Author’s response to reviews

Title: Triple-A Syndrome with Prominent Ophthalmic Features and a Novel Mutation in the AAAS Gene: Case Report

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The reviewers raise several interesting and important points. We will address each in turn.

1. Elias Traboulsi
   a. Dr. Traboulsi is rightly concerned about the decreased best-corrected visual acuity in this patient. At the time of examination, we felt the most likely explanations for his decreased acuity were superficial punctate keratopathy and possibly amblyopia. Similarly, we felt that the keratopathy and decreased tear production might cause the photophobia. We assumed that the red-green color deficiency was likely unrelated, given its prevalence in the male population. There was nothing on fundus examination to suggest a retinal dystrophy and there is no known association between triple-A syndrome and retinal degeneration. That said, Dr. Traboulsi is quite correct in raising the possibility of an "occult" cone dystrophy—a diagnosis that can only be excluded by ERG. We have revised our discussion to specifically mention that possibility. Because this patient traveled a long distances to come to the NIH for diagnosis, it is unlikely that we would be able to have him return for further testing.
   b. We have included the near visual acuity testing, as requested. The dysregulation of accommodation and/or the decrease in best-corrected visual acuity appear to affect near vision as well as distance vision.

2. Henry Houlden
   a. We have included additional details in the endocrine and neurologic assessments. The presentation of adrenal unsufficiency was typical of this disease and nerve conduction studies were not performed.
   b. In the case of this subject, both mutations are expected to cause premature truncation of the protein. While sequencing of control chromosomes is required in cases of missense changes of unknown significance, it is likely not required here. However, sequencing of 100 controls was previously done in Dr. Stratakis’ lab and no such changes have been previously noted. This information is included in the text of the manuscript.