Leigh Syndrome - A Rare Case Report

Shreya Soni¹, Atul Mishra²

¹3rd Year PG, Department of Ophthalmology, Katihar Medical College
²Professor and HOD, Department of Ophthalmology, Katihar Medical College

Abstract: Leigh syndrome is a rare neurological, progressive, mitochondrial condition that causes multiple system failure with a prevalence of 1:40,000. It is characterised by motor/intellectual developmental delay as well as symptoms of and signs for brain stem/basal ganglia involvement. Vision loss, nystagmus, strabismus, ophthalmoparesis, and optic atrophy are examples of ocular symptoms.

Keywords: Leigh syndrome, Subacute necrotising encephalopathy, mitochondrial disorder

1. Case Report

On June 5, 2021, the paediatric department recommended a two-year-old female kid to the dept of ophthalmology to seek for an ocular cause of vision loss and nystagmus. The mother served as the informant and reported symptoms included a decline in alertness and a history of seizures dating back a year with a frequency of once every two to three months. The child’s prenatal history was uncomplicated. The youngster was found to have dystonia with hypotonia, delayed developmental milestones, and to be afebrile. All four limbs had hypotonia, with the lower limbs having more of it. Deep tendon responses were heightened and the Babinski sign was positive on both sides.

When examined for extraocular signs, the infant had both eyes fixed on a light. The pupils were round, regular, and light-responsive. There were less lateral gaze movements. There was horizontal nystagmus. There was latent convergence squint. Bilateral flat white discs with clearly defined edges and healthy blood arteries were discovered during a funduscopy. The image appeared to show signs of optic atrophy (primary). The periaqueductal grey material, basal ganglia (mainly Putamen), medial thalamus, substantia nigra subthalamic nuclei, both sides cerebellar hemispheres (mainly fourth ventricle), both sides corona radiata, midbrain and posterolateral callosal-septal interface all displayed lesions that were hypointense on T1WI, hyperintense (Figure2,3,4) Subacute necrotizing encephalopathy in active phase was suggested of the lesions. Serum electrolytes were normal. Serum creatinine was 0.7mg/dl, blood urea was 21 mg/dl, which were normal. Serum lactate was 3.9mmol/L which was raised.

Figure 1: Child with Leigh syndrome with delayed milestones

Figure 2: Represent subsacute necrotising encephalopathy involving the basal ganglia, substantia nigra, putamen shown by focal hyperintensities in the region.
2. Discussion

A uncommon, neurological, progressive metabolic condition called Leigh syndrome. Juvenile subacute encephalomyelopathy is another name for it. The disease was initially characterised in 1951 by British neuropsychiatrist Archibald Denis Leigh. It is characterised by the central nervous system's dysfunction. It normally begins between ages of 3 months and 2 years when it first manifests, however some children may not show characteristics of disease till much later years. Children that are affected typically exhibit symptoms within initial year of life, including feeding issues, vomiting, and failure to thrive. Generalized weakness, dystonia, altered muscle tone, cerebellar ataxia, missed developmental stages or regression of the completed milestones, vision loss, tachypnea, and seizures are symptoms of Leigh syndrome that worsen with time.

Lactic acidosis episodes affect the renal and breathing systems. Because the brain is unable to govern how muscles contract, the muscular system throughout the body is compromised. Nystagmus, optic atrophy, and ophthalmoparesis are ocular symptoms. Hypertrophic cardiomyopathy and ventricular septal abnormalities are cardiac symptoms. Arterial Blood Gas for acidosis, blood lactic acid, CSF lactic acid and pyruvic acid levels, a kidney function test, and an electrolyte analysis should all be performed. The most distinctive neuro-radiological MRI results include B/L symmetrical focal hyperintensities at different levels in the basal ganglia, thalamic, substantia nigra, and brainstem nuclei. The putamen is notably engaged in the basal ganglia.

On MR spectroscopy in a study by Barkovich AJ et al. showed a rise in lactic acid from patients' afflicted areas. The diagnosis of Mitochondrial Encephalopathies must take into account MR Spectroscopy results, clinical symptoms, and laboratory results. The Leigh syndrome has a wide range of clinical characteristics and is unique for lacking a defined biochemical or molecular malfunction. Typical MRI brain abnormalities and clinical symptoms were often used to make the diagnosis. Diffusion weighted MRI displays acute phases of limitation. N-acetyl aspartate(NAA) peak level is lowered in MR spectroscopy, whereas lactate peak level is enhanced due to dysfunction of OXPHOS16. Neural and/or axon loss and necrosis cause a decrease in NAA level.

Leigh syndrome can be brought on by mutations in one of more than thirty distinct genes, either in nuclear DNA (gene SURF1 and several COX assembly factors) on the long arm of chromosome nine (producing autosomal recessive inheritance infrequently) or in mitochondrial DNA (mtDNA), causing maternal inheritance. Mutations in nuclear or mtDNA-encoded genes cause abnormalities of oxidative phosphorylation, which in turn causes a shortage.
of ATP in the cellular environment, which results in basal ganglia and brain stem cell death. Pyruvate dehydrogenase complex (PDHC), an enzymatic complex in the glycolysis pathway, is affected by another nuclear DNA mutation that results in Leigh syndrome and causes pyruvate accumulation and lactic acidosis. Therefore, genetic testing for both parents and children is necessary. The primary cause of mortality is respiratory failure. Within a few years of the commencement of symptoms, death frequently results from gradual respiratory failure.

Perinatal asphyxia, carbon monoxide poisoning, thiamine deficiency, Wilson’s diseases, biotin-responsive basal ganglia illness, kernicterus, methanol toxicity and a few distinct types of encephalitis are among the differential diagnoses.

3. Conclusion

When a child exhibits ocular symptoms such as vision loss, nystagmus, strabismus, ophthalmoparesis, and optic atrophy in addition to the foregoing neurological symptoms and an MRI that reveals abnormalities indicative of sub acute necrotizing encephalopathy, Leigh syndrome should be suspected. This should encourage more research, including blood/CSF lactate measurements and renal function tests. It is necessary to conduct more enzymatic and genetic research on the kid and parents if suitable clinical and laboratory conditions are available. Despite the exceedingly poor prognosis of this disorder, which often results in mortality in initial years of life, the child can get adequate supportive care if the diagnosis is confirmed early, depending on a syndromic strategy with the proper examinations and analysis.

References