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REPLY

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We thank Dr. Khan for his letter in response to our recent case series.[1] We fully agree that genetic testing does not replace, but rather complements, careful clinical phenotyping and history gathering. Khan outlines the ocular findings of *CLN3*-associated neuronal ceroid lipofuscinosis (NCL) that are distinct from other pediatric-onset retinal dystrophies and reiterates the importance of asking specific questions that might suggest neuropsychiatric symptoms. However, it is also important to acknowledge that there are often constraints that limit a clinician's ability to comprehensively phenotype children as an awake ophthalmic evaluation and ancillary testing require a certain level of cooperation. Additionally, the positive and negative predictive value of an elicited history in a child can be limited. The purpose of our case series is to highlight the varying presentations, some not classic, of children diagnosed with NCL prior to the onset of clear neurologic symptoms and to remind providers that NCL should be considered in the differential diagnosis and pretest counseling is critical.

How clinicians integrate genetic and phenotypic information to establish a "clinical-molecular" diagnosis is a topic of much attention.[2,3] We reemphasize that as next-generation sequencing is used increasingly in clinical practices, our understanding of the phenotypic and molecular spectrum of genetic disease continues to expand. Therefore, we caution against dismissing genetic testing results based on clinical findings alone. Perhaps the distinctions between clinical entities as we currently understand them are not so distinct after all.

References

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