Abstract
Leigh Syndrome (LS) is a subacute necrotizing encephalomyelopathy characterized by bilateral symmetrical necrotic lesions of gray matter nuclei in the basal ganglia, diencephalon, cerebellum or brainstem. The onset is usually in early infancy and patients manifest a heterogeneous set of symptoms, such as regression or psychomotor delay, weakness, hypotonia, truncal ataxia, intention tremor associated with lactic acidosis in the blood, cerebrospinal fluid or urine. The diagnosis of Leigh’s disease should be considered in appropriate clinical and laboratory settings whenever symmetrical hypodensities are encountered in the putamina and midbrain on CT and further investigated with MRI. Neuroradiological examinations, when performed, showed lesions in brainstem and basal ganglia in LS and dystonia patients. A positive result at MRI investigation could address the diagnosis of dystonia or LS although exceptions to this correlation have been reported.

Key words: Leigh’s Syndrome, MRI investigation, coenzyme Q10.
INTRODUCTION

Leigh Syndrome (LS) is a sub acute necrotizing encephalomyelopathy characterized by bilateral symmetrical necrotic lesions of gray matter nuclei in the basal ganglia, diencephalon, cerebellum or brainstem. The onset is usually in early infancy and patients manifest a heterogeneous set of symptoms, such as regression or psychomotor delay, weakness, hypotonia, truncal ataxia, intention tremor associated with lactic acidosis in the blood, cerebrospinal fluid or urine. It is the most frequent cause of inherited Mitochondrial disorder in infancy (1:40,000) [1]. LS inheritance is complex since patients may present mutations in mitochondrial DNA (mtDNA) or in nuclear genes, which predominantly encode for proteins involved in respiratory chain structure and assembly or in coenzyme Q10 biogenesis [2]. Among maternally inherited forms, most of the mutations lay within genes encoding Complex I (ND1-6) and V (ATP6, ATP8) mitochondrial subunits [3]. However the genetic cause of a number of cases of Leigh syndrome remains unknown, despite the presence of a specific biochemical defect in many of them. Despite its considerable clinical, genetic and biochemistry heterogeneity, the basic neuropathological features in children affected are almost identical; which are focal, bilateral, and symmetric necrotic lesions associated with demyelination, vascular proliferation and gliosis in the brainstem, diencephalon, basal ganglia, and cerebellum [4]. It is possible to come to a diagnosis of probable SNE during life on the basis of clinical signs and symptoms, mode of inheritance, metabolic abnormalities, and neuroimaging findings [5,6]. We report a rare case which presented clinically as a neurodegenerative disorder and diagnosed as Leigh syndrome on MRI.

CASE PRESENTATION

A 8 months old male child admitted in Pediatrics department brought by mother as reliable information with chief complaints of developing of both eye lids since 8 days.

Past history: Child was apparently asymptomatic 10 days back, had a history of vomiting for 3 days, multiple episodes/day, vomits milk, non projectile, non bilious, no blood in vomit and on further questioning to mother it was revealed that the child has loss of neck holding and dull activity positive.

General examination: Child was dull, afebrile, pulse rate: 108 bpm, respiratory rate: 20 bpm, CFT < 3 seconds, Heart, Lungs were clear, par abdomen: soft, Liver 2cm decreased RCM, CNS:AF, Tone normal in all limbs, 180° Flip test - Normal.

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Power                Right         Left

UL          3/5             3/5
LL          3/5             3/5

DTR’S B -   ++            ++
   T -    +             +
   K -    +++           +++
   A -    ++            ++

Planters -   ↑             ↑
B/L Pupils - NSRL.

Laboratory investigations
Serum electrolytes, complete blood count: RBC, Hemoglobin were found to be normal, WBC - 13,000; differential count: Neutrophils - 30 (40-75%), Lymphocytes - 65(20-45%), were found to be abnormal, Eosinophils, Monocytes, Basophils were found be normal. Peripheral blood smear revealed an impression of RBC: Normocytic & Hypochromic. WBC- Leucocytosis. Platelets – Thrombocytosis and count was found to be normal.

Differential diagnosis
CT scan brain plain done which show an impression of bilateral basal ganglia hypo-density, inborn errors of metabolism-Leigh, hallervorden-spatz syndrome. Magnetic resonance imaging was performed and which finally revealed an impression of Symmetrical T₂/ Flair hyper intensity with diffusion restriction in bilateral caudate and lenti form nucleus medial peri ventricular thalami and periadeductal white matter. s/o Leigths disease. Based on the above complaints and laboratory investigations the condition was finally confirmed as LEIGH’S disease.

Treatment
Initially symptomatic treatment was given, which was followed by Tab.Thiamine (vitamin B₁) - 75mg/PO/OD, Cap.Coenzyme Q 10 - 30mg/PO/TID, Inj.Optineuron - 3ml/IV/OD × 3days with oral feeds which was continued for 15 days and patient was discharged with the same medications.
Figure 1 & 2 Denotes Symmetrical T₂/ Flair hyper intensity with diffusion restriction in bilateral caudate and lenti form nucleus medial peri ventricular thalami and periadeductal white matter.

DISCUSSION

Leigh’s disease or SNE is a rare progressive neurological disorder of the childhood. Age of onset of symptoms is usually less than 2 years (infantile form), but others may present in childhood (juvenile form) and unusually in adulthood. It presents early in life with psychomotor regression, abnormal muscle tone, weakness, dystonia, brainstem and cerebellar dysfunction (ataxia), visual loss, missed milestones or regression of the achieved milestones, tachypnea, and seizures [7-9]. Neuroimaging plays an important role in diagnosis of patients with Leigh syndrome. These high T2 signals on MRI reflect the spongiform changes and vacuolation in the affected brain structures. Specific therapy for mitochondrial disorders in children is not available. The results and prognosis are variable. A high-fat, low-carbohydrate diet may be followed if a gene on the X chromosome is implicated. Thiamine (vitamin B₁) may be given if a deficiency of pyruvate dehydrogenase is known or suspected [10-12]. Marked improvement was observed with riboflavin, which nearly normalized the adenosine triphosphate production. Rapid clinical and biochemical improvement was observed in patients with acute central respiratory failure with the use of intravenous soya bean oil (Ketogenic emulsion). Ketogenic diet has been found to improve the outcome in those with a deficiency of pyruvate dehydrogenase. The use of coenzyme Q10, thiamine, and carnitine may cause a decrease in severity of symptoms in a few cases.
CONCLUSION

The diagnosis of Leigh’s disease should be considered in appropriate clinical and laboratory settings whenever symmetrical hypodensities are encountered in the putamina and midbrain on CT and further investigated with MRI. Neuroradiological examinations, when performed, showed lesions in brainstem and basal ganglia in LS and dystonia patients. A positive result at MRI investigation could address the diagnosis of dystonia or LS although exceptions to this correlation have been reported. With appropriate investigations, accurate diagnosis and prompt institution of adequate supportive therapy, symptomatic amelioration can be achieved, thereby adding life to the limited years of survival of these children. Further research aimed at prenatal identification of the responsible mutations and prevention of the disease is warranted.

REFERENCES


