ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 11 | November - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL AND NEUROIMAGING CORRELATES OF LEIGH SYNDROME , A CASE SERIES AND REVIEW OF LITERATURE

Paediatrics

Dr.Dadireddy Leela Prasanna* Pediatric Junior Resident, Narayana Medical College And Hospital, Nellore-524003. Andhra Pradesh. *Corresponding Author

Dr. Vaka Haripriyanka Pediatric Junior Resident, Narayana Medical College and Hospital, Nellore- 524003. Andhra Pradesh.

ABSTRACT

Leigh syndrome, also referred to as Sub acute necrotising encephalopathy usually presents with symptoms like developmental delay, regression of neurological skills and sudden death. Approximately 25% of the patients are abnormal at birth with features like hypotonia, lactic acidosis, feeding problems, hypoglycemia, hyperbilirubinemia, cardiac complications, seizures and/or hyperammonemia. Here, we present 6 cases of Leigh's disease , who presented within 6 months of life with neurological regression and hypotonia as the predominent manifestations with MRI findings showing Bilateral symmetrical hyperintensities in T2 weighted images which are characteristic findings in Leigh's disease.

KEYWORDS

Leigh syndrome, neurodegenerative disease , subacute necrotising encephalopathy, mitochondrial dysfunction.

INTRODUCTION:

Leigh syndrome (LS), also referred to as subacute necrotising encephalopathy, was first described by the British psychiatrist and neuropathologist Denis Archibald Leigh in 1951.

On the basis of the definition used by the Online Mendelian Inheritance in Man Database (OMIM 256000) which defines Leigh syndrome as (1) neurodegenerative disease with variable symptoms due to (2) mitochondrial dysfunction caused by a hereditary genetic defect accompanied by (3) bilateral CNS lesions that can be associated with further abnormalities in diagnostic imaging.

The term "Leigh-like syndrome" is used when the above criteria are only partly met or when patients present with atypical symptoms, laboratory findings or radiologic features. But the overall clinical picture suggestive of Leigh syndrome . The term "genetically confirmed Leigh syndrome" refers to cases of Leigh syndrome for which a genetic etiology has been identified (accounts 50% of all Leigh syndrome patients). Few reports of cases detailing imaging findings in children with genetically confirmed Leigh syndrome do exist. Here we review the clinical features and imaging studies of Leigh syndrome and describe the neuroimaging findings and clinical presentation of 6 children.

CASE SERIES:

The original case described by Denis Archibald Leigh in 1951 ,was a case of a 7-month-old boy, who presented with progressive neurological symptoms with developmental regression, somnolence, bulbar palsy and spasticity of the limbs. The child was born at term and appeared completely normal until 6 weeks before admission. The disease onset was probably triggered by an infection. Postmortem investigations revealed focal, bilateral symmetrical subacute necrotic lesions, extending from the thalamus to the pons, the inferior olives and the posterior columns of the spinal cord.

Prior to the availability of MRI , diagnosis was made exclusively on postmortem pathological examination. The ready availability of MRI in the 1980s enabled a diagnosis of Leigh syndrome to be made premortem by combined imaging and clinical findings.

Leigh syndrome has its onset typically lies within the first year(s) of life and is often followed by rapid deterioration.

Most children show normal prenatal growth and are term at birth.

Presenting symptoms of Leigh syndrome include developmental delays, regression of neurological skills and sudden death as mentioned earlier .The remaining patients present as an acute episode which is often triggered by metabolic challenges secondary to acute infection. During recurrent episodes, patients develop hypotonia , breathing irregularities, ptosis, ataxia, nystagmus, seizures, spasticity/ dystonia, dysphagia, or psychomotor retardation. Symptoms can persist but often improve following the acute episode. Extra-central nervous system findings in Leigh syndrome include polyneuropathy, myopathy, diabetes mellitus, short stature, hypertrichosis, cardiomyopathy, anemia, sleep disturbances, renal failure, gastrointestinal dysfunction, hearing loss, failure to thrive, retinitis pigmentosa, cranial nerve palsies and scoliosis. The outcome of Leigh syndrome remains poor, with the majority of affected individuals dying before 3 years of age from sudden respiratory failure .

Of our 6 cases ,3 were boys and 3 were girls . The age at presentation was less than 6 months in all the 6 cases. All are delivered at term . Presenting symptoms in order of frequency was seizures ,altered sensorium, neuro regression, hypotonia, decreased acceptance of feeds, irritability, lethargy and visual impairment.

The clinical manifestations in our patient population are similar to those described previously in the literature, with neurological regression and hypotonia as the most common manifestations.

Neuroimaging was done which showed:

Bilateral, symmetrical hyperintensities in T2-weighted images as a characteristic finding in LS . These lesions are commonly found in the basal ganglia, especially in the putamen, or in variable areas within the brain stem such as the substantia nigra, the nucleus rubra and the medulla oblongata.

As MRI has become clinically available, imaging characteristics of Leigh syndrome have been reported; however . Here we review the imaging studies of our 6 patients. One Child showed B/L symmetrical hyperintense foci showing diffusion restrictions in B/L putamen. Basal ganglia lesions were found in 3 children , with compromise of the caudate nuclei and lentiform nuclei in 2 children.

Follow up MRI was done in 3 of 6 patients. The extent of the lesions progressed over time in 2 children. One had resolution of the lesions in restricted diffusion imaging and decreased size of the lesions .

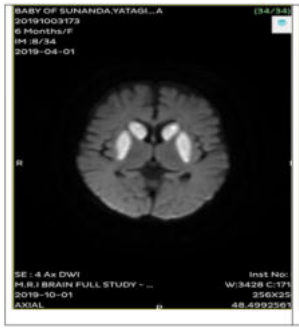

Fig 1

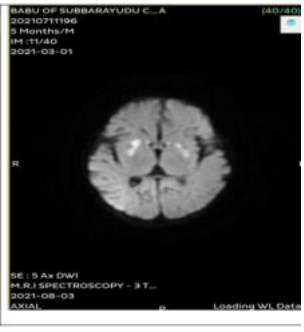

Fig 2

Fig 1 : Axial Diffusion Weighted Image showing areas of restriction in Bilateral Caudate nucleus and Lentiform nucleus .

Fig 2: Axial Diffusion Weighted Image showing patchy areas of diffusion restriction in Bilateral putamen .

Laboratory features:
Arterial blood gas analysis showed metabolic acidosis with elevated lactate levels and ammonia levels in all 6 children. Hypercarbia is seen in 2 children. CSF analysis done in all cases showed elevation of pyruvate and lactate levels. Other metabolic parameters were normal. Complete blood picture showed anemia in 4 children

Treatment:
Specific treatment for Leigh syndrome is not available and therapeutic options are limited. But a range of vitamins, including riboflavin, thiamine and coenzyme Q10 are given to improve mitochondrial function. Symptomatic treatment is usually given to improve the ATP production and to lower the lactate levels. Ketogenic diet is found to improve the clinical features. Antiseizure medication is suggested for seizure control . Phenobarbitone and valproic acid should be avoided because of their inhibitory effect on mitochondrial respiratory chain. The above cases responded to thiamine, riboflavin, Coenzyme Q10, supportive treatment and symptomatic treatment for seizures.

DISCUSSION:
The diagnosis of Leigh's disease should be considered in appropriate clinical and laboratory settings whenever symmetrical hypodensities are encountered in the putamen and midbrain on CT which should be further confirmed with MRI. Our experience suggest that any bilateral symmetric T2 hyperintensities involving multiple brainstem nuclei/ structures associated with basal ganglia abnormalities in a child with neurological problems should prompt the clinician to consider Leigh syndrome and conduct further investigations such as measurement of blood and/or CSF lactate, and respiratory chain enzymes activities. Neuro-radiological discriminative observation is very useful in guiding the clinicians for the most appropriate enzymatic and genetic study in these patients. Though mitochondrial diseases cannot be cured completely, efforts for prevention and prenatal diagnosis are still in the nascent stage. With appropriate investigations, accurate diagnosis and prompt institution of adequate supportive therapy, symptomatic amelioration can be achieved . Finding an underlying genetic cause in LS patients can be challenging. However, it can be facilitated if clinical and biochemical evidence is carefully evaluated.

REFERENCES:
1. Richard EBehrman, Robert MKliegman, Hal BJenson, et al: Nelson's Text Book of Pediatrics 17thEdition. Saunders Ltd, Pennsylvania 2004, p2027
2. Mannan AASR, Sharma MC, Shrivastava P, Ralte AM, Gupta V, Behari M, Sarkar Chitra: Leigh's syndrome-Clinical Brief. Indian J Pediatr 2004, 71(11):1029-1033
3. 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
4. A rare mitochondrial disorder: Leigh syndrome a case report by etl.Dhananjay Y Shrikhande1, Piyush Kalakoti2*, MM Aarif Syed2, Kunal Ahya2, Gurmeet Singh.