# Co-occurrence of Incomplete Achromatopsia and Microcornea Syndrome in a Single Family: Genetic Insights and Clinical Characterization

## Introduction

Achromatopsia is a rare form of retinal dystrophy characterized by reduced visual acuity, pendular nystagmus, light sensitivity, impaired color vision, and central vision loss. Mutated ADAMTS18 has been found to lead to retinal dystrophy and microcornea, Myopic Chorioretinal Atrophy, and dysmorphic facial features. Herein, we reported a single Iranian family with six affected individuals caused by novel pathogenic variants in PDE6H and ADAMTS18.

## Methods

Whole-Exome Sequencing was performed on the proband, identifying two novel genetic variants. Sanger sequencing confirmed these findings and was used to assess zygosity in other family members. Clinical assessments were conducted for the affected individuals.

## Results

Two novel variants were identified in six individuals within the family: PDE6H (NM_006205.3:c.35C>G; p.Ser12Ter) and ADAMTS18 (NM_199355.4:c.3139C>T; p.Arg1047Ter). The proband and two sisters were homozygous for the PDE6H variant and heterozygous for the ADAMTS18 variant, presenting with reduced visual acuity, color discrimination issues, photophobia, and myopia.

Ellipsoid zone disruption and pendular nystagmus were also noted in two and three patients, respectively. Two second-generation family members, born to non-consanguineous parents, were heterozygous for the PDE6H variant and homozygous for the ADAMTS18 variant, exhibiting microcornea, myopia, telecanthus, punctual atresia, and strabismus.

## Conclusion

Mutations in PDE6H and ADAMTS18 can cause a broad range of ophthalmic disorders. Three out of six reported cases suffer from incomplete achromatopsia, and two suffer from microcornea and myopia.

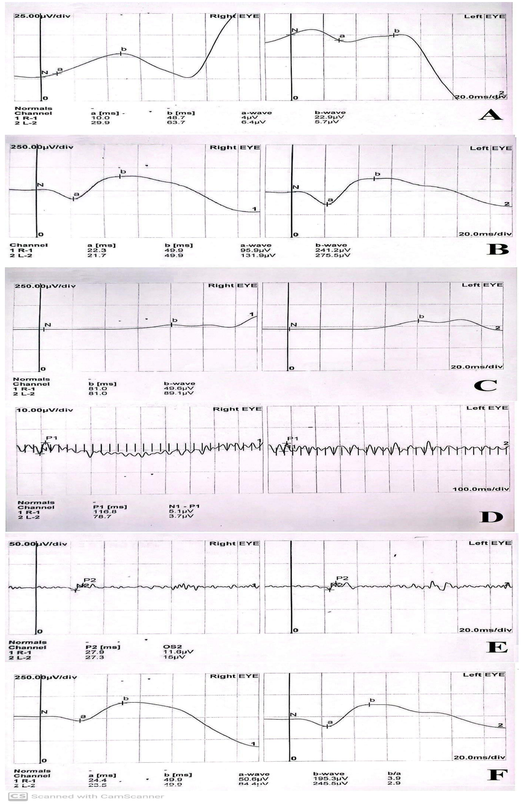



**Figure 1**. Electroretinogram of the proband. A: Photopic 3.0 ERG, B: Scotopic 10.0 ERG, C: Scotopic 0.01 ERG, D: Photopic 3.0 Flicker 30Hz ERG, E: Scotopic 3.0 Oscillatory Potential ERG, F: Scotopic 3.0 ERG.

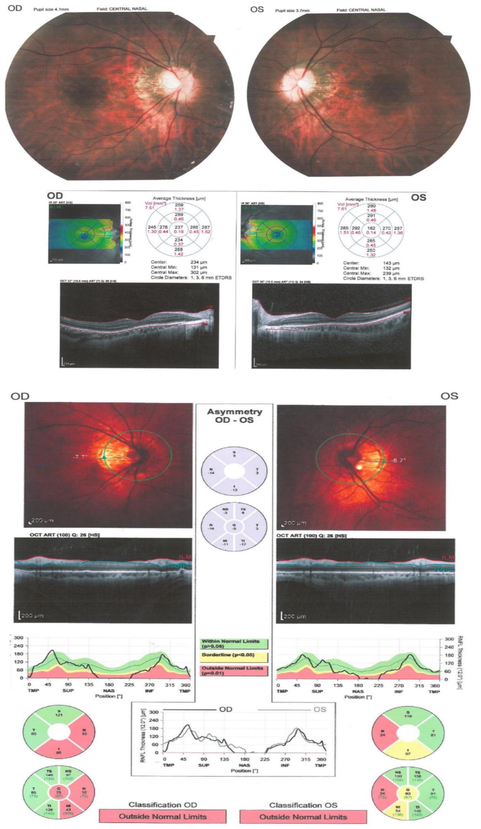



**Figure 2**. Optical coherence tomography and fundus photos of the proband. Foveal thinning in his left eye and ellipsoid zone disruption in both eyes are present.

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