CR1-4 Phenotype–genotype correlation of the first patient with a homozygous missense variant *RPE65* c.499G>T, p. (Asp167Tyr)

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Abstract Published: 16 March 2023

60th Annual Symposium of the International Society for Clinical Electrophysiology of Vision (ISCEV 2023 Kyoto)

Documenta Ophthalmologica **volume 146**, pages3–65 (2023)

Background

This case report aims to present the specific phenotype–genotype correlation of the first patient with pigmentary retinopathy (RP) caused by the homozygous missense variant *RPE65* c.499G>T, p. (Asp167Tyr).

Case report

A 66-year-old male diagnosed with a homozygous missense variant *RPE65* c.499G>T, p. (Asp167Tyr) presented with light perception in the right eye (RE) and amaurosis in the left eye (LE). He had manifested nyctalopia since early childhood but completed his college education according to the regular program. Full-field stimulus testing (Metrovision, Perenchies, France) detected responses of 43 dB, 26 dB, and 53 dB to white, red, and blue light, respectively, in the RE, while in the LE, no response was evoked. The Optos® California (Optos Inc., Marlborough, MA, USA) ultra-widefield imaging depicted extensive chorioretinal atrophy with clumped nummular pigmentary changes and obliterative sclerosis of retinal vessels in the mid- and far periphery. Short-wavelength fundus autofluorescence was absent.

Conclusions

In contrast with typical perivascular bone spicule clusters of relocated RPE cells, the patient presented a distinctive pattern of reactive RPE changes: rounded, heavily pigmented nummular flecks clustered against Bruch's membrane as reported in choroideremia, RP-86, and RP-87 with choroidal involvement. We hypothesize that the lower expression level of RPE65 or the rapid degradation of the variant protein enables RPE cells to stay in situ as opposed to exhibiting migration to perivascular inner retinal sites. The observed phenotype is thus associated with less severe visual deterioration in adolescence. The melanin with its pro-oxidative potential could potentially advance chorioretinal atrophy in later stages.