CASE REPORT

Lowe Syndrome (Oculo-cerebro-renal Syndrome of Lowe): A Case Report from Eastern India

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Abstract:
Lowe syndrome (the oculocerebrorenal syndrome of Lowe, OCRL) is a rare X-linked recessive metabolic disorder that primarily affects eyes, kidneys and brain. It is caused by the deficiency of enzyme phosphatidylinositol 4, 5-bisphosphate 5-phosphatase. The gene coding for this enzyme, OCRL1 and mutations in it are responsible to cause Lowe Syndrome. We report a 6 years old boy from Eastern India, with Lowe Syndrome. Diagnosis was suggested by typical features in the MRI of the brain along with other clinical feature and investigation.

Keywords: Lowe syndrome; OCRL; Cataract.

Introduction:

Lowe syndrome (the oculocerebrorenal syndrome of Lowe, OCRL) is an uncommon, panethnic, X-linked recessive metabolic disorder described by Lowe and coworkers in 1952 [1]. It is a multisystem disorder which primarily affects the eyes, nervous system, and kidneys. It is characterized by congenital cataracts, infantile glaucoma, neonatal or infantile hypotonia, intellectual impairment, and renal tubular dysfunction (Fanconi syndrome). Tentative prevalence is 1 in 500,000 of general population. The mutation of the gene *OCRL1* localized at Xq26.1, coding for the enzyme phosphatidylinositol, bisphosphate 5 phosphatase, PtdIns P2, in the trans-Golgi network is responsible for the disease. Both enzymatic and molecular testing is available for confirmation of the diagnosis and for prenatal detection of the disease [2]. Clinical features include congenital cataract, glaucoma, miotic pupils, nystagmus, corneal keloids as ocular involvement, infantile hypotonia, areflexia, seizures, mental retardation, behavioral abnormalities as cerebral involvement and fanconi syndrome, renal tubular acidosis and gradual impairment of glomerular function as renal involvement. Although the child was treated by different subspecialist but proper diagnosis was not predicted in the beginning, as there was no team approach. We should treat a patient as a whole & team approach is needed to diagnose a rare syndrome like Lowe syndrome.

Case Report:

A six years old male patient came thrice in different hospitals at different departments. At one month of age the baby presented for the first time with bilateral congenital cataract and glaucoma which were treated by ophthalmologist.

Next time the patient came with lower limb injury for which X-ray was done. X ray showed features of rickets (Fig. 1, 2, 3). Relevant blood examination showed low phosphorus level with raised alkaline phosphatase and normal serum calcium. Urine examination revealed albumin, sugar and phosphate in urine suggesting renal tubular dysfunction. Blood gas analysis revealed acidosis. USG of abdomen showed bilateral small kidneys.

The patient came for the third time and was admitted for convulsion in our hospital at the age of six years. Along with other routine investigations, the patient was referred to our department for MRI of brain. MRI brain was performed in our Magnetom Concerto (Siemens Medical System) which showed periventricular hyperintensities on T2W and FLAIR images with tiny cystic lesions within (Fig. 4, 5, 6, 7). The cysts were hypointense on T1W and FLAIR images (Fig. 7, 8). The cerebellum, basal ganglia and subcortical white matter were not involved.

Based on the previous history of ocular and renal in-

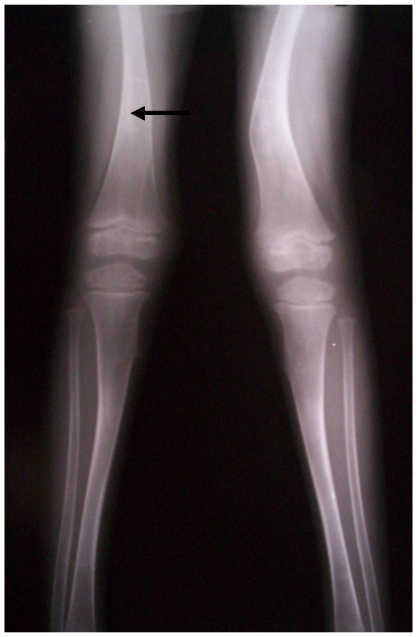

Fig. 1: X-Ray PA View of the Both Lower Limbs Show Bowing of Lower Femur and Tibia, Genu Valgus

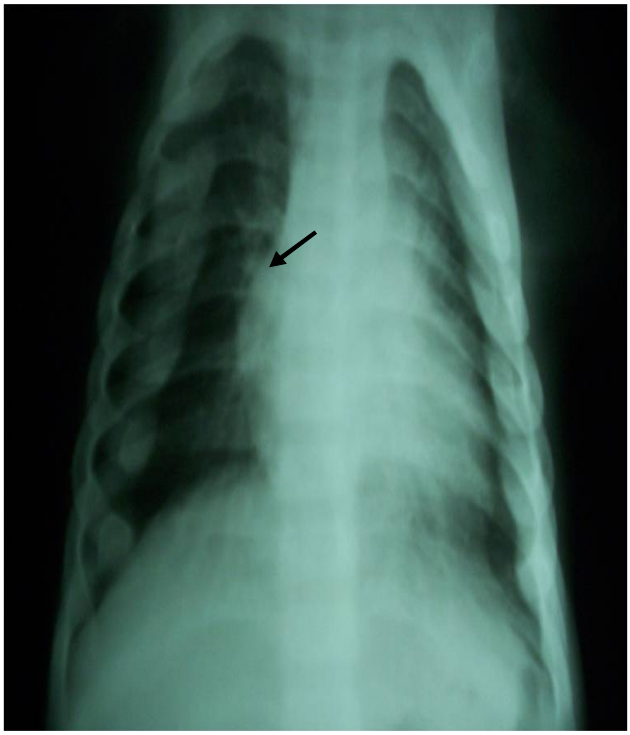

Fig. 2: Chest X-Ray PA View Shows Rachitic Changes in the Ribs

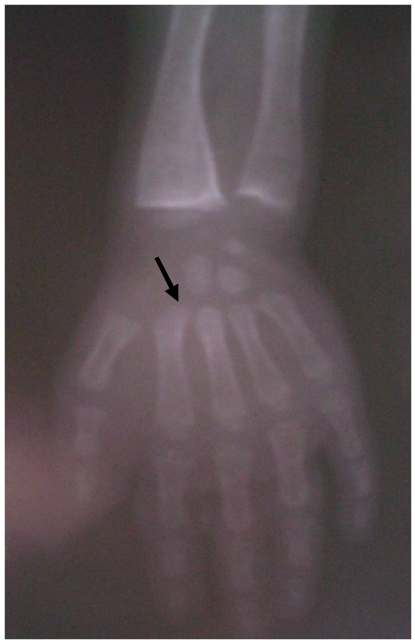

Fig. 3: X-Ray of Right Hand PA View Shows Oteopenia and Metaphyseal Increased Density

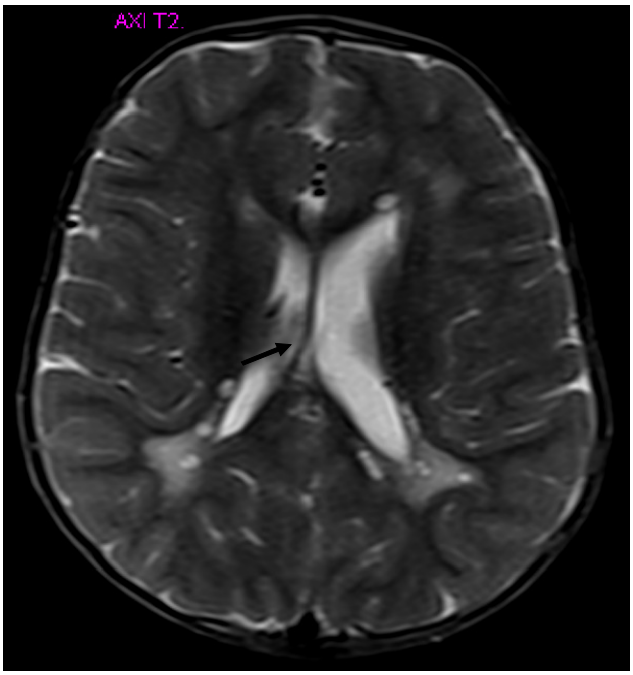

Fig. 4: Axial T2 Weighted Images Shows Hyper Intensities in the Periventricular White Matter. Multiple Small Oval Shaped Hyperintense (CSF Intensity) Lesions are Noted Around the Periventricular Region with Mild Dilatation of the Ventricular System

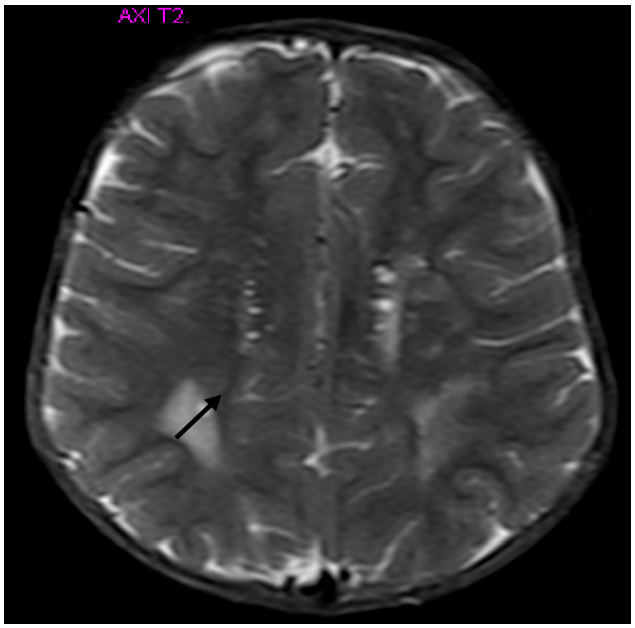

Fig. 5: Axial T2 Weighted Images Shows Ill-Defined Hyperintensities in the Region of Centrum Semiovale

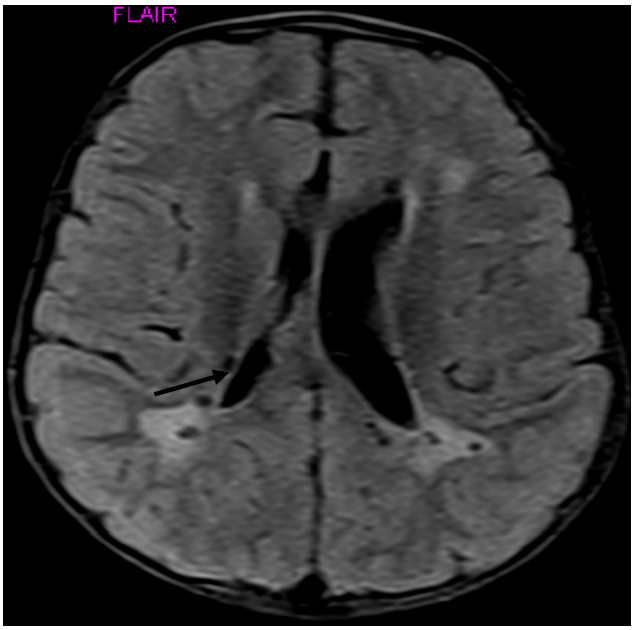

Fig. 7: Axial FLAIR Image Shows Periventricular Hyper Intensities with Multiple Hypo Intense Cystic Lesions

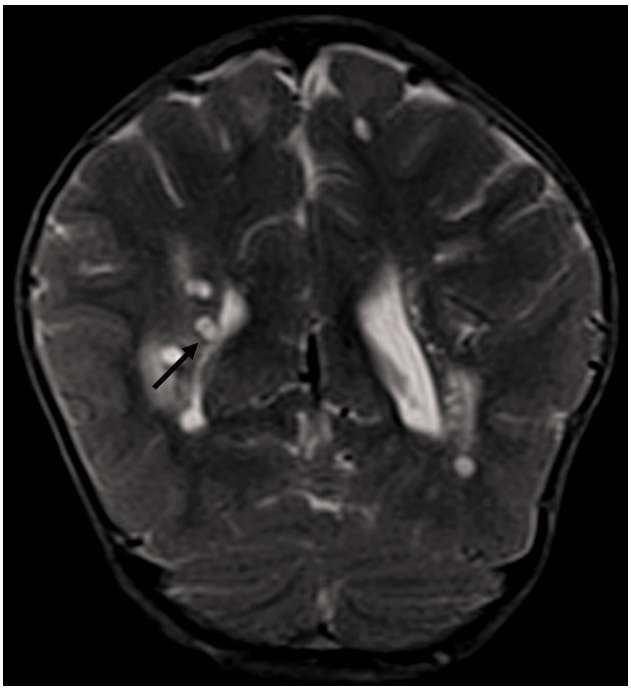

Fig. 6: Coronal T2 Weighted Image Shows Hyper Intensities in the Periventricular Region with Multiple Cystic Lesions Within. the Lesions are not Involving Cerebellum and Corpus Callosum

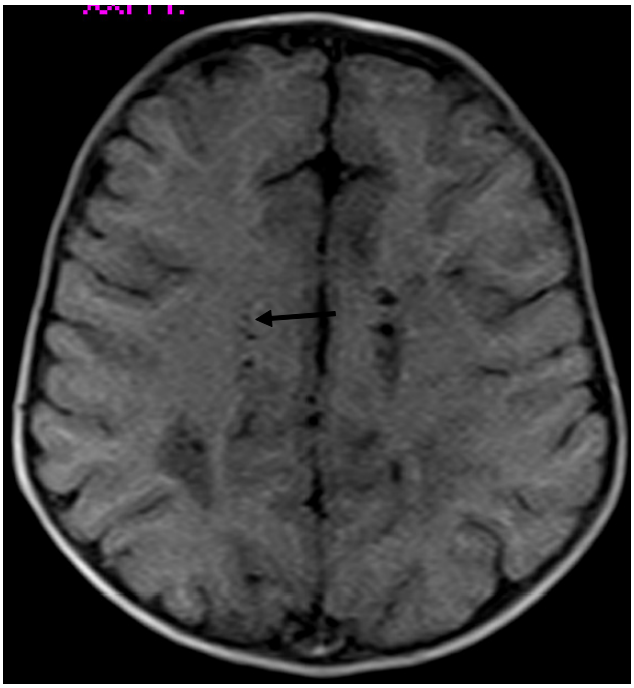

Fig. 8: Axial T1 Weighted Image Shows Hypointensities in the Periventricular Region and Centrum Semiovale and Multiple Hypointense Cystic Lesions Within.

volvement, the cerebral lesions pointed towards the diagnosis of oculo-cerebro-renal syndrome of Lowe. MR spectroscopy could not be done as it was not available in that scanner.

Discussion:

MR imaging findings in Lowe syndrome include patchy areas of high-signal changes on T2W and FLAIR images that are hypointense on T1-weighted images. At the same time there may be small, well-defined, punctate, cyst-like changes, which follow the signal pattern of CSF. The lesions are usually bilateral [3, 4, 5, 6]. Cranial MR examination of our patient shows similar bilateral hyper intensities on T2 weighted images with tiny cysts in the periventricular regions.

Past reports attribute that the hyper intensities mostly in the bilateral periventricular regions and centrum semiovale are due to demyelination [7, 4] or gliosis [8] and not necessarily correlated with the severity of clinical manifestations [8]. Recent studies and neuropathological data show evidences that these are due to gliosis. Schneider and Sener [5, 4] described cases with proton MR spectroscopy reporting prominent peaks of myoinositol which is a glial marker, suggesting the presence of gliosis [9].

In OCRL patients there is deficiency of phosphatidylinositol, bisphosphate 5 phosphatase, located in the Golgi apparatus, which catalyzes the hydrolysis of the 5-position phosphate and regulates cellular levels of phosphatidylinositol 4, 5-biphosphate (PtdIns 4, 5-P2), a metabolite involved in Golgi vesicular transport. This enzymatic deficiency leads to accumulation of PtdIns 4, 5-P2 in lysosomal membranes and therefore causes increased extracellular release of lysosomal enzymes [10]. This would be responsible for developmental defects in the lens and abnormal renal and neurological functions. In CNS the accumulation of lysosomal products can lead to dilatation of perivascular spaces [5], whereas extracellular release of lysosomal enzymes can lead to toxic gliotic reactions [5].

In our patient, ocular involvement (bilateral cataract and glaucoma) and renal involvement (renal tubular dysfunction, renal rickets) were viewed as isolated entities when attended. However, after the highly suggestive MR picture of brain, we reviewed the past history of the patient and detailed work up was done. Although similar tiny cystic lesions and periventricular hyper intensities on long TR sequences can be found in different conditions with dilated perivascular spaces including mucopolysaccharidosis, white matter injury etc. The diagnosis was suggested in the perspective of ocular and renal involvement in the same patient. Any further investigation like genetic mutation, enzymatic analysis and response to treatment with golgi complex are not possible with this patient because of our socio-economic condition.

Inspite of multisystem involvement, patients with Lowe syndrome survive for about 30-40 years. Renal insufficiency [9] is the usual cause of death. Medical management includes correction of electrolytic imbalance, supplementation of calcium, vitamin- D, phosphate, potassium and relation with speech, occupational and physiotherapy. Surgical intervention combines ophthalmologic intervention and includes treatment of cataract, glaucoma and orthopedic intervention including corrections of scoliosis and long bone deformities.

Conclusion:

The moral of the story is, in these days of specialization we often analyze patient's complaints in isolation and miss a multisystem disorder or a syndrome. We should treat a patient as a whole and a team approach is needed to diagnose a rare syndrome like Lowe syndrome. The role of radiologist is crucial in the diagnosis of rare syndromes or diseases with multisystem involvement. The scrutiny of the patients past health records and analysis of present clinical sce-

nario can only lead to the correct diagnosis.

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