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Case Report

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TWO DIFFERENT SPECTRUM OF PRESENTATION OF LEIGHS SYNDROME IN SAME FAMILY -A RARE CASE REPORT

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ABSTRACT

Leigh syndrome is a progressive neurodegenerative disorder; begins most commonly in infants between the ages of three months and two years. It presents with variable clinical features like swallowing difficulties, developmental delay / regression, and signs and symptoms of brain stem and/or basal ganglia involvement. Raised lactate levels in blood and/or cerebrospinal fluid and characteristic symmetrical necrotic lesions in the basal ganglia and/or brain stem on T2-weighted Magnetic resonance imaging of brain clinches the diagnosis. Here we report two siblings, who presented to us with different spectrum of clinical features.

KEY WORDS: Leigh syndrome, clinical Features, Lactate, MRI Brain.

BACKGROUND

Leigh syndrome is a rare inherited neurometabolic disorder named after Archibald Denis Leigh (1915-1998), a British neuropsychiatrist who first described the condition in 1951.[1] Most cases of Leigh's disease become apparent during infancy with feeding and swallowing problems, vomiting, failure to thrive, delayed motor mile stones, seizures, hypotonia,

pyramidal or extrapyramidal signs.[2]Death usually occurs within a few years after onset of symptoms, typically from progressive respiratory failure.[3,4]The pattern of inheritance may be Autosomal / X-linked recessive or mitochondrial or sporadic. The underlying defect can be at any of the sites in the enzyme pathway for respiratory metabolism. Regardless of the genetic basis, it results in an inability of the complexes to perform their role in oxidative phosphorylation. The resultant chronic lack of energy leads to cell death, affecting central nervous system and inhibiting motor functions. In case of Leigh disease, crucial cells in the brainstem and basal ganglia are affected. The characteristic MRI findings help to clinch the diagnosis. Here we report two siblings, who presented to us with different spectrum of clinical features.

CASE 1: A 9month old female child born to a non-consanguineous couple presented with complaints of 2 episodes of generalized tonic clonic seizures in the last 1 month, following which mother noticed that the child was unable to hold neck, or roll over, or sit with support. She also gave history suggestive of recurrent apneic attacks since the last 3 months. No history of fever/ altered sensorium at any point of time. Prior to this the child was otherwise normal.

The child was delivered by NVD, birth weight- 3kg. Antenatal/perinatal/postnatal history was uneventful. No h/o abortions/stillbirths/IUD.

This child has two elder siblings. First sibling is normal female child. Second child is a male, with history of global developmental delay and swallowing difficulty.

On examination child was alert and conscious, had microcephaly (HC-40cm) with FTT (Wt-5.4kg). She recognized her mother and had social smile. On physical examination, she was noted to have generalized hypotonia, sluggish deep tendon reflexes and extensor plantar.

Case 2: Her elder brother, now 4.5years, was born by vaginal delivery with no significant antenatal history, weighing 3.5 kg at birth with normal Apgar scores. Mother noticed problem while swallowing milk from the 3 months of age, delayed developmental milestones, and apnea infrequently. On examination he had microcephaly (HC = 46cm), weight and height for age was<3rd centile; sits without support; hypotonia of all four limbs with extensor plantar. Laboratory investigations of these two siblings (Table 1) and MRI Brain reports are shown in fig.1 & fig.2 .The radiological findings on MRI established the clinical diagnosis of a neurodegenerative disease as Leighs syndrome.

Table 1-Routine laboratory investigations of two siblings

S.No	Investigations	Case I	Case II
1	Hb	12gm/dl	8gm/dl
2.	WBC Count	9900 cells/cu.mm	9500 cells/cu.mm
3.	Platelets	3.5 lakhs/cu.mm	5.5 lakhs/cu.mm
4.	Random Blood Sugar	72mg/dl	84 mg/dl
5.	ABG	Compensated Metabolic Acidosis	Compensated Metabolic Acidosis
6.	Serum Lactate	6.2 mmol/L	5.2mmol/L
7.	2D ECHO	Normal Study	Normal Study
8.	EEG	Normal Study	Normal Study
9.	LFT and RFT	Normal	Normal

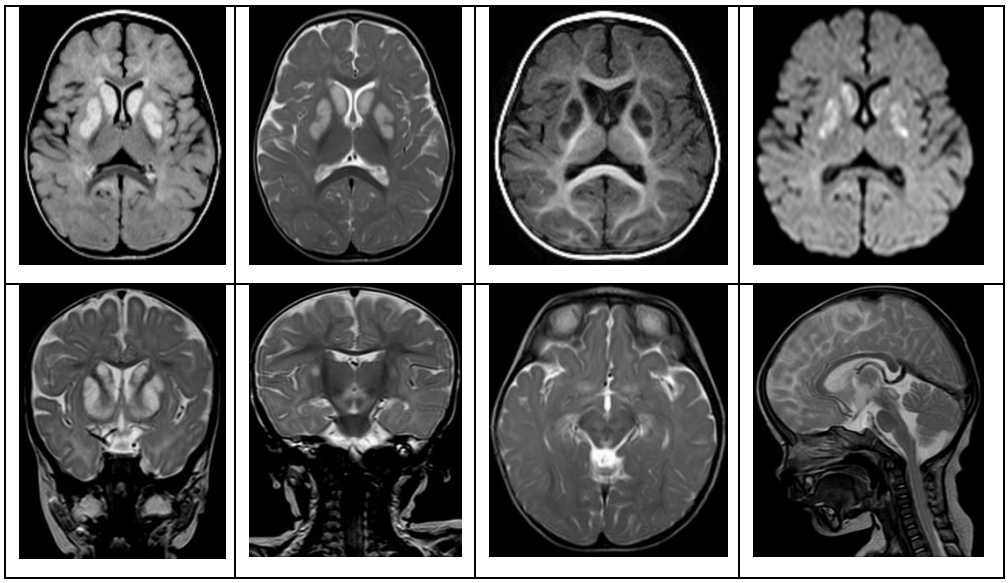

Figure.1: MRI Brain showing bilateral hyper intense lesions of basal ganglia, thalamus and midbrain in T2W & diffusion weighted images in case 1

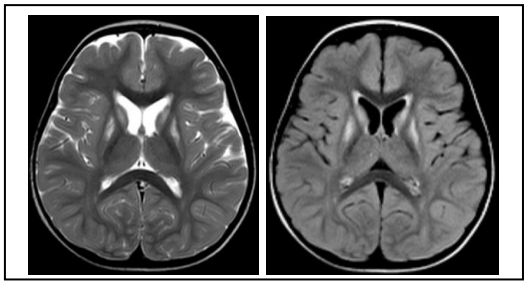

Figure. 2: MRI Brain showing bilateral hyper intense lesions of basal ganglia,T2W & flair in case 2.

DISCUSSION

Leigh disease, also known as sub acute necrotizing encephalomyelopathy **(**SNEM**),** is a progressive neurodegenerative disorder.

The estimated prevalence of Leigh Syndrome was 2.05 cases per 1,00,000. [5]The preschool incidence of Leigh syndrome was 1 in 32, 000.[6] This progressive disorder begins in infants between the ages of three months and two years.

The clinical presentation of Leigh syndrome is highly variable. The earliest signs may be poor sucking ability, and the loss of head control and motor skills.[7]Our two cases presented classically with regression of milestones in first case and swallowing problems and developmental delay in second case, although he was misdiagnosed as a case of cerebral palsy previously because of developmental delay and microcephaly. Both the cases had history of apnea starting from 3-6months of age with more frequent episodes in 1st case which could be due to significant brainstem involvement.[8]

Stringent diagnostic criteria for Leigh syndrome were defined by Rahman et al [1996]: (1)Progressive neurologic disease with motor and intellectual developmental delay(2)Signs and symptoms of brain stem and/or basal ganglia disease(3)Raised lactate concentration in blood and/or cerebrospinal fluid (CSF);(4) One or more of the following features: Characteristic features of Leigh syndrome on neuroimaging (OR) Typical neuropathologic changes: multiple focal symmetric necrotic lesions in the basal ganglia, thalamus, brain stem, dentate nuclei, and optic nerves. (OR)Typical neuropathology in a similarly affected sibling.[9,10]

Neuroimaging[10,11] plays an important role in diagnosis of patients with Leigh syndrome. The most characteristic neuroradiological findings are bilateral, symmetric focal hyperintensities in the basal ganglia, thalamus, substantia nigra, and brainstem nuclei at various levels on T2-weighted MRI. In the basal ganglia, the putamen is particularly involved.[12] In 2005, Hombal and Narvekar[13] reported Leigh syndrome in a 3-year-old child with regression of milestones and involuntary movements diagnosed based on neuroimaging.

In 2010, Dhananjay Y Shrikhande**,** PiyushKalakoti[14] reported a7 months old child with status epilepticus, delayed developmental milestones and regression of achieved milestones, diagnosed on MRI as Leigh syndrome.

In both of our cases, clinical presentation is variable but the imaging findings suggested a progressive neurodegenerative disorder with the possibility of a mitochondrial encephalopathy. This is consistent with the neuro-radiological findings in previous reports of Leigh Syndrome.

Conditions that can appear similar to Leigh's disease include perinatal asphyxia, kernicterus, thiamine deficiency, Wilson's disease, biotin-responsive basal ganglia disease, and some forms of encephalitis. Perinatal asphyxia can cause bilateral ganglia lesions and damage to the thalamus, which are similar to the signs seen with Leigh syndrome.

When hyperbilirubinemia is not treated with phototherapy, the bilirubin can accumulate in the basal ganglia and cause lesions similar to those seen in Leigh syndrome. This is not common since the advent of phototherapy.[15]

There is currently no effective treatment. A high-fat, low-carbohydrate diet may be followed if a gene on the X chromosome is implicated in an individual. Thiamine (vitamin B_1) may be given if a deficiency of pyruvate dehydrogenase is known or suspected. The symptoms of lactic acidosis are treated by supplementing the diet with sodium bicarbonate or sodium citrate; Dichloroacetate may also be effective in treating Leigh syndrome-associated lactic acidosis; research is ongoing on this substance.[7]Coenzyme Q10 supplements have been seen to improve symptoms in some cases.[16]

We discharged the two siblings with co enzyme Q, B-Complex vitamins, sodium bicarbonate tablets and phenytoin syrup for first case. They came for follow up after a month, with not much improvement.

CONCLUSION

Leighs disease is a rare disease which mimics various disorders. It requires high degree of suspicion and correlation of clinical, laboratory and neuroimaging features to bring about a diagnosis.

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REFERENCES

1. Psychiatric Bulletin 22(10): 648. 1998. doi:10.1192/pb.22.10.648. Retrieved 16, October 2013.
2. Richard EBehrman, Robert MKliegman, Hal BJenson, et al: Nelson’s Text Book of Pediatrics 17th Edition. Saunders Ltd, Pennsylvania: 2004; 2027.

3. Barkovich AJ: Toxic and metabolic brain disorders. In:Pediatric Neuroimaging. New York: Raven Press 1995; 55-106.
4. Geyer CA, Sartor KJ, Prensky AJ, et al: Leigh disease (subacute necrotizing encephalomyelopathy): CT and MR in five cases. J Comput Assist Tomogr 1988; 12: 40-44.
5. Castro-Gago M, Blanco-Barca MO, Campos-Gonzalez Y, Arenas-Barbero J, Pintos-Martinez E, Eiris-Punal J: (Epidemiology of pediatric mitochondrial respiratory chain disorders in northwest Spain). Pediatr Neurol 2006; 34(3): 204-11.
6. Darin N, Oldfors A, Moslemi AR, Holme E, Tulinius M: The incidence of mitochondrial encephalomyopathies in childhood: clinical features and morphological, biochemical, and DNA anbormalities. Ann Neurol 2001; 49(3): 377-83.
7. "NINDS Leigh's Disease Information Page". National Institute of Neurological Diseases and Stroke. www.ninds.nih.gov/disorders/leighsdisease/leighsdisease.htm. NIH. 16 December 2011. Retrieved 25 November 2013.
8. Teofilo L. Lee- Chiong Sleep: A Comprehensive Handbook. Copyright ©, John Wiley& Sons, Inc. Chapter: 2006; 66: 518.
9. David R Thorburn, PhD and Shamima Rahman, FRCP, FRCPCH, PhD. (Mitochondrial DNA-Associated Leigh Syndrome and NARP), October 30, 2003; Last Update: April 17, 2014.
10. Rahman S, Blok RB, Dahl HH, et al: (Leigh syndrome: clinical features and biochemical and DNA abnormalities). Ann Neurol 1996; 39(3): 343-51.
11. Bhavsar VM, Kumta NB. (Leigh's subacute necrotizing encephalomyelopathy: possible diagnosis by C.T. scan.) Indian J Pediatr. 1991; 58(3): 375-7.
12. Ghosh D, Pradhan S. (Ante mortem diagnosis of Leigh's disease. Role of magnetic resonance study.) Indian J Pediatr. 1996; 63: 683-691.
13. AG Hombal, VN Narvekar: (Leigh's Disease (Subacute Necrotising Encephalomyelopathy) - A Case Report.) Ind J Radiol Imag 2005; 15(2): 217-219.
14. Dhananjay Y Shrikhande, Piyush Kalakoti, (A rare mitochondrial disorder: Leigh syndrome - a case report) Italian Journal of Pediatrics 2010; 36:62 doi:10.1186/1824-7288-36-62.
15. Baertling F, Rodenburg RJ, Schaper J et al. (A guide to diagnosis and treatment of Leigh syndrome). J. Neurol. Neurosurg. Psychiatr. June 2013; 85: 257–265.
16. Leigh Syndrome. Online Mendelian Inheritance in Man. McKusick-Nathans Institute of Genetic Medicine. 13 March 2013. Retrieved 25 November 2013.