Phenotype in homozygous and heterozygous carriers of BEST1 mutations in autosomal recessive Bestrophinopathy

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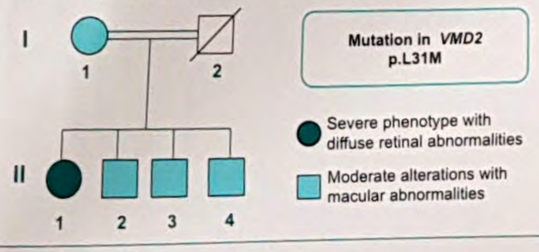
Introduction

Autosomal recessive Bestrophinopathy (ARB) was first recognized by Burgess et al[1] in 2008. It is part of the retinal diseases spectrum caused by mutations in the *BEST1* gene.
We report the phenotype and genotype results in a family including a patient with ARB we report phenotype characteristics of heterozygous carriers.

Patients and methods

We did a clinical and molecular genetic study of a consanguineous Tunisian family of a patient affected with ARB. DNA sample from the index patient was subjected to whole exome sequencing (WES). Variants localized in homozygous regions were validated by Sanger sequencing. Familial segregation was performed.

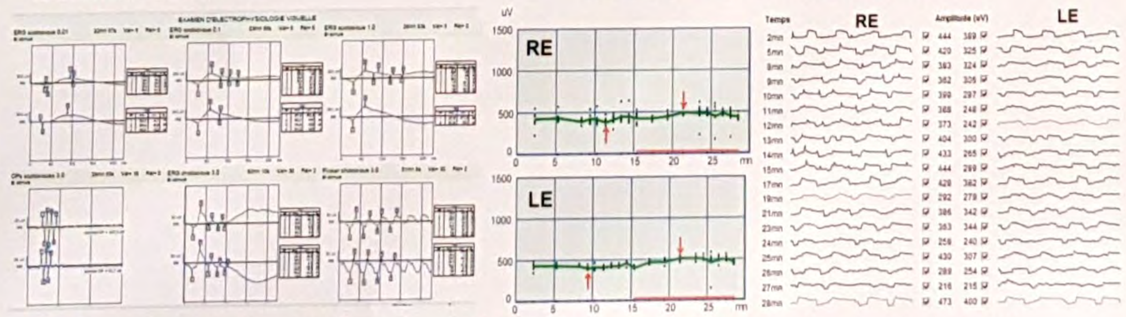


Results

Index patient (**II-1**) was 50 years old with history of occludable narrow anterior chamber
angle treated with YAG laser peripheral iridotomy in both eyes.
She reported visual loss from the second decade of life. BCVA = 3/10 RE , 2/10 LE.

- **Color fundus photography (CFP)** revealed macular central vitelliform lesions with

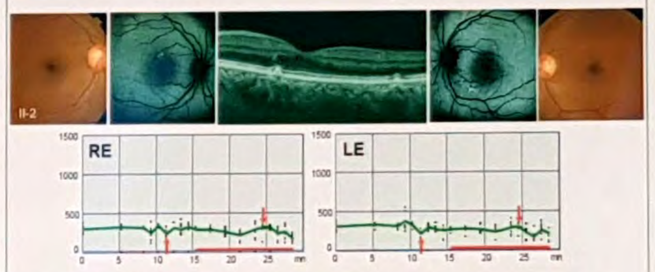
- **FAF:** Central macular hypo-FAF surrounded by markedly increased autofluorescence
- **SS-OCT:** Hyperreflective accumulations on RPE, cystoid intra-retinal and serous subretinal fluid accumilation.



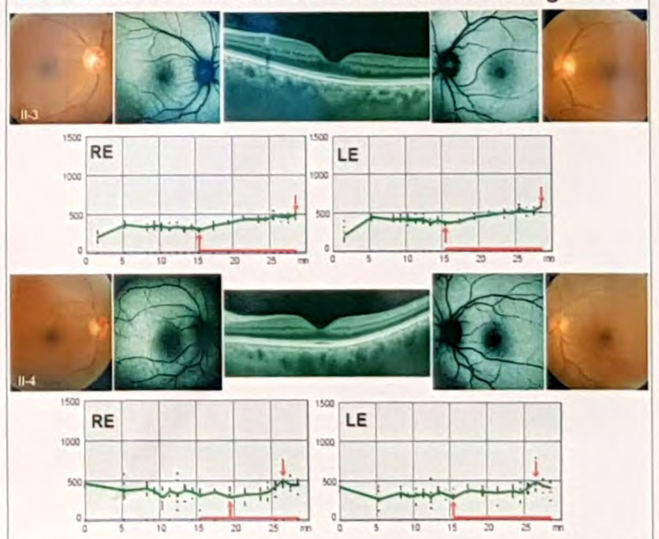
- **ERG:** moderate reduced response in both scotopic and photopic conditions.
- **EOG:** reduction in the light rise.

This patient had a **novel homozygous mutation p.[L31M],[L31M] in *BEST1***.

- **The brother** (**II-2**) complained of hemeralopia.
CPF & FAF: Yellowish FAF deposits in the macula.
EOG: Severe reduction in the light rise.



- **The brothers** (**II-3 and II-4**) were asymptomatic.
CPF &FAF: Normal. **EOG:** reduction in the light rise.



All the brothers were **heterozygous** carriers of the ***BEST1* mutation**.

- **The mother (I-1)** was also heterozygous carrier of the *BEST 1* mutation.

Discussion and conclusion

ARB has been hypothesized to represent the human "null" phenotype for Best1.[1,2] Previous studies showed that heterozygous parents of the proband did not have any abnormal fundus findings and their EOG was normal.[3,4]
We identified a novel mutation in a Tunisian family with ARB. This mutation expands the mutation spectrum of *BEST 1* and helps to further study molecular pathogenesis of ARB.
Contrary to what is known, we had affected patients carrying heterozygous mutations with a reduced EOG light rise in all of them.

1- Burgess et al. Am. J. Hum. Genet. 2008; 82:19–31.
2- Pomares et al. Invest. Ophthalmol. Vis. Sci. 2012; 53:532–537.
3- Boon et al. Prog. Retin. Eye Res.. 2009; 28:187–205.
4- Marmorstein et al. Prog. Retin. Eye Res. 2009; 28:206–228.