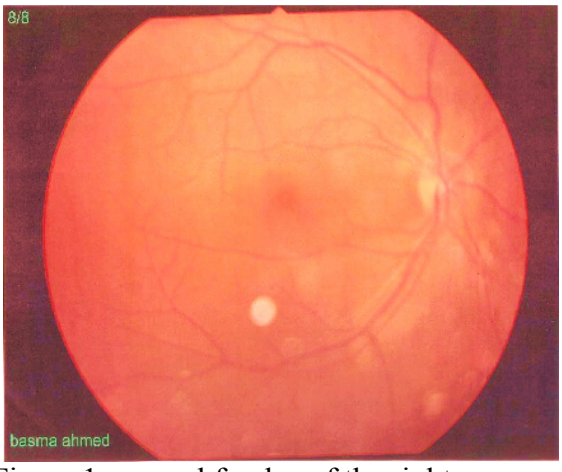

Figure 1: normal fundus of the right eye

The left eye examination revealed peri-papillary choroidal neovascular membrane involving the papillo-macular region with sub-retinal hemorrhage and retinal edema (Figure 2).due to unseen pathology, possiblely para-macular telangectasia or choroidal tear.

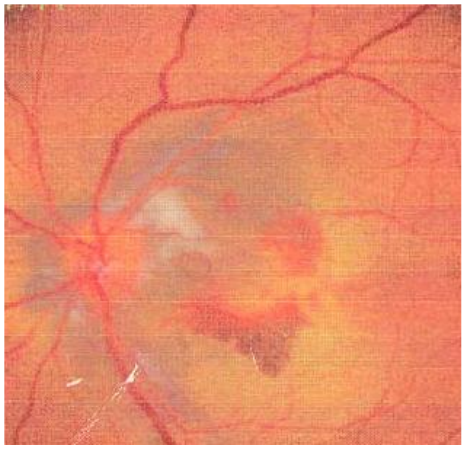

Figure 2: Patient with per papillary choroidal neovascular membrane involving the papillo-macular region in the left eye.

The patient was treated with an off-label intravitreal bevacizumab injection of 2.5 mg

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(0.1 ml of avastin Genetech Inc, San Francisco, CA at concentration of 25 mg /ml)
The consent of the patient was obtained after explaining the risks and benefits of the treatment.
Three months following the intravitreal injection the visual acuity of the left eye improved to 6/6 (Figure 3).

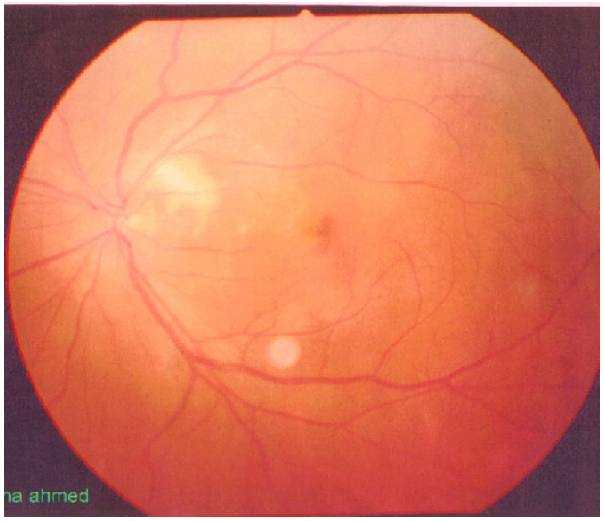

Figure 3: Patient left eye after treatment

We observed rapid resolution of the choroidal neovascular membrane and sub-retinal hemorrhage and retinal edema with an excellent improvement in visual acuity.

Case Report -2

A 30- year-old man presented with Metamorphopsia of the right eye. He was systemically healthy Visual acuity was 1/60 in the right eye and 6/5 left eye respectively. Examination of the right eye revealed multifocal choriditis with choroidal neovascular membrane. A fluoresceine Angiogram was performed (Figure 4)
The left eye was within normal limits. The patient was treated with an off-label intravitreal bevacizumab injection of 2.5 mg of (0.1 ml of avastin Genetech Inc, San Francisco, CA at a concentration of 25 mg /ml)
The consent of the patient was obtained after explaining the risks and benefits of the treatment.

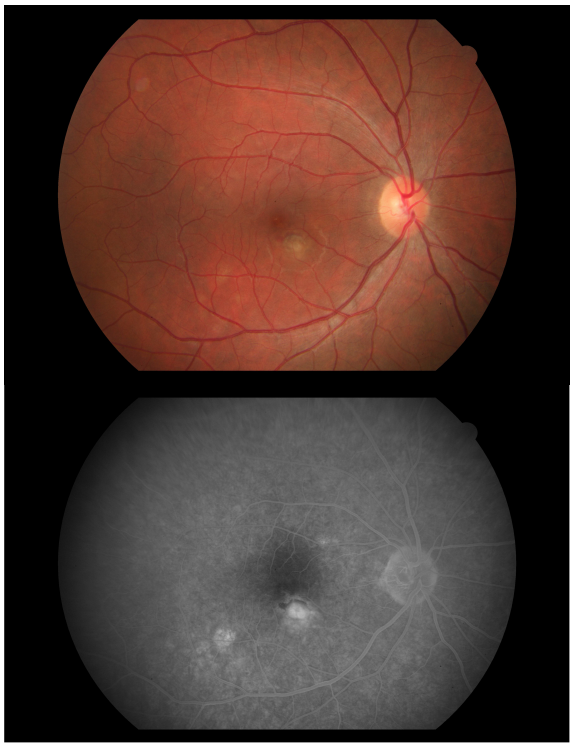

Figure 4: patient with multi-focal choriditis of the right eye and fluoresceine angiography demonstrated multifocal lesions affecting retinal pigment epithelium and choroid.

The condition improved on follow up and after 3 months the best vision of the right eye was 6/6 and the lesion resolved with only persistence extra foveal scar (Figure 5).

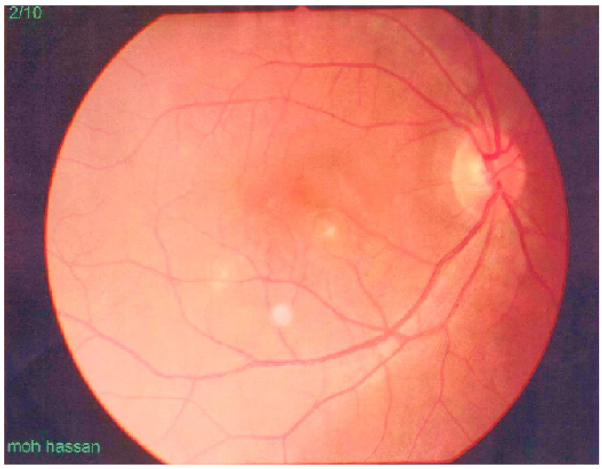

Figure 5: patient right eye after treatment

Discussion

Bevacizumab was primarily developed for the treatment of a variety of solid tumors 3-5 .In 2004, the FDA approved bevacizumab for treatment of metastatic colorectal cancer in combination with standard chemotherapy 4

It also showed benefit of improved vision in neovascular AMD and reduction of macular edema in diabetic retinopathy.

Most of the published reports are either small case series or anecdotal reports. However, extensive publications on intravitreal bevacizumab suggest that the drug has shown its beneficial effect at least in short-term follow-up and appears to be a part of preferred practice in the treatment of the CNV or retinal vascular disease.

No systemic or serious drug-related adverse events were observed. Subconjuctival hemorrhage and conjunctival hyperemia were observed frequently at the injection site.

Ocular complications due to injection procedure like both infectious and sterile endophthalmitis were reported in one study 7 the incidence of culture-positive endophthalmitis was 0.87%, while in other reports no case was observed; this difference could be due to following strict asepsis during the drug administration. Sterile endophthalmitis could occur due to solvent agent.

Intravitreal Bevacizumab has also been used in the treatment of aggressive posterior retinopathy of prematurity 6. Anecdotal reports also show the effect of intravitreal bevacizumab in the treatment of central retinal vein occlusion, branch retinal vein occlusion, and neovascular glaucoma.

The cases we report here were pooled from different patients who received bevacizumab for treatment of neovascular membrane due to different causes as age-related macular degeneration, central retinal vein occlusion, post traumatic choroidal tears, or due angioid streaks.

All patients received intravitreal bevacizumab 2.5mg/0.1ml under good aseptic conditions . No case had ocular or systematic complications.

All cases gained best vision and resolution of the fundus lesions with in 3 months of follow- up.

These cases illustrates that intravitreal bevacizumab has possible role in the treatment of the above conditions with regression of neovascular membrane and subsequent visual improvement ,although a much longer follow up and a larger prospective study is required to reach a conclusive result.

References

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