Atypical Pediatric Autosomal Recessive Bestrophinopathy with Multifocal Extramacular Deposits: A Case Report

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Abstract
Autosomal recessive bestrophinopathy (ARB) is a rare inherited retinal dystrophy caused by mutations in the BEST1 gene, characterized by subretinal accumulation of vitelliform material and retinal pigment epithelium dysfunction. We report the case of a 7-year-old child presenting with progressive visual loss in the right eye. Fundus examination revealed bilateral vitelliform lesions associated with multiple extramacular deposits, with marked asymmetry between both eyes. Multimodal imaging, including optical coherence tomography (OCT), fundus autofluorescence, and fluorescein angiography, demonstrated subretinal hyperreflective vitelliform material, pseudoserous retinal detachment, cystoid macular edema (CME), and subretinal fibrosis in the right eye. Electro-oculography showed a markedly reduced Arden ratio, while electroretinography revealed both photopic and scotopic dysfunction. Genetic analysis confirmed a mutation in the BEST1 gene, establishing the diagnosis of autosomal recessive bestrophinopathy. No specific treatment was initiated, and regular follow-up was recommended. This case highlights the phenotypic variability of ARB and emphasizes the importance of multimodal imaging and genetic testing for accurate diagnosis and management.

Keywords:
Bestrophinopathy,Vitelliform deposits
Electro-oculography.

Introduction

Autosomal recessive bestrophinopathies (ARB) are a group of inherited macular dystro--phies secondary to mutations in the BEST1 gene. They are characterized by the accumulation of subretinal vitelliform material related to functional impairment of the retinal pigment epithelium (RPE). ARB is associated with a markedly reduced light peak on electro-oculography (EOG), as well as progressive retinal dysfunction on electroretinography (ERG). Patients with ARB commonly present with decreased visual acuity and diffuse RPE irregularities associated with scattered punctate flecks, which differ from extramacular vitelliform lesions. Clinical presentation is variable, ranging from the typical “egg-yolk” macular lesion to atypical forms with diffuse deposits, cystoid macular edema (CME), or subretinal fibrosis. We report the case of a 7-year-old child presenting with autosomal recessive bestrophinopathy.

Case Report

A 7-year-old child with no significant past medical history presented with progressive visual loss in the right eye. Ophthalmologic examination of the right eye revealed a best-corrected visual acuity of 2/10 with an unremarkable anterior segment examination. Fundus examination demonstrated a yellowish, round, elevated, well-circumscribed vitelliform lesion with an “egg-yolk” appearance located in the intermaculopapillary region. A second macular lesion surrounded by a pigmented border with retinal pigment epithelium (RPE) alterations was also noted, along with multiple whitish deposits outside the macular area (Figure1-A)..

In the left eye, best-corrected visual acuity was 9/10 with a normal anterior segment examination. Fundus examination showed a small yellowish, round, elevated macular lesion associated with multiple extramacular

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deposits(Figure 1-B).. Fundus examination of both parents was normal

Multimodal imaging allowed better characterization of the lesions. Macular OCT of the right eye revealed heterogeneous hyperreflective vitelliform material located beneath the photoreceptor layer, contained within an optically empty space corresponding to a pseudoserous retinal detachment, associated with fibrosis and cystoid macular edema (CME). In the left eye, OCT also demonstrated subretinal hyperreflective vitelliform material within a pseudoserous retinal detachment associated with CME (Figure 2).

Fundus autofluorescence revealed multiple diffuse hyperautofluorescent lesions, including the intermaculopapillary lesion, while the right macular lesion displayed a heterogeneous pattern. Fluorescein angiography showed early inhomogeneous hyperfluorescence of the vitelliform material persisting into the late phases without leakage (Figure 3).

Electro-oculography demonstrated a markedly reduced Arden ratio associated with ERG abnormalities, including decreased photopic and scotopic responses.

The diagnosis was confirmed by genetic analysis, which identified a mutation in the BEST1 gene. No specific treatment was initiated, and regular follow-up was recommended for the patient as well as for siblings.

Discussion

Bestrophinopathies are a group of inherited macular dystrophies caused by mutations in the BEST1 gene. They result from dysfunction of the bestrophin-1–dependent chloride channel at the level of the RPE, leading to the accumulation of lipofuscin and subretinal vitelliform material(1). Autosomal recessive bestrophinopathies differ from Best disease by their recessive inheritance pattern (neither parent is affected) and the presence of multiple macular and extramacular vitelliform deposits. These recessive forms are rare (1/45 “Best” families in referral centers). This entity should be considered in multifocal forms of Best disease. (2)The macular and extramacular material is vitelliform and hyperautofluresent scattered throughout the retina vary in size and may sometimes appear punctate(3).

The marked asymmetry and presence of extramacular deposits suggest phenotypic variability. Bilateral CME and right subretinal fibrosis indicate a potentially complicated course that may negatively affect visual prognosis.(4)

The absence of abnormalities in the parents may be explained by incomplete penetrance or a de novo mutation. Confirmation by electro-oculography and genetic analysis of the BEST1 gene is essential to establish the diagnosis and provide appropriate genetic counseling.(5)

Visual prognosis may be poor in cases progressing to complete chorioretinal atrophy or choroidal neovascularization. Few cases have been reported, and long-term follow-up remains limited since this entity was only clearly distinguished in 2008. Currently, there is no treatment for vitelliform deposits.(6)

Conclusion

This case illustrates an atypical pediatric form of autosomal recessive bestrophinopathy characterized by asymmetric involvement and multiple extramacular deposits. Multimodal imaging is essential for diagnosis and follow-up. Genetic confirmation is recommended to refine the nosological classification and optimize patient management.

Declarations

Ethics approval and consent to participate

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this review.

Consent for publication

All authors consent to publication

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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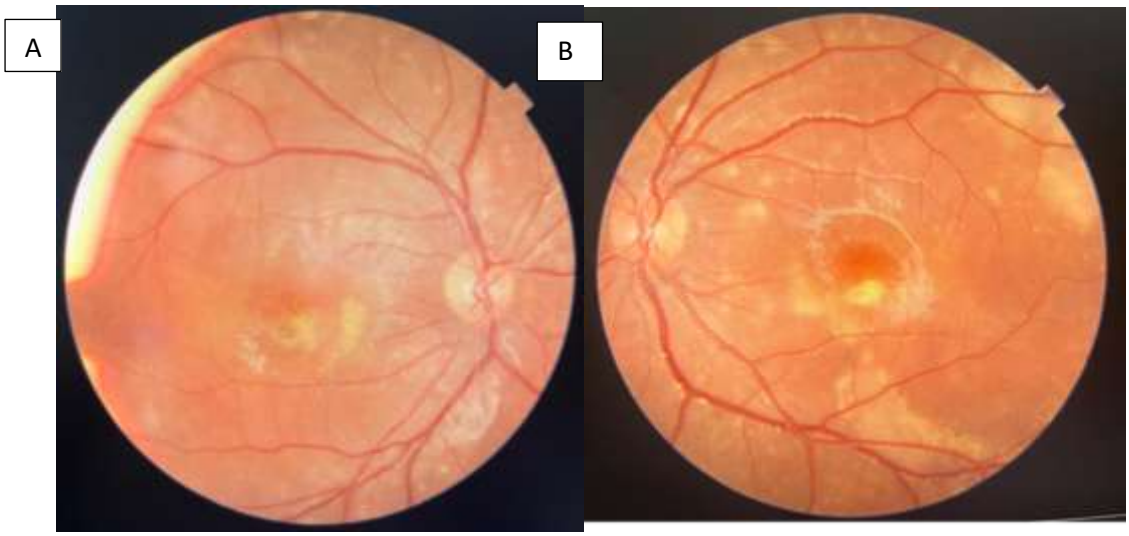

Figure 1: Retinography of both eyes with yellowish oval macular lesion and extra-macular lesions A: right eye /B: left eye

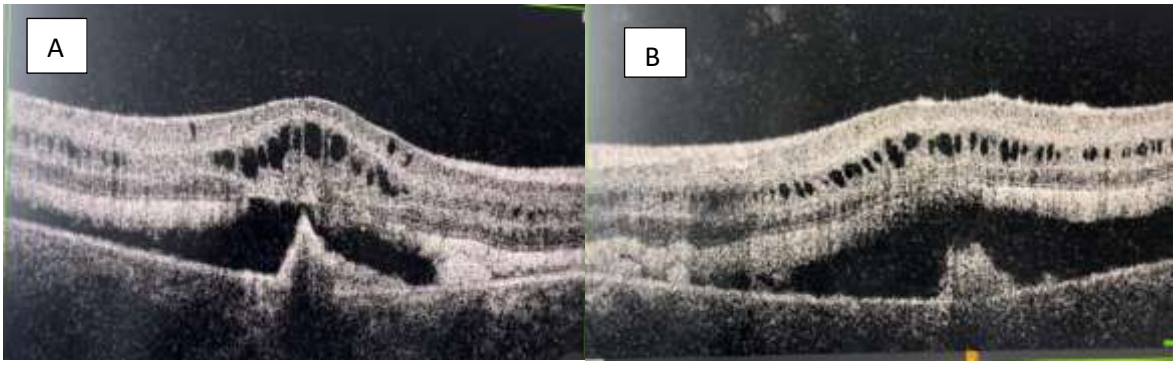

Figure 2: Macula OCT (Optical coherence tomography) showing seroretinal detachment with altered retinal pigment epithelium with cystoid macular edema in the right eye (A), seroretinal detachment and hyperreflective subretinal deposits in the left eye.

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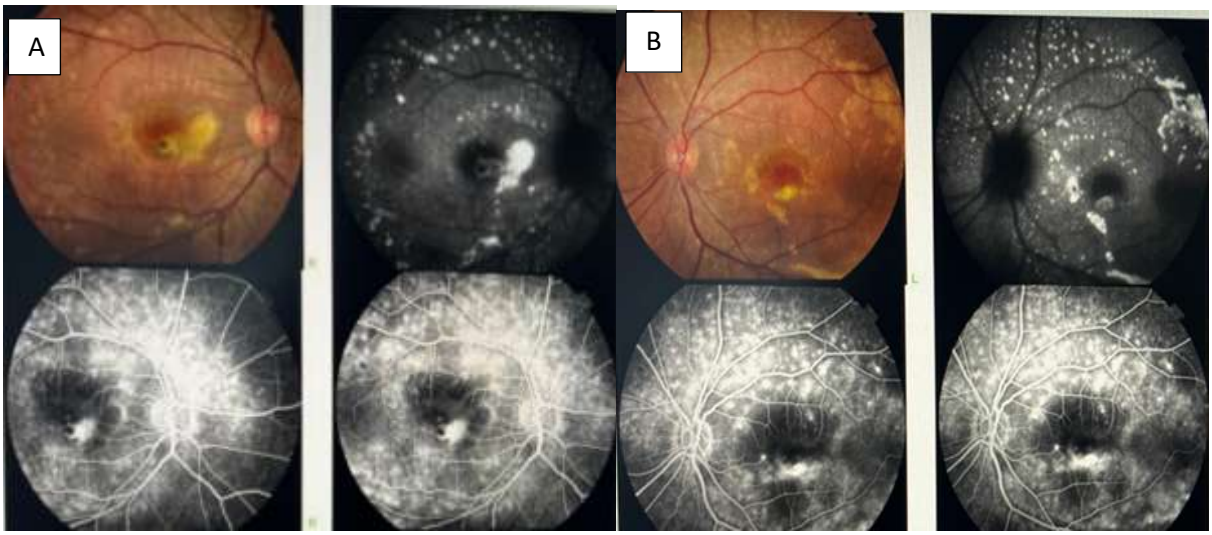

Figure 4 : Color fundus photography, fundus autofluorescence, and fluorescein angiography of the right eye in a child with autosomal recessive bestrophinopathy.**A:** right eye /**B:** lefteye.
Color fundus image (top left) shows a yellowish vitelliform lesion with an "egg-yolk" appearance associated with retinal pigment epithelium alterations and multiple extramacular whitish deposits. Fundus autofluorescence (top right) demonstrates multiple hyperautofluorescent lesions, including the vitelliform lesion and scattered extramacular deposits. Early- and late-phase fluorescein angiography (bottom images) reveal inhomogeneous hyperfluorescence of the vitelliform material without leakage.

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