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LETTER TO THE EDITOR (BY INVITATION)

Mitochondrial A3243G mutation results in corneal endothelial polymegathism

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We would like to thank Finsterer and Zarrouk-Mahjoub for their interest in our recent findings. Macular dystrophy due to the mitochondrial DNA (mtDNA) A3243G point mutation can manifest with associated ocular and systemic features that are important for specialists to identify [1]. Our case series suggests that corneal endothelial polymegathism is associated with mtDNA A3243G mutations, and in agreeance with the responding authors, our original submission emphasizes that future prospective studies are necessary to determine the utility of corneal endothelial polymegathism as a biomarker for mitochondrial diseases [2].

The aim of our observational study was to report and characterize a novel corneal finding in this disease entity in cross-section, rather than conduct a longitudinal study assessing the clinical manifestations of the mitochondrial DNA point mutation A3243G and treatment options. As such, it was not feasible to assess for subclinical manifestations in other organ systems or recruit family members for further evaluation by virtue of our study design.

With regard to the rate of heteroplasmy, a correlation between the degree of polymegathism and heteroplasmy rate was observed amongst the patients that underwent pyrosequencing. However, we purposely refrained from emphasizing this relationship given the small number of patients. Moreover, when assessing rates of heteroplasmy in lymphocytes, the exact rate of heteroplasmy may not be equivalent to that of the corneal endothelium.

All five patients described in our study presented with macular dystrophy. No patient had a past ocular history or evidence of congenital cataracts, optic atrophy, or iris atrophy on our clinical exam. Only one patient (Patient 1) had sensorineural hearing loss. We excluded patients with other known causes of well-established corneal endothelial dystrophy, such as Fuchs' endothelial corneal dystrophy and posterior polymorphous corneal dystrophy, as these would provide a confounding variable. Finally, we agree with the responding authors that polymegathism in diabetes could be secondary to an underlying mitochondrial genetic defect. However, answering this interesting question requires a larger study.

References

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