
OCRL1 & Lowe Syndrome

What is Lowe Syndrome?

- Lowe Syndrome is an inherited condition caused by changes in the OCRL1 gene which affects the eyes, brain and kidneys.
- It almost exclusively occurs in males.

What is OCRL1, and how do changes in OCRL1 affect the kidneys?

- The OCRL1 gene plays a number of roles, both in cell structure and function.
- Changes in this gene leave kidney cells unable to reabsorb important nutrients into the bloodstream.
- Instead, they are excreted in urine, causing a number of problems such as increased urination, dehydration and overly acidic blood.
- This abnormality of the kidneys generally begins showing signs after the first year of life, and can eventually lead to kidney failure.

Do these changes have effects on other parts of the body?

- Changes in OCRL can have a number of effects on the eyes:
 - Boys with Lowe syndrome are born with cataracts in each eye.
 - Around half of all affected boys develop high pressure in the eye (glaucoma) that can damage the eyes enough to cause blindness if not treated.
 - A small number may develop growths on the corneas called keloids during late childhood and adolescence which can eventually lead to blindness.
- The loss of salt and nutrients due to kidney dysfunction may impair growth and result in soft, bowed bones (rickets), as well as bone fractures and abnormal curving of the spine (scoliosis).
- These changes in OCRL1 also have implications for physical and intellectual development.
 - Intellectual ability can range from normal to severely impaired.
 - There can be significant behavioural problems such as severe temper tantrums, attention deficit disorder and obsessive behaviour.
- The boys are born with poor muscle tone. This can contribute to feeding difficulties, problems with breathing and delayed motor development (i.e. sitting, walking).
- Some children may have seizures.

How is Lowe Syndrome treated?

- Cataracts are removed as soon as possible, usually within the first few months of life. Unfortunately, vision is generally still poor after surgery and the child will need to wear glasses, contacts or both.
- Glaucoma may be treated with medicated eye drops, however surgery is usually necessary.

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- Corneal keloids can sometimes be removed but often recur.
 - Early intervention programs that include physical therapy, occupational therapy, speech and language therapy, special education services, and services for visually impaired are recommended and should begin in early infancy.
 - Tube feeding may be required if there are feeding difficulties due to poor muscle tone.
 - Oral supplements are used to replace lost nutrients.
 - Oral phosphate and oral calcitriol are used to treat (or prevent) rickets. Bone density should be monitored periodically.
 - Seizure disorders are treated with anticonvulsant medications.
 - Kidney failure has been treated successfully with dialysis and kidney transplantation in some late-adolescent adult men.

How is this change passed down through a family?

- Normally you have two copies of every gene – one from each parent. However, in the case of certain genes, only one copy is passed to males. OCRL1 is an example of such a gene.
- These genes are found on the X ‘sex chromosome’ – males have one X chromosome and one Y chromosome, while females have two X chromosomes.
 - Males only have one copy of OCRL1. If this copy is faulty, the syndrome will develop.
 - Females have two copies of OCRL1. If one copy is faulty, she will not develop the syndrome as the other copy functions normally.
 - However, most female carriers have changes in the lens of their eye, although this typically doesn’t have an impact on their sight.
- A faulty copy cannot be passed from an affected father to their son as the father only passes the unaffected Y chromosome to his son.
- Some cases can result from new changes in the gene and there is no family history of the syndrome.

Should my family members be tested?

- If there is a history of Lowe Syndrome in the family, genetic counselling can help assess risks before planning for a child.