IMAGING OF JUVENILE ONSET LEIGH SYNDROME: A CASE REPORT AND SHORT REVIEW OF LITERATURE

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Abstract
Leigh's disease is a rare entity affecting the central nervous system generally of infants, incidence being 1 in 40,000. Rarely, it occurs in teenagers and adults. The diagnosis is difficult and still continues to challenge the clinicians on the basis of history; hence the role of imaging is very crucial. The neuropathy encountered in the disease is commonly associated with features of demyelination, presenting rarely in acute form. A case of Juvenile Leigh Disease is reported here presenting with an acute polyneuropathy. Neuroimaging confirmed it to be a case of Leigh disease.
Keywords: Basal ganglia, CT, Encephalopathy, Juvenile, Leigh, Putamina, MRI

1. Introduction

Leigh's disease is a rare inherited progressive neurometabolic disorder first described by Leighs in 1951[1] affecting CNS generally of infants between the ages of three months and two years. Prevalence of the syndrome was 2.05/1,00,000 with incidence of 1/40,000.[2,3]

In India, Bhavsar, Kumta[4] on CT and later in 1996 Ghosh and Pradhan[5] on MRI diagnosed Leigh Syndrome suspected clinically. So neuroimaging is of immense help to the clinicians in the diagnosis. Most common neuropathy is chronic neuropathy with features of demyelination, which can be the presenting manifestation. On rare occasions, the neuropathy encountered can represent a more acute process.[6]

2. Case Report

A thirteen years old male presented with history of fever and generalised colonic tonic seizures 2 months back and on presentation again since 10 days. At admission, he was uncooperative and disoriented.Later the fever settled down with gradually progressive spastic paraparesis, associated dysphagia, nasal regurgitation and abnormalities of the psychomotor skills.

Clinical examination revealed horizontal nystagmus, absent gag reflex , intermittent myoclonus but no cerebellar signs.CNS examination showed spastic lower limbs with power of 1/5 in lower limbs and 3/5 in upper limbs, all reflexes exaggerated and bilateral extensor plantars .Laboratory examination shows microcytic anaemia and metabolic acidosis.

The patient underwent Computed Tomography in the department and Axial CECT showed bilaterally symmetrical non enhancing hypodensities in Substantia nigra, basal ganglia & thalami. To confirm the findings MRI was done and on Axial T1weighted MR image bilaterally symmetrical hypo intense lesions in basal ganglia & thalami were observed .Axial T2 weighted & FLAIR MR images at same level showed the bilaterally symmetrical hyperintense lesions in same region along with bilateral symmetrical involvement of central tegmental tracts, Peri-aqueductal grey matter, Substantia nigra & dorsal midbrain was also noticed.

Hence, based on the clinical history and imaging findings diagnosis of Leigh disease was made.

3. Discussion

Leigh syndrome is the most common clinical phenotype of mitochondrial disorders in childhood. Despite its considerable clinical, genetic and biochemistry heterogeneity, the basic neuropathological features in children affected by Leigh syndrome 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.

The diagnostic criteria are (1) progressive neurological disease with motor and intellectual developmental delay;(2) signs and symptoms of brainstem and/or basal ganglia disease; (3) raised lactate levels in blood and/or cerebrospinal fluid (CSF); and (4) characteristic

symmetric necrotic lesions in the basal ganglia and/or brainstem.[3]

There are at least four genetically determined causes of Leigh Syndrome .[7]: Pyruvate dehydrogenase complex deficiency, complex I deficiency, complex IV deficiency (COX), and complex V (ATPase deficiency). These enzymes, when defective, are known to disturb oxidative phosphorylation and lead to failure of organs with high oxidative metabolic demand such as neuro-muscular system. All the five complexes except complex II are heterogeneous in their origin i.e. components of all the four complexes are encoded by both nuclear and mitochondrial genomes.

Neuroimaging [5,7] plays an important role in diagnosis as well as follow up of patients with Leigh Syndrome. Putaminal involvement has been reported to be the constant feature, and several reports have supported this statement.[8] CT scans may reveal bilateral symmetric areas of low attenuation involving the basal ganglia(Figure-1).

On MR imaging, signal changes characterized by low signal on T1 weighted images and high signal on T2 weighted images, have been most commonly reported in the putamen, basal ganglia, thalamus,periaqueductal grey matter and brainstem (Figure-2,3). Cortical and cerebellar involvement might also accompany the basal ganglia and brain stem lesions. Involvement of cerebral white matter has only been reported in a few cases.

On Diffusion Weighted sequence the affected regions show restriction of diffusion in the acute phase. MR spectroscopy of the basal ganglia typically demonstrates high lactate levels, decrease in NAA/creatine levels and elevation of choline/creatine ratio. These metabolites are useful indicators of prognosis and response to therapy.[9]

Bilateral symmetric T2 prolongation involving multiple brainstem nuclei/structures associated with basal ganglia abnormalities in a child with neurological problems should prompt the clinician to consider Leigh syndrome.Mitochondrial disease cannot be cured completely. Efforts for prevention and prenatal diagnosis are still in the nascent stage.

Hence, neuroradiological discriminative observation is very useful in guiding the clinicians for the most appropriate enzymatic and genetic study in their patients.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.

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Figure-1.Axial CECT showing bilaterally symmetrical non enhancing hypodensities in basal ganglia & thalami.

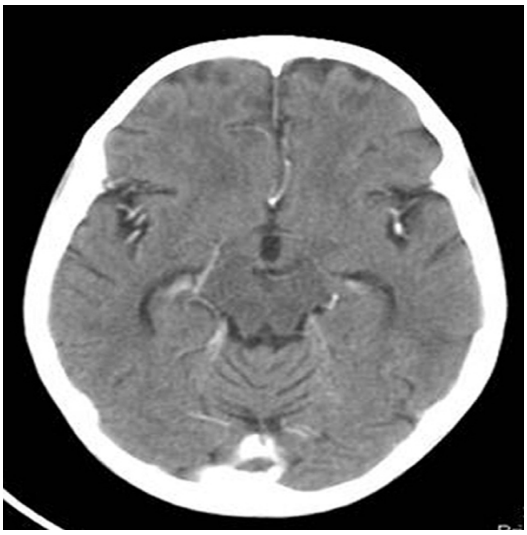

Figure-2.Axial T2 weighted MR image showing bilaterally symmetrical hyperintense lesions in basal ganglia & thalami.

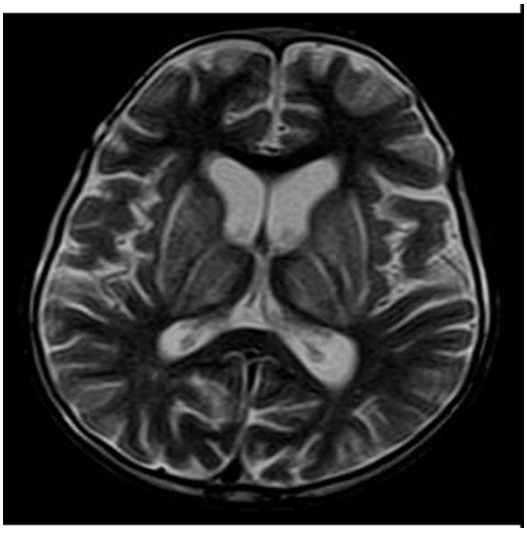

Figure-3.Axial T2 weighted MR image showing bilateral symmetrical involvement of substantia nigra & dorsal midbrain.