

## Case Report

# Esotropia in the Context of Maculopathy Compatible with Autosomal Recessive Bestrophinopathy

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Submitted: 24 September 2017

Accepted: 10 October 2017

Published: 12 October 2017

ISSN: 2333-6447

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**OPEN ACCESS****Keywords**

• Recessive; Bestrophinopathy; Esotropia; Maculopathy; Best; Dystrophy

**Abstract**

**Introduction:** Best's vitelliform maculopathy is an autosomal dominant macular dystrophy associated to a mutation in the bestrophin-1 (*BEST1*) gene. There are some recessive inherited cases called autosomal recessive bestrophinopathy (ARB).

**Case presentation:** We present a case of a 5 year old boy with hyperopia and accommodative esotropia. Best corrected visual acuity was 100/200 in the right eye (RE) and 80/200 in the left eye (LE). He only had one great-grandfather who became blind in late childhood as relevant family history. Biomicroscopic fundus examination revealed yellowish deposits in the macular region and mid periphery, subfoveal serous detachment and retinal pigment epithelium (RPE) irregularities in both eyes.

**Discussion:** ARB is an unusual, early-onset maculopathy, with autosomal recessive inheritance pattern, in contrast to Best's classical dominant disease. ARB patients present retinal deposits and RPE irregularities, hyperopia and shallow chamber. Strabismus may be associated and surgery might be required in some cases. The diagnosis of suspicion is based on clinical ophthalmological examination, family history and electro-oculogram (EOG) test, but should be confirmed by genetic studies.

**ABBREVIATIONS**

RE: Right Eye; LE: Left Eye; AO: Both Eyes; ARB: Autosomal Recessive Bestrophinopathy; FA: Fluorescein Angiograph; OCT: Optical Coherence Tomography; EOG: Electro-Oculogram; ERG: Electroretinogram; RPE: Retinal Pigment Epithelium; DP: Dioptres; CNV: Choroidal Neovascularization; AMD: Age-Related Macular Degeneration

**INTRODUCTION**

Best's vitelliform macular dystrophy (Phenotype MIM number 153700/ Gene MIM number 607854) is typically a bilateral maculopathy with onset in childhood. The mode of inheritance is autosomal dominant but the expression and the penetrance are highly variable. Nevertheless, there are some cases described in the literature with recessive inheritance pattern, called autosomal recessive bestrophinopathy (ARB) (Phenotype MIM number 611809/ Gene MIM number 607854). These dystrophies are frequently associated with high hyperopia and strabismus, as in the case reported in this paper.

**CASE PRESENTATION**

A 5-year-old boy came to the office to be examined due to some educational problems at school. His mother referred no other

major medical concerns but admitted that the patient showed a more "awkward behavior" compared to her other children. Reviewing ophthalmological family history, the patient only had some hyperopic family members and a great-grandfather that became blind for unknown reasons when he was about 12-14 years old.

Non-corrected visual acuity on Snellen's chart was 40/200 in RE and 30/200 in LE. Cycloplegic subjective refraction was +7.50-0.75°150° in RE and +8.00-0.25°10° in LE.

Pupillary reflexes were normal and a 12 prismatic diopter esotropia with RE dominance was found on cover test.

Slit-lamp anterior segment examination showed that the cornea and lens were clear, and the anterior chamber was not shallow.

Findings on fundus examination included yellowish deposits at the macular region and mid periphery associated to a macular serous detachment in both eyes, resembling the pseudohypopyon stage of Best's vitelliform maculopathy (Figure 1). Vitritis was absent and peripheral retina remained normal as well as the optic nerve and arterial and venous vessels.

High resolution optical coherence tomography (OCT) showed a subfoveal and inferotemporal serous detachment with



**Figure 1** Posterior pole retinography. Blue arrow shows yellow deposit outside the macular region.

mild macular atrophy and irregularities of the retinal pigment epithelium (RPE) that suggested chronicity (Figure 2).

On fluorescein angiography (FA), a window defect was observed corresponding to the area of the RPE atrophy. Subretinal deposits were seen as patchy hyperfluorescent lesions without leakage (Figure 3).

Complete electrophysiology study was performed finding an Arden Index below standard values, corresponding to 1.3 in RE and 1.6 in LE (normal values >1.8) on electro-oculography (EOG).

A complete pediatric workup excluded other immune or infectious diseases associated.

The parents' fundus examination did not showed any lesions.

The full hyperopic correction based on the cycloplegic refraction was prescribed to correct the hyperopic defect, improving the visual acuity to 100/200 in RE and 80/200 in LE.

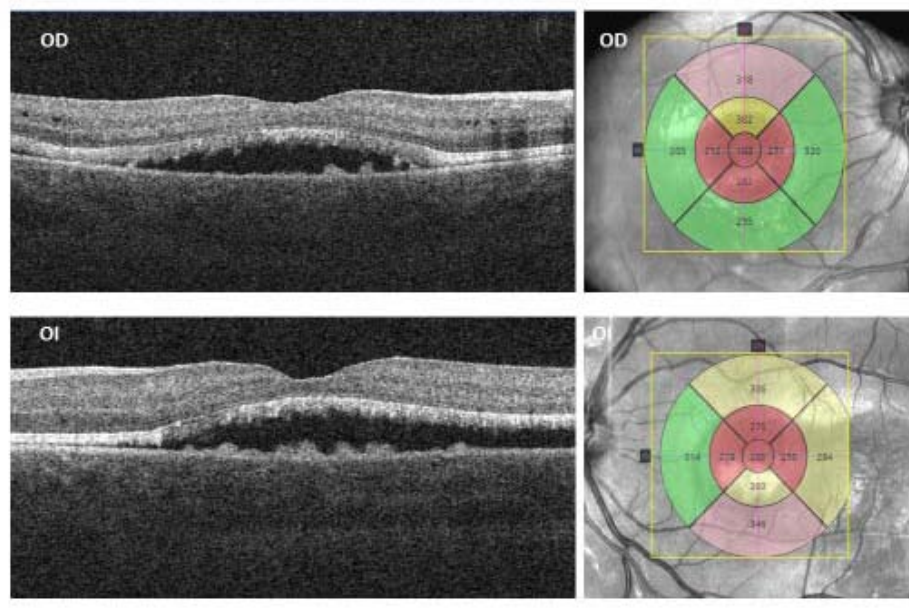
The accommodative esotropia was also fully corrected after the prescription of spectacles.

Genetic studies are being carried out to confirm the suspected diagnosis of ARB with mutation in *BEST1* gene.

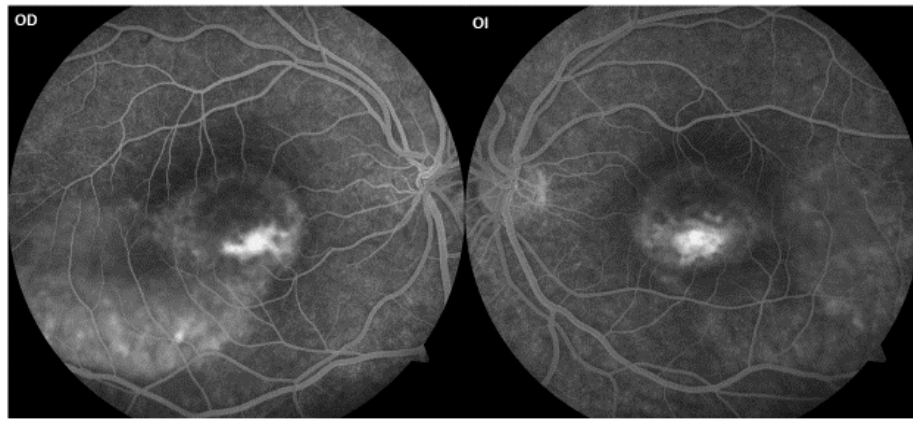
## DISCUSSION

The *BEST1* gene encodes the bestrophin-1 protein which acts in RPE. Mutations in this protein cause a spectrum of diseases called *bestrophinopathies*, including Best's vitelliform macular dystrophy, adult onset foveomacular vitelliform dystrophy, autosomal dominant vitreoretinchoroidopathy and autosomal recessive bestrophinopathy. Some cases of age-related macular degeneration (AMD) are related to this protein [1].

The case presented has the phenotype that corresponds to the unusual disease autosomal recessive bestrophinopathy (ARB) [2,3].



**Figure 2** Optical coherence tomography (OCT). Subfoveal serous detachment.



**Figure 3** Fluorescein angiography (FA). Patchy hyperfluorescence.

It has been described in patients presenting with low vision (about 60/200) at early stages (between 4-40 years of age) highly hyperopic, short axial lengths and shallow anterior chamber predisposing to angle-closure even at early age. The characteristic fundus findings include atrophic changes at the RPE, yellowish deposits in macular area and mid periphery and macular serous detachment that eventually leads to macular fibrosis and fibrotic scars. However, classic vitelliform lesions are not usually found.

The mode of inheritance and the genetic examinations that are still being carried out will reveal the type of mutation present in our patient. These will allow us to achieve the differential diagnosis between Best's disease and ARB [4-6]. Best's vitelliform macular dystrophy is a well-defined autosomal dominant maculopathy, whereas in ARB, the recessive pattern is caused by heterozygous or homozygous mutations in *BEST1* gene [7-9]. This gene encodes bestrophin-1, a transmembrane protein that regulates chloride channels that are crucial for transepithelial fluid and ion transport at the RPE cells, decreasing or suppressing this channel's activity [10]. It has been hypothesized that the ARB could associate the null phenotype of bestrophin in humans through a markedly reduction or even absence of bestrophin-1 function.

The diagnosis should be suspected on the basis of clinical ophthalmological examination, family history and ocular electrophysiology [11,12]. The EOG is of great value since it is based in the study of the RPE function. It corresponds to the absent light rise due to changes in chloride channels leading to a reduction in Arden Index.

OCT is a main diagnostic tool [13,14], showing retinal oedema, serous subretinal fluid and in some chronic cases, fibrosis. FA confirms the same features and helps us to rule out the presence of choroidal neovascularization (CNV), which could also be associated. Nevertheless, the ultimate diagnosis must be acquired by genetic screening [15].

Differential diagnosis includes Stargardt's disease, familial drusen, vitelliform macular dystrophy, AMD, central serous chorioretinopathy and chorioretinitis [16].

The appropriate management of this disease goes through

treating the refractive error and amblyopia, as well as strabismus treatment if needed. These measures can improve the visual prognosis and quality of life of patients [17]. In some cases, prophylactic iridotomies may be necessary to prevent angle-closure, thus close observation with gonioscopy is suggested. In case of CNV, intravitreal anti-vascular endothelial growth factor (VEGF) can be used. Cystoid macular oedema could be treated with oral acetazolamide.

In the near future, genetic therapy could be the treatment for this *BEST1* gene mutation related diseases.

At the moment, our aim is to assist other ophthalmologists to recognize this unusual disease, emphasizing the magnitude of the EOG utility for bestrophinopathies diagnosis.

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#### Cite this article

Guadilla AM, Rodriguez M, Modamio-Gardeta L, Martín, Ancochea G, Del Barrio I, et al. (2017) Esotropia in the Context of Maculopathy Compatible with Autosomal Recessive Bestrophinopathy. *JSM Ophthalmol* 5(3): 1059.