REVIEW ARTICLE

Lowe Syndrome

Sowndariya Perumal

Received on: 13 October 2022; *Accepted on:* 13 November 2022; *Published on:* 31 December 2022

Abstract

Lowe syndrome or Oculocerebrorenal Syndrome of Lowe (OCRL) is a rare disorder characterized by multiple features occurring mainly in males. Its prevalence is approximately 1 in 500,000. Its systemic manifestations include mental retardation, hypotonia and kidney dysfunction in the form of Fanconi syndrome. It causes physical and mental handicaps and mental problems. Children with Lowe syndrome and glaucoma often require surgery to treat their glaucoma. Lowe syndrome is a condition that primarily affects the eyes, brain, and kidneys. It is brought on by a single faulty gene on the X-chromosome, which prevents the production of enzymes. Treatment aids in surviving, but mental capacity is compromised. The severity of neurological and renal manifestations affects quality of life.

Keywords: Creatine phosphokinase test, Glomerular filtration rate, Intraocular pressure, Magnetic resonance imaging, Oculocerebrorenal syndrome of Lowe.

Pondicherry Journal of Nursing (2022): 10.5005/jp-journals-10084-13150

Introduction

Lowe syndrome or OCRL is a rare disorder characterized by multiple features occurring mainly in males. Its systemic manifestations include mental retardation, hypotonia, and kidney dysfunction in the form of Fanconi syndrome. Specifically, its ocular manifestations include congenital cataracts, corneal keloid, and infantile glaucoma. Lowe syndrome is an X-linked recessive disorder with the key mutation in the *OCRL* gene.[1]

Definition

A rare multisystem disorder characterized by congenital cataracts, glaucoma, intellectual disabilities, seizures, postnatal growth retardation, and renal tubular dysfunction with chronic renal failure.[2]

Other Names

- Brain–eye–nose syndrome
- Syndrome Lowe oculocerebrorenal
- Eye–brain–neural syndrome
- Lowe's oculocerebrorenal syndrome
- 4,5-Bisphosphate-5-phosphatase phosphatase deficiency[3]

Prevalence

Its prevalence is about 1 in 500,000. Conditions have been documented in Asia, Europe, Japan, and North and South America. According to estimates, there are 1 to 10 men for every million individuals.[3]

Etiology

The *OCRL* gene is the primary cause of the X-linked recessive illness known as Lowe syndrome. A man may acquire a novel mutation spontaneously without any prior family history, or he may inherit a mutation from his mother who carries a mutant copy of the *OCRL* gene.[4]

Department of Medical Surgical Nursing, Kasturba Gandhi Nursing College, Puducherry, India

Corresponding Author: Sowndariya Perumal, Department of Medical Surgical Nursing, Kasturba Gandhi Nursing College, Puducherry, India, Phone: +91 8667312006, e-mail: sowndariyabalu05@gmail.com

How to cite this article: Perumal S. Lowe Syndrome. Pon J Nurs 2022;15(3):73–76.

Source of support: Nil

Conflict of interest: None

Risk Factors

Both the mother's OCRL mutation carrier status and the male gender are risk factors.[4]

Pathophysiology

Inositol 5-phosphatase, which has the substrates P1 and P2, is a key mutation in the *OCRL* gene, which codes for the enzyme OCRL-I. When P1 and P2 levels rise, levels of OCRL level 1 are low. This enzyme primarily targets organelles like endosomes and the Golgi apparatus. Protein trafficking, segregation, actin cytoskeleton polymerization, phosphoinositides, and cellular physiological processes like cytokinesis, actin cytoskeleton remolding, and motility all depend on the concentration of P1 and P2 substrates. This enzyme, which interacts with clathrin, is crucial for endosome and trafficking functions. Protein trafficking abnormalities occur at the kidney level. It is necessary for the differentiation and migration of epithelial cells in the eye, and ocular disorders are poorly understood.[5]

Symptoms and Signs

- Each eye has cataracts that are present from birth.
- Glaucoma
- Motor development is delayed and there is poor muscle tone (hypotonia).

© The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

- There are many degrees of intellectual disability, from mild (10–25%) to severe (50–65%).
- Seizures and behavioral issues
- A male victim grows something on his corneas known as keloids, and eye cornea in one or both eyes (blindness).
- Fanconi-type proximal tubular dysfunction brought on by amino acid, bicarbonate, and phosphate loss into the urine.
- Short height
- Tooth cysts
- Abnormal tooth dentin development
- Skin growths
- Soft bones, skeletal abnormalities (rickets), bone fractures, and scoliosis are all symptoms of vitamin D insufficiency.
- Joint degeneration without inflammation
- Delayed bleeding syndrome[6]

Test for Diagnosis

It is based on results from genetic testing and a newborn's physical examination.

History Collection

In a newborn male patient with congenital cataracts, central hypotonia, and central nervous system delay, it should be suspected. There may be male relatives with similar findings in the family history. Mothers of affected children may exhibit snowflake-shaped radial cortical ventricular opacities.

Physical Examination (Ophthalmological Abnormalities)

Patients with Lowe syndrome have a generally poor visual prognosis because of a variety of abnormalities. Vision is rarely 20/100 or greater. Cataracts are frequently seen even at 20 weeks of pregnancy. Bilateral cataracts in newborns are possible. Fifty percent of patients have glaucoma, nystagmus, and keloid.

Nervous System Disorders

At birth, there is severe hypotonia and a lack of the deep tendon reflex. It might make essential processes like birth breathing more difficult. The ability to move is significantly delayed. There may be signs of mental disability, and the majority exhibit maladaptive behaviors such as tantrums, irritation, and unresolved conduct. Additionally, patients may experience febrile convulsions or seizures.

Kidney Abnormalities

- Fanconi syndrome.
- Failure to thrive may present due to mineral wasting.
- Chronic renal failure.
- Renal tubular dysfunction.

Laboratory Investigation

A metabolic acidosis, a reduced glomerular filtration rate, hypokalemia, a vitamin D insufficiency, increased creatine phosphokinase test, and liver transaminases are all revealed by serologic tests. Urine analysis reveals proteinuria and aminoaciduria. Light ventriculomegaly and periventricular cystic lesions are visible on MRI. The posterior pole cannot be seen on an ocular ultrasonography B scan because of the cataract. Reduced OCRL-1 inositol polyphosphate 5-phosphatase activity in cultured skin fibroblasts is the basis for the diagnosis. If the *OCRL* gene mutation has been identified in one or more affected male relatives or the carrier mother, prenatal diagnosis is made through biochemical testing (enzyme assay) or molecular genetic testing, by either electromyography or electroencephalography.[7]

Management

General Management (Vision Disabilities)

It is advised to have cataract surgery for congenital cataracts. Within the first 3 months of life, cataract surgery is advised to prevent amblyopia. Infants are typically left aphakic, which increases the risk of problems and necessitates more procedures. Contact lenses or aphakic glasses are crucial for developing vision. Surgery is necessary to treat glaucoma and Lowe syndrome in children. The cornerstone of glaucoma care includes goniotomy, trabeculotomy, and tube shunt procedures. Children should get routine glaucoma screenings.

Systemic Abnormalities

Early physical therapy is necessary for hypotonia. Antipsychotics will be administered for maladaptive behavior. For nervous abnormalities, people utilize clomipramine, paroxetine, and risperidone. Treatment options for renal tubular acidosis include sodium bicarbonate or other alkalis. Infants with the resulting dehydration may need intravenous fluids. Additionally, calcium and parathyroid hormone levels must be closely monitored, and vitamin D supplements must be adjusted accordingly to prevent the development of rickets.

Standard Therapies

- Feeding issues caused by low muscular tone may necessitate tube feedings and treatment, and gastrointestinal reflux therapy with human growth hormones to quicken growth.
- Early cataract removal is utilized to encourage the best possible visual development.
- The use of contact lenses and eyeglasses can enhance vision.
- Lubricants, topical steroids, cyclosporine, and antimetabolites are used to treat corneal keloids in patients undergoing lamellar keratectomy or corneal transplant surgery.
- Treatment for proximal tubular dysfunction of the Fanconi type involves oral sodium and potassium bicarbonate or citrate supplementation.
- Treatment for renal bicarbonate losses that is alkalizing.
- Rickets is treated with oral calcitriol and phosphate.
- Periodically checking on bone density is recommended. Bone reabsorption is aided by phosphorus supplementation.
- For severe or worsening scoliosis, joint hypermobility, and cutaneous cysts that are uncomfortable or impede function, bracing or surgery may be necessary.
- Anticonvulsants are used to treat seizure disorders.
- Behavior modification and medication are offered for behavioral issues.
- It is advised that early intervention programmers, which should start in early infancy, include physical therapy, occupational therapy, speech and language therapy, special education services, and services for visually impaired children.
- Dialysis and other therapies have been effective in treating end-stage renal disease kidney transplant.
- In order to address platelet dysfunction, tranexamic acid has been employed.[8]

Surgical Management

Ocular

In order to maximize visual potential, the congenital cataract must be surgically removed, ideally within the first 6 weeks of life. Instrumentation using a mechanized vitrector is necessary. The likelihood of a secondary membrane forming is decreased by the complete removal of all lens material combined with a primary posterior capsulotomy and an anterior vitrectomy. Following surgery, aphakic correction must be started right away.[8]

Diet

To replenish urinary water losses with fluid, supplements with phosphate should be suggested. A low-protein diet and vitamin D are recommended.[8]

Outpatient Care

Keep an eye on your alignment, refraction, optic disk, intraocular pressure, and any signs of glaucoma. Amblyopia is monitored and appropriately treated. Watch your kidney health. Arthritis, tenosynovitis, and joint edema should be monitored and treated. Fractures frequently occur. Keep an eye out for hypotonia and growth. Speech treatment, genetic counseling, and physical therapy are recommended.[8]

Prevention (Prenatal Examination)

Amniocentesis or sample of chorionic villus, 99% sensitivity of prenatal enzyme test for male fetuses, and using family-linked markers or directly detecting mutant alleles in DNA are recommended.[8]

Complications

Ocular

Eye blindness (congenital cataracts are left untreated), nystagmus, amblyopia, and strabismus)

Renal

If the condition is left untreated, gradual renal failure may happen by the second or third decade.

Neurologic

Mental impairment, seizures, and motor development are delayed.

Orthopedic

Fractures, swelling of a joint, tenosynovitis, rickets, osteomalacia, and osteopenia can occur.[8]

Prognosis

The severity of neurological and renal manifestations affects the quality of life. Rarely does a person live above the age of 40, and deaths typically happen between the ages of 20 and 40 as a result of renal illness, hypotonia, increased susceptibility to infectious diseases, seizures, and sudden demise. The oldest Lowe syndrome patient reported to have passed away at age 54.[8]

Nursing Management of Lowe Syndrome

Optimizing patient quality of life needs a multidisciplinary and interprofessional team approach to therapy in the nursing management of Lowe syndrome. In order for the entire care team to work from the same correct, current information, and better optimize care, each member of the interprofessional team must be able to get in touch with the other team members and maintain accurate records of all observations and interactions with the patient.[9]

Preoperative Care

- Gather the medical history from the past, which should include information on Lowe syndrome, Fanconi syndrome-related renal involvement, cataracts, hypertension, intellectual disability, short stature, and osteopenia with a history of prior femur fractures.
- Gather previous surgical history, which included a kidney biopsy at the age of 16, surgery on the tear ducts, and orthopedic surgery for femur fractures.
- Keep an eye on the patient's speech and movement abilities.
- Use gentamicin and codeine to test for allergies.
- There was a considerable maternal history of hypertension and a family history of two maternal uncles who had Lowe syndrome.
- Administer drugs including amlodipine (5 mg oral tablet by mouth once daily) for hypertension, potassium citrate, sodium citrate, and ergocalciferol, as well as growth hormone (1.6 mg subcutaneous injection every night) for short height.
- The preoperative laboratory examination included electrolytes, renal function, coagulation function, blood glucose, and hepatic function. Low serum potassium (3.2 mEq/L) and low serum bicarbonate (18 mEq/L) levels were also monitored.

Intraoperative Care

- Rocuronium (15 mg) was used during surgery to decrease neuromuscular blockade, and direct laryngoscopy was used for endotracheal intubation. To ease breathing problems, bag-valve-mask ventilation was used during intraoperative treatment.
- Tranexamic acid (50 mg/kg bolus dose followed by an infusion at 5 mg/kg/h) was given to prevent fibrinolysis and to reduce intraoperative blood loss.
- Desflurane was titrated to keep the bispectral index between 50 and 60 while anesthesia was maintained during spinal surgery. Sufentanil was infused at a rate of 0.1–0.3 gm/kg/h.
- To reduce intraoperative blood loss, clevidipine was given to keep the mean arterial pressure between 55 and 70 mm Hg. A dose of 0.15 mg/kg of methadone was given to provide postoperative analgesia. We recorded motor-evoked potentials and somatosensory-evoked potentials as part of our baseline neurophysiological monitoring.
- Using a prone cushion, the patient was turned and placed prone on the Jackson table.
- With a typical sinus rhythm, the intraoperative heart rate ranged from 60 to 100 beats per minute.
- No allogeneic blood components were given. An estimated 650 mL of blood was lost. A total of 1100 mL of 5% albumin and Normosol-R® were given as fluids throughout the procedure.
- Sugammadex was used to break up any remaining neuromuscular blockage. Based on intraoperative arterial blood gas and electrolyte levels, sodium bicarbonate, potassium chloride, and calcium chloride were given. The patient was made supine once the surgery was finished, and his trachea was extubated while he was still conscious.
- Watch out for patients who need surgery may experience intraoperative problems due to impaired hemostasis.

Perioperative Care

During surgery, it's important to keep an eye out for things like hypotonia, chronic metabolic acidosis, electrolyte imbalances, bone fragility, and problems managing the airway.

Postoperative Care

- Monitor vital signs.
- After surgery, acetaminophen (15 mg/kg) was injected intravenously along with hydromorphone in increasing doses to relieve pain.
- Hydromorphone was given *via* nurse-controlled analgesia to control postoperative discomfort.[10]

Who can't Receive the Treatment?

Children or infants with other uncommon genetic conditions are ineligible for therapy for Lowe syndrome.[11]

Considerations of Treatment

Infection, inflammation, and bleeding after cataract surgery. Antipsychotic medication side effects include nausea, increased appetite, weight gain, lethargy, drowsiness, sleeplessness, dry mouth, and impaired vision.[11]

India's Treatment Cost

It ranges in price from ₹500 to 20,00000.[11]

Conclusion

Lowe syndrome is an X-linked recessive disorder that primarily affects men. It is brought on by a single faulty gene on the X-chromosome, which prevents the production of enzymes. Treatment aids in surviving, but mental capacity is compromised.

References

1. Stephen C, Dryden MD, Fowler BT, Philip S, Patel AS, DelMonte DW et al. Lowe syndrome. March 30, 2022, available from https://eyewiki.aao.org/Lowo-Syndrome.
2. Bokenkamp A. Oculocerebrorenal syndrome of Lowe, available from www.orpha.net.com. Accesssed date: 14 September 2022.
3. Medlineplus. Bethesda (MD): National Library of Medicine, updated: June 24; cited: July 1, 2020, available from https://medlineplus.gov/.
4. Lewis RA, Robert L. Lowe syndrome – rare disease. NORD Member Organizations, available from https://rarediseases.org. Accesssed date: 27 August.
5. Alcorn DM, Lee AG. Lowe syndrome (oculocerebrorenal syndrome). March 21, 2017, Medscape, Available from https://emedicine.medscape.com.
6. Health Jade Team for Lowe Syndrome, available from http://healthjade.net.com. Accesssed date: 12 June 2022.
7. Wikipedia. Oculocerebrorenal syndrome, available from https://en.m.wikipedia.org. Accesssed date: 23 June 2022.
8. Mestrovic T News medical and life science. 2015, updated on September 25, 2022, available from https://www.news.medical.net.com.
9. Murdock N, Chou E. Oculocerebrorenal syndrome article – StatPearls. 2022, available from https://www.statpearls.com.articlelibrary. Accesssed date: 13 September 2022.
10. Malik B, Walia H, Martin DP, Tobias JD. Anesthetic management of an adolescent with Lowe syndrome during posterior spinal fusion. J Med Cases 2017;8(12):388–392. DOI: https://doi.org/10.14740/jmc2949w.
11. Kumar R. Lowe syndrome: cost and side effects. Lybrae.net, available from http://www.lybrate.com. Accesssed date: 11 May 2022.