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Response to Finsterer's "Exclude hereditary and acquired differential disorders before attributing retinoschisis to Kears-Sayre syndrome"

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We thank Dr. Finsterer for his interest in our article and his erudite comments on the differential diagnosis of retinoschisis. Indeed, many of the conditions he cites were mentioned specifically within the discussion of the article and we elaborated in some cases on our reasons for these diagnoses to be more or less likely. Given that we neither sent whole exome sequencing nor chromosomal studies on this patient, it may be useful to briefly discuss why we would think other diagnoses were less likely.

X-linked retinoschisis was considered and effectively ruled out with single gene sequencing. The retinal phenotype/ERG of the patient does not fit with autosomal recessive bestrophinopathy, choroideremia, or Goldmann-Favre Syndrome. The patient with the complex chromosomal rearrangement described by Bagheri et al. presented with multiple other systemic abnormalities, including seizures, dysmorphic features and mental/growth retardation (1). Such multisystemic presentations are expected in patients with clinically significant, unbalanced chromosomal abnormalities. As mentioned in the discussion, we cannot exclude myopic retinoschisis (although patients tend to have higher refractive errors) and stellate non-hereditary idiopathic foveal retinoschisis (SNIFR) is a diagnosis of exclusion. The patient had not suffered electrical shock or trauma. Autosomal recessive familial retinoschisis (2) was considered, but CRB1 sequencing was not pursued. To our knowledge a total of two families in the world have been described with this condition and the likelihood of coming upon the third in the setting of another rare genetic condition with known retinal pathology seemed improbable in the extreme. Overall, we would submit that having an atypical retinal presentation of a known genetic syndrome with known retinal involvement is more likely than having two very rare conditions simultaneously in the same patient.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

There was no family history, which should have been noted in our report, and the mother of the proband had tested negative. To our knowledge, there are no reports of maternal transmission of a deletion of this size in the mitochondrial genome in KSS.

In the era of readily available whole exome or gene panel testing, it is tempting to always throw the proverbial kitchen sink at patients regardless of their underlying phenotype or diagnosis. While this approach may have merits, we would submit that deciding on the pre-test probability of a genetic diagnosis before sending a test, as argued eloquently by Stone et al. (3), increases the overall sensitivity and decreases the cost of testing. Indeed, genetic testing does not always result in clear answers and identifying variants of unknown significance in genes with important medical significance can muddy the diagnostic waters as much as clarify them.

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