Leber Congenital Amaurosis

WHAT IS LEBER CONGENITAL AMAUROSIS?

Leber Congenital Amaurosis (LCA) is a spectrum of inherited (genetic) conditions that causes poor vision. Findings commonly appear within the first 6 months of life and may worsen over time. LCA is caused by a defect in the cells that detect light in the retina (rods and cones).

HOW COMMON IS LCA?

Overall, it is rare (2–3 cases per 100,000 births), but about 10-18% of all cases of congenital blindness or severely reduced vision in children are caused by LCA — making it the leading cause of inherited blindness in children.

HOW IS LCA INHERITED?

LCA is usually inherited in an autosomal recessive fashion. Both parents carry one copy of a recessive gene. If both parents are unaffected but carry the recessive gene, there is a 25% chance that each child will have LCA. Several genetic defects have been found that cause LCA — most of which are inherited in a recessive fashion. A couple of genes, however, reportedly have been involved in a rare form of dominant inheritance. In the latter case, one mutated copy of the gene from an affected parent or a new mutation in the child would lead to LCA.

WHAT ARE THE SYMPTOMS AND SIGNS OF LCA?

The most common early symptom is nystagmus (shaking of the eyes), and it is usually evident within the first few months of life. As a child gets older, poor vision/tracking, sensitivity to light, and poking/rubbing of the eyes with a fist or finger may be noted. The ophthalmologist may notice slow reaction of the pupils, and severe hypermetropia (a need for glasses). The retina usually looks normal in early life but, abnormal retinal pigment, narrowing of the retinal blood vessels, and pale optic disc may appear. Other associated findings as children get older may include corneal problems (e.g. keratoconus), cataract, and glaucoma. Some genetic subtypes predispose to early onset kidney failure and these patients require renal surveillance.

HOW IS LCA DIAGNOSED?

LCA is usually diagnosed by an ophthalmologist based on history and the physical findings on exam. An electroretinogram (ERG) is often utilized to test the function of the rods and cones of the retina and is performed with special equipment. Other modalities that have been explored and assist with evaluation include optical coherence tomography (OCT) and autofluorescence imaging of the retina. If LCA is suspected clinically, genetic testing should be performed. Almost 80% of patients will have a diagnostic genetic test which can aid in prognosis, family planning, and determining treatment options. Specific genetic subtypes of LCA predispose patients to nephronophthisis and kidney failure; patients with these genetic subtypes should be referred to a nephrologist. Genetic testing can identify carriers of the condition among other family members. Genetic counseling is recommended for affected families.

HOW IS LCA TREATED?

In December 2017, the first gene therapy treatment for a genetic retinal degeneration was approved for RPE65-associated LCA. Patients who have biallelic mutations in the RPE65 gene may benefit from this treatment. More information is available on the Genetic Eye Disease Task Force page on the AAPOS website, and at Luxturna. Routine examinations by an ophthalmologist are recommended for all LCA patients to diagnose/treat other eye problems and prescribe glasses if necessary. Low vision aids to maximize visual function can be very useful for patients with LCA and a formal low vision evaluation is recommended soon after diagnosis to allow appropriate services to be accessed. Educational programs and support agencies for the visually impaired (and their families) are important. Some genetic subtypes of LCA have associated kidney dysfunction and/or developmental delays making referral to appropriate specialists very important.

WHAT IS VISION LIKE FOR PEOPLE WITH LCA?

Best attainable vision is somewhat variable for people with LCA. Vision is typically 20/200 or less, while no light perception is uncommon. Vision sometimes improves slightly in the first years of life as the brain develops but usually plateaus or even deteriorates in later life.

ARE THERE OTHER PHYSICAL PROBLEMS ASSOCIATED WITH LCA?

Most children with LCA are otherwise healthy. Neurologic, skeletal, muscular, heart, ear, and kidney abnormalities have been reported in some patients; in patients with NPHP5-associated LCA kidney dysfunction almost always develops with other genetic subtypes carrying an increased but variable risk. Genetic testing and communication with a child's pediatrician can help guide medical surveillance. Most children with LCA have normal intelligence.

IS THERE RESEARCH BEING DONE TO LEARN MORE ABOUT LCA?

Currently, there is active research being done on LCA.

Resources

- ClinicalTrials.gov — Currently active studies
- Lighthouse Guild — Tele-support group for parents

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