

Case Report

Intra-Vitreous Injections of Bevacizumab in Choroidal Neovascularization Complicating Best Vitelliform Macular Dystrophy: Case Report of a Child

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Abstract

A 15-year-old child followed for Best vitelliform macular dystrophy presented to the clinic with an abrupt visual impairment of his left eye. Fundus examination showed bilateral vitelliform lesions, with serous retinal detachment and adjacent retinal hemorrhage in the left eye. Fluorescein angiography and optical coherence tomography confirmed the diagnosis of type-2 choroidal neovascularization complicating the Best disease. The juxtafoveal location of the choroidal neovascularization prompted us to realize monthly intra-vitreous injections of bevacizumab. After the fourth injection, we observed visual and anatomical improvement that remained stable after a 12-month follow-up. It's important to look for complications in front of a sudden decrease in visual acuity in Best disease.

Keywords: Best disease; Macular dystrophy; Choroidal neovascularization; Intra-vitreous injections; Bevacizumab

Introduction

Best Vitelliform Macular Dystrophy (BVMD) is among the most common genetic macular degeneration typically occurring bilaterally with juvenile-onset [1]. The development of choroidal neovascularization (CNV) is an uncommon complication with no proven effective treatment modality at this time.

Case Presentation

We report the case of a child followed for BVMD who presented to the ophthalmology clinic for a sudden visual impairment that happened to be caused by choroidal neovascularization.

Results

We report the case of a 15-year-old male diagnosed with BVMD seven years earlier based on electrophysiological examination (perturbed electro-oculography and subnormal Arden ratio). Visual acuity remained stable at 20/32 in both eyes during five years, then the patient was lost to follow-up for 30 months, before attending the ophthalmology clinic for a bilateral rapidly progressive decrease of vision and metamorphopsia, mostly in the left eye.

Best-Corrected Visual Acuity (BCVA) was 20/40 OD and 20/160 OS. Intraocular pressure was normal. Fundus examination revealed bilateral foveal fibrotic vitelliform lesion, surrounded by a serous retinal detachment (SRD) and an inferior macular microhemorrhage in the left eye (Figure 1).

Left eye fluorescein angiogram showed a lesion that hyperfluoresces in the early stages due to a pigment epithelial window defect, maintains well-demarcated borders, and leaks late suggestive of an active subfoveal choroidal neovascularization. Inferior to this lesion, we found a localized hypofluorescence area caused by the masking effect of subretinal haemorrhage (Figure 2).



Figure 1: Fundus photography of both eyes: oval macular dystrophy with an irregular greyish appearance in the left eye associated with retinal serous detachment and sub-foveal intraretinal haemorrhage.

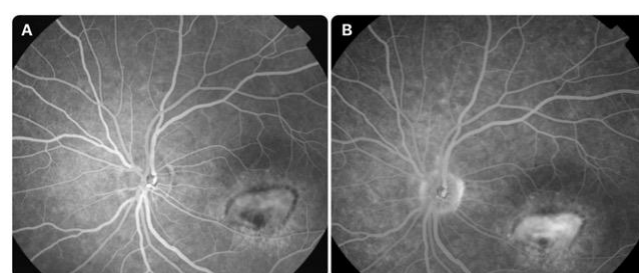


Figure 2: Fluorescein angiogram of the left eye. (A): hyperfluorescence at mid-phase angiography (B): suggestive of pre-epithelial choroidal neovascularization.

Left eye Optical Coherence Tomography (OCT) showed a diffuse inhomogeneous area of choroidal hyper-reflectivity suggestive of CNV associated with a complete shadowing of the underlying retinal pigment epithelium and choroid indicative of a serous pigment epithelium detachment (Figure 3).

Given this clinical presentation of BVMD complicated by type-

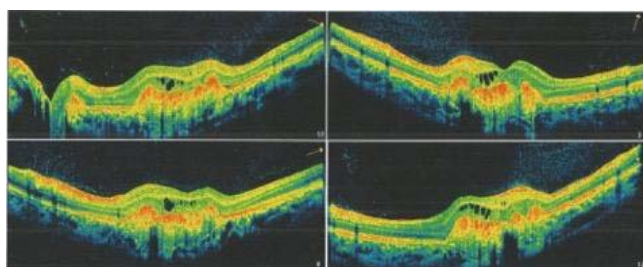


Figure 3: Optical coherence tomography of the left eye before bevacizumab intra-vitreous injections: hyperreflective lesion in front of the pigmentary epithelium compatible with a choroidal neovascularization associated with cystoid foveae of intraretinal oedema and a peripheral subretinal hyporeflective space suggestive of retinal serous detachment.

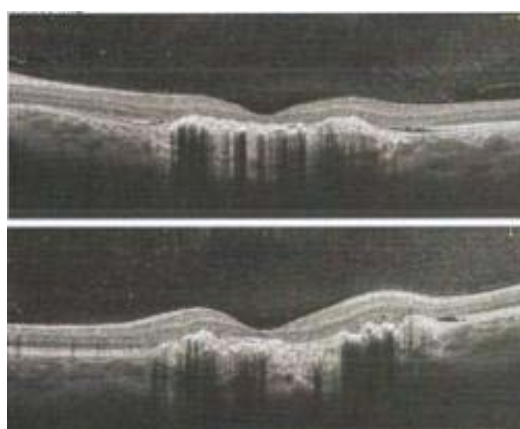


Figure 4: Fundus photography (A) and Optical Coherence Tomography (B) of the left eye five months after starting the treatment: resorption of intraretinal haemorrhage, regression of retinal serous detachment, scarring fragmentation of the vitelline lesion and retraction of the choroidal neovascularization with a hypo-reflective residual blade at the margins of the lesion.

2 choroidal neovascularization, and after parental consent, we performed four intravitreal injections of 1.25 mg of bevacizumab in the left eye under local anaesthesia, at one-month intervals, without any adverse event. As the fourth injection had no positive effect after a good initial response, we decided to stop the injections.

At one month after the fourth injection, visual acuity improved to 20/32 OS and the metamorphopsia disappeared. Intraocular pressure remained normal. Fundus examination showed retraction of the CNV and resorption of the subretinal haemorrhage. OCT showed resorption of the intraretinal oedema in the left eye with a significant reduction of the SRD but a hyper-reflective layer persisted at the edges of the lesion and the vitelliform material resorbed partially (Figure 4).

At six months after the fourth injection, visual acuity has steadied to 20/32 OS, and after one year of follow-up, the appearance of the macula remained stable with no recurrence of intra- or sub-retinal fluid.

Discussion

Best vitelliform macular dystrophy is a hereditary degenerative maculopathy, usually bilateral, with an autosomal dominant transmission and a variable expressivity and penetrance due to mutations in the BEST1 gene located on chromosome 11 [1]. The

product of this gene is the protein Bestrophin-1, a transmembrane protein whose expression is associated with chloride channels in the Retinal Pigment Epithelium Cells (RPE). Alteration of ions flow would explain both electrophysiological findings and accumulation of a yellow pigment named lipofuscin in the macular subretinal space.

Despite the striking macular lesions exhibited in patients with BVMD that we usually classify into several evolutionary phenotypic stages (pre-vitelliform, vitelliform, pseudohypopic, vitelliruptive, and atrophic stages), the majority maintains good VA over their life, and therefore any sudden visual impairment results from complications. Subretinal neovascularization is an uncommon complication observed in 15% of all cases predominantly in the later stages [2].

Fundus Autofluorescence (FAF) shows hyper-autofluorescence during the earlier vitelliform stages characteristic of the egg-yolk appearance, although in late stages hypo-autofluorescence predominates due to the atrophy of the RPE.

Optical Coherence Tomography (OCT) can be used to localize the vitelliform lesion and evaluate the presence of subretinal fluid or RPE atrophy but FAF remains the gold standard to look after an active Choroidal Neovascularisation (CNV) [3].

This CNV tends to be self-limiting in young people, probably due to the hyper-function of the RPE in the area of the lesion and the production of inhibitors of neovascularization [4].

There is a lot of controversy in the treatment of these CNVs because of the lack of randomized studies comparing the different treatment options:

- Therapeutic abstention in cases of non-significant vision loss or extensive hemorrhage [5].
- Direct laser photocoagulation in cases of extra-foveolar CNV, or photodynamic therapy using Verteporfin [6].
- Anti-Vascular Endothelial Growth Factor (VEGF) therapy, including intravitreal injection of bevacizumab [7], association bevacizumab-triamcinolone or ranibizumab, has been reported more recently as an option for treating CNV.

Bevacizumab, used in our patient, inhibits vascular endothelial growth factor resulting in regression of CNV and resolution of macular edema. It's used in children on an experimental basis, without pre-established safety consensus, but no prospective study with conclusive results on the potential adverse effects exists currently.

Choroidal neovascularization complicating BVMD generally requires a reduced number of antiangiogenic injections compared to other macular dystrophies [8] associated to an improvement of the visual function without recurrence in most cases, [9] highlighting relatively non-aggressive character of this CNV. Observation findings by Leu et al. [10] and Cakir et al. [8] reported both morphological and functional gains after one single intravitreal injection of bevacizumab and bevacizumab-triamcinolone respectively.

For our case, only four injections enabled complete closure of the neovascular lesion, allowing prompt vision recovery although a fibrotic scar holding a SRD blade persisted, after 12-month follow-up with no recorded side-effects.

Conclusion

Though the rapid recovery of visual acuity prompted the authors to recommend the use of antiangiogenic agents in the context of CNV complicating Best disease, larger series with extended follow-up periods are required to define their place in the available therapeutic armamentarium and to assess their possible adverse effects in young patients.

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