Genetics and Ocular Disorders: A Focused Review

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KEYWORDS

• Eye disease • Genetics • Genetic testing • Pediatrics

KEY POINTS

- Increasingly accurate phenotyping leads to better genetic evaluation.
- Genetic eye conditions may be due to a common cellar defect (eg, ciliopathies or RASopathies).
- Early-onset retinal dystrophies may be associated with renal disease.
- An understanding of genetic testing helps clinicians identify shortcomings in testing which may lead to a better understanding of the most appropriate test for a given ocular condition.
- Dedicated genetic counselors within ophthalmic and pediatric clinics are likely to improve the delivery of clinical care in these settings.

INTRODUCTION

Genetic eye disease is a vast topic. So many areas of interest exist and so many enormous developments have occurred that providing a comprehensive discussion in a short review such as this is impossible. Therefore, this article concentrates on some new concepts in ophthalmic genetics, and also provides some strategies that may help pediatricians cope with all of the new information in the world of genomics. This article also helps identify patients who might benefit from genetic evaluation and provides some idea of how to interpret those genetic results.

The pediatrician and ophthalmologist often work as a team to determine a diagnosis to account for all physical and developmental anomalies that might present in a child. Whenever concern exists about a child's development, it is important for an ophthalmologist to conduct an evaluation to assess vision and possible related eye anomalies.

The newborn screening examination and the family ocular history provide critical information to pediatricians. Any anatomic anomaly seen by the pediatrician might indicate a genetic disease, which might impact not only the child's vision but also the

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overall health of the child. For example, a lens opacity could represent galactosemia. Conversely, if a history exists of a genetic eye defect, the baby should have an immediate thorough evaluation. For example, a family might have a history of incontinentia pigmenti. This disease can variably affect the retinas of different people. A mother might have normal vision, but her child could inherit a form of the disease that will cause blindness if treatment is not obtained before the retinas detach. Therefore, the pediatrician can help prevent total loss of vision if a child with incontinentia pigmenti is referred immediately for retinal examination regardless of the parent's vision.

SELECTED CLINICALLY IMPORTANT OCULAR PHENOTYPE/GENOTYPE CORRELATIONS

This section presents either recent information that is important to know or older information that is still so important that it needs to be revisited.

Lids

Lymphedema-distichiasis syndrome

This syndrome is caused by mutations in FOXC2 and has significant variability of expression.[1] Distichiasis (the growth of extra eyelashes, ranging from a few extra eyelashes to a full extra set on both the upper and lower lids) is the most common clinical feature, followed by lymphedema, which typically has its onset at puberty and not at birth (Milroy disease). Therefore, any child with distichiasis should be genetically tested for this condition.

Cornea

Corneal lesion and trisomy 8 mosaicism

Corneal lesions present as a flat reticular-appearing white lesion usually extending from the limbus into the cornea; fine blood vessels are usually present and the lesion is not elevated (**Fig. 1**).[2] This lesion is most commonly seen in trisomy 8 mosaicism, and the affected child may seem normal, and therefore testing (see later discussion) should be considered.

Iris

Iris anomalies and ACTA2

Cysts from the iris pigment epithelium at the pupillary margin are also called *iris flocculi* (**Fig. 2**). If a patient has parents or siblings with the same condition or has a family history of cardiac problems or vascular dissection, then ACTA2 analysis should be considered.[3] Congenital mydriasis with persistent pupillary membranes has also been found to be associated with ACTA2 mutations.[4]

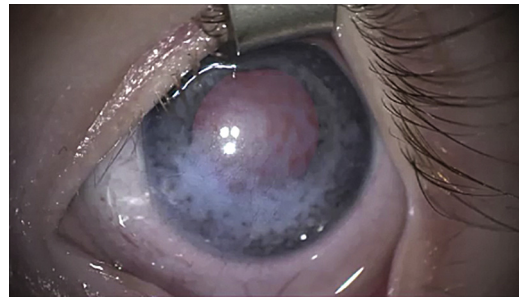

Fig. 1. This corneal lesion is unilateral; there is a flat reticular pattern with fine vessels. If seen, trisomy 8 mosaicism should be excluded.