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Leigh Syndrome - A Rare Case Report

Shreya Soni[1], Atul Mishra[2]

[1]3rd Year PG, Department of Ophthalmology, Katihar Medical College

[2]Professor 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. [1] 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 calloso-septal interface all displayed lesions that were hypointense on T1WI, hyperint (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

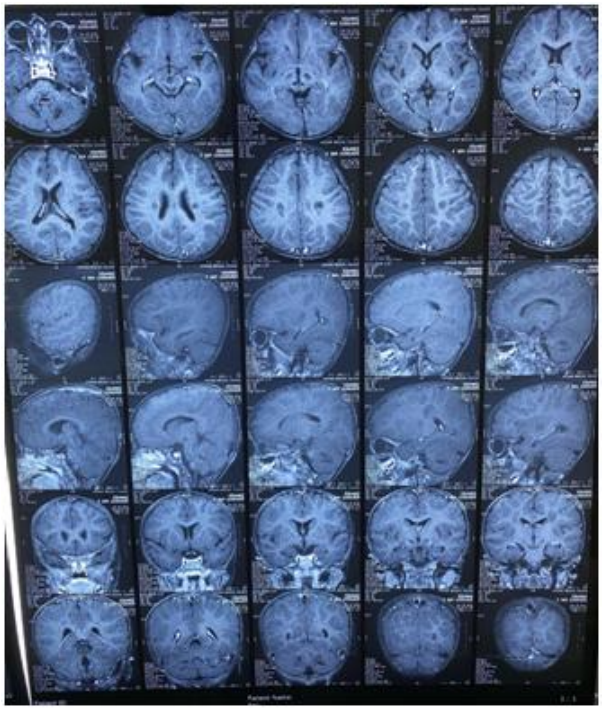

Figure 2: Represent subscute necrotising encephalopathy involving the basal ganglia, substantia nigra, putamen shown by focal hyperintensities in the region.

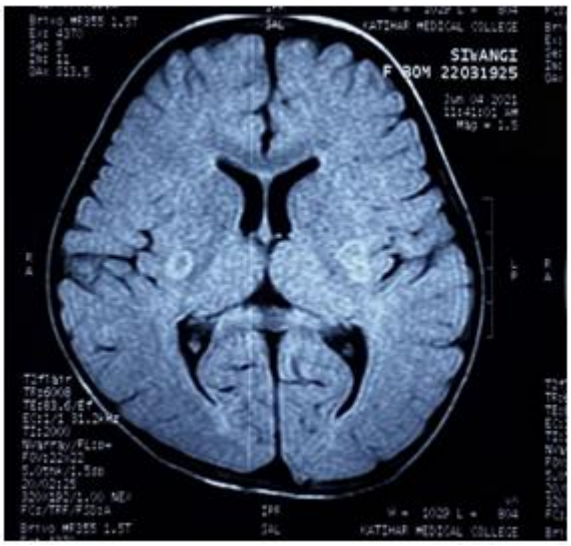

Figure 3

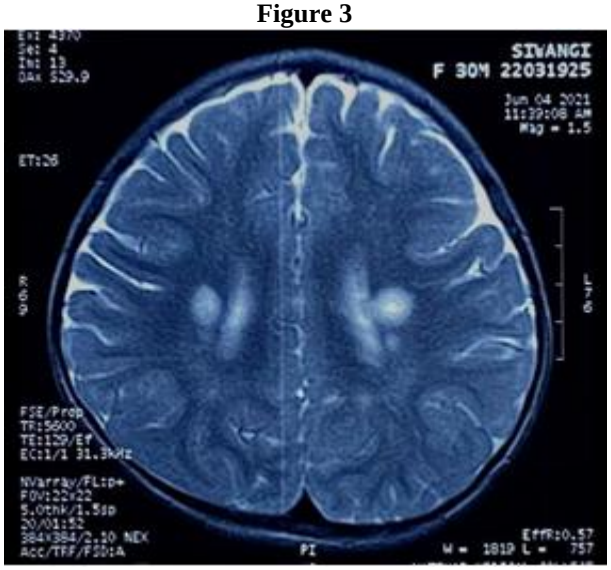

Figure 4

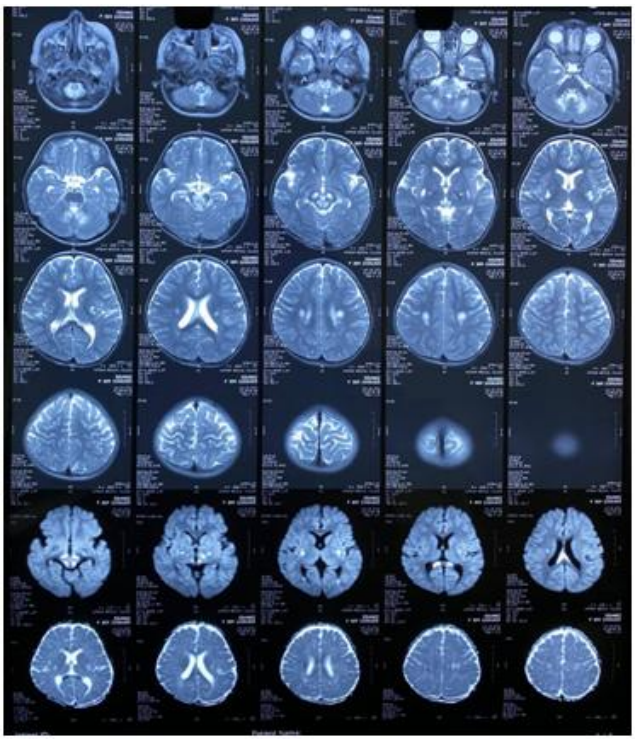

Figure 5

Figure 3, 4, 5: Bilateral symmetrical altered signal intensity area involving B/L corona radiata, B/L lentiform nucleus and midbrain appearing hypointense on T1WI , hyperintense on T2WI, center of lesions partially suppressed on FLAIR and restriction noted on DWI

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. [2,5] 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. [2,6] 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.[2,5] . 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.[5,7,2]

On MR spectroscopy in a study by Barkovich AJ et al. showed a rise in lactic acid from patients' afflicted areas[14]. 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.[2,15]. 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. [10,12,14] 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.[13,16] Therefore, genetic testing for both parents and children is necessary. The primary cause of mortality is respiratory failure. [15] Within a few years of the commencement of symptoms, death frequently results from gradual respiratory failure. [3]

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.[10]

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

[1] Leigh D. Subacute necrotizing encephalomyelopathie in an infant. J Neurol Neurosurg Psychiatry. 1951; 14: 216–21.
[2] Crimi M, Papadimitriou A, Galbiati S, Palamidou P, Fortunato F, Bordoni A, Papandreou U, Papadimitriou D, Hadjigeorgiou GM, Drogari E, Bresolin N, Comi GP. A new mitochondrial DNA mutation in ND3 gene causing severe Leigh syndrome with early lethality. Pediatr Res. 2004; 55: 842-46.
[3] Cacic M, Wilichowski E, Mejaski-Bosnjak V, Fumić K, Lujić L, Marusić Della Marina B, Hanefeld F. Cytochrome c oxidase partial deficiency-associated leigh disease presenting as an extrapyramidal syndrome. J Child Neurol. 2001; 16: 616–19.
[4] Menkes JH. Textbook of child neurology. 5th edi. London, Williams and Wilkins, 1995, p 850.
[5] Montpetit VJA, Andermann F, Carpenter S, Fawcett JS, ZborowskaSluis D, Giberson HR. Subacute narcotizing encephalomyelopathy. Brain. 1971;94:01-30.
[6] Sparaco M, Bonilla E, DiMauro S, Powers J. Neuropathology of mitochondrial encephalomyopathies due to mitochondrial DNA defects. J Neuropathol Exp Neurol. 1993;52:01-10.
[7] Lee H-F, Tsai C-R, Chi C-S, Lee H-J, Chen CC-C. Leigh syndrome: clinical and neuroimaging follow-up. Pediatr Neurol. 2009;40:88-93.
[8] Sofou K, De Coo IF, Isohanni P, Ostergaard E, Naess K, De Meirleir L, et al. A multicenter study on Leigh syndrome: disease course and pre- dictors of survival. Orphanet J Rare Dis. 2014;9:52.
[9] Jabeen SA, Sandeep G, Mridula KR, Meena AK, Borgohain R, Sundaram C. Adult-onset Leigh's disease: A rare entity. Annals of Indian Academy of Neurology. 2016;19(1):140.
[10] Arii J, Tanabe Y. Leigh Syndrome: Serial MR Imaging and Clinical Follow-up. AJNR Am J Neuroradiol. 2000;21:1502-09.
[11] Davis PC, Hoffman JC, Braun IF, Ahmann P, Krawiecki N. MR of Leigh's Disease (Subacute Necrotizing Encephalomyelopathy). AJNR. 1987;8:71-75.
[12] Sijens PE, Smit GPA, Rödiger LA, Van Spronsen FJ, Oudkerk M, Rodenburg RJ, et al. MR spectroscopy of the brain in Leigh syndrome: Brain & Development. 2008;30:579-83.
[13] Aydina H, Kizilgöz V, Hekimog˘ lu B. Leigh Syndrome: Cranial MRI and MR Spectroscopy Findings. Fırat Tıp Dergisi. 2011;16(2):102-05.
[14] Barkovich A, Good W, Koch T, Berg B. Mitochondrial disorders: Analysis of their clinical and imaging characteristics. AJNR. 1993;14:1119-37.
[15] Jiang YW, Qin J, Yuan Y, Qi Y, Wu XR. Neuropathologic and clinical features in eight Chinese patients with Leigh disease. J Child Neurol. 2002;17(6):450-52.
[16] Ruhoy IS, Saneto RP. The genetics of Leigh syndrome and its implications for clinical practice and risk management. The Application of Clinical Genetics. 2014;7:221-34. doi:10.2147/TACG,46176