Int J Biol Med Res.2015;6(1):4790-4792

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

A Two Case Series of Different Disorders Causing Leigh Syndrome

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ARTICLE INFO

Keywords:

Leigh's syndrome
mitochondrial
lactate peak
cavitation
succinate peak.

ABSTRACT

Aim and Objective: To study the neuroimaging findings of Leigh syndrome with complex I and II deficiency in infants. Materials & Methods: We present two cases; children aged 3 years and 15 months. Patients underwent MRI brain scans after taking proper consent. Result: First patient showed imaging features of less common complex I deficiency with extensive white matter hyperintensities with areas of cavitation and high lipid and lactate peaks on MRS in 3 year old male, with complaints of developmental delay , fever and dystonia. Second patient showed imaging findings of a rarer complex II deficiency due to succinate dehydrogenase deficiency with diffuse periventricular & deep cerebral white matter, callosal and thalami T2 hyperintensities with decreased ADC values, sparing of basal ganglia and characteristic succinate peak along with inverted lactate peak on MRS in a 15 month old child, with complaints of developmental delay and ataxia.

Introduction

Leigh syndrome is a symptom complex with characteristic, but variable, clinical and pathological manifestations. Affected infants and children typically present toward the end of first year of life with hypotonia and psychomotor deterioration. Ataxia, ophthalmoplegia, ptosis, dystonia, and swallowing difficulties almost inevitably ensue.

The disorder seems to be the result of defective terminal oxidative metabolism from any of a number of causes that are likely to impair energy production.

Many disorders can result in Leigh syndrome, indeed, mutations of both mitochondrial and nuclear DNA, involving genes coding for proteins in respiratory chain complexes I, II, III, IV &V, mitochondrial tRNA, pyruvate dehydrogenase complex, and coenzyme Q10 have been shown to cause Leigh syndrome.

Four groups generally account for a large majority of cases these include, Leigh to pyruvate dehydrogenase deficiency, Complex IV, V and I respectively.

Results

Case 1:

Clinical details: A 3 year old male child born to non-consanguineous married couple. Baby cried at birth. He now presents with developmental delay, fever and dystonia

Imaging: MRI brain plain was done and showed findings of T1 hypointense and T2 & FLAIR symmetrical confluent hyperintensities with interspersed areas of FLAIR hypointensities (indicative of complete cavitation) in the periventricular, fronto-temporo-parietal white matter and corpus callosum.The hyperintensities in the white matter are seen to reach upto the cortex.

On Diffusion Weighted Imaging, there is seen peripheral restriction along the confluent areas.

Mild vermian atrophy and giant cisterna magna is seen.

On MR spectroscopy in the frontal white matter, markedly elevated lipid and lactate peak and reduced NAA peak is seen.

Based on the imaging findings we conclude that it's a mitochondrial disorder with features of Leigh syndrome due to Complex I deficiency.

Fig1) T1 sagittal images shows hypointense cavitatory areas in the fronto-parietal white matter and corpus callosum (arrows)

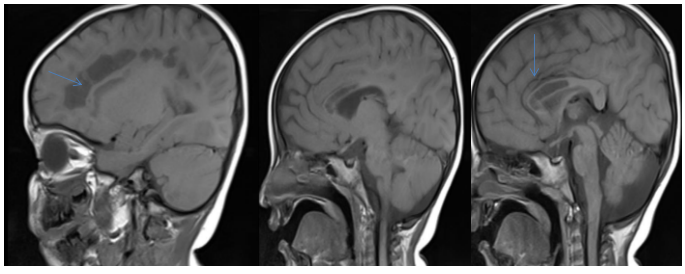

Fig2) T2 axial images shows hyperintense areas in the fronto-parietal white matter and corpus callosum

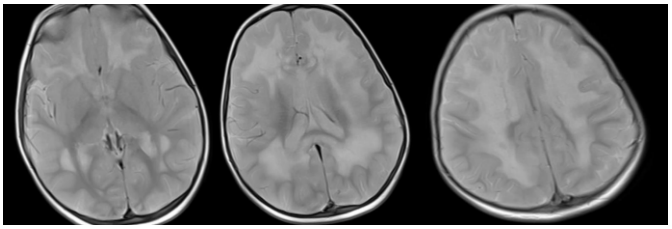

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Fig 3) T2 coronal images show hyperintense areas with interspersed cavities (arrows) in the fronto-parietal white matter and corpus callosum

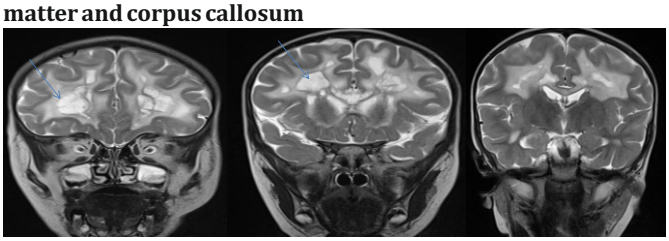


Fig 4) FLAIR sagittal and axial images show hypointense areas with interspersed cavities in the fronto-parietal white matter and corpus callosum (arrows)

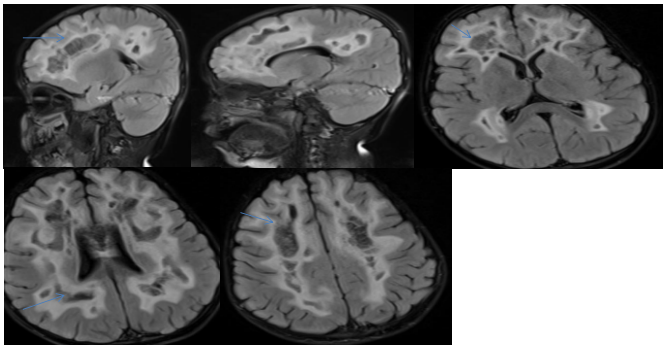


Fig 5) DWI axial images show hyperintense areas of restricted diffusion with interspersed cavities in the fronto-parietal white matter and corpus callosum

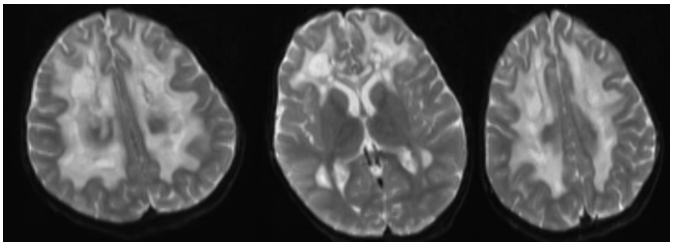
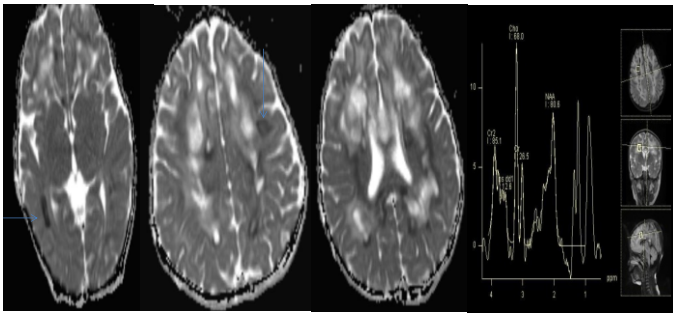


Fig 6) ADC axial images show peripheral hypointense areas (arrows) with interspersed cavities in the fronto-parietal white matter and corpus callosum.

MR spectroscopy in the frontal white matter, markedly elevated lipid and lactate peak and reduced NAA peak is seen.



CASE 2:

CLINICAL DETAILS:A 15 month old male child born to non-consanguineous married couple with an uneventful perinatal history. He now presents with developmental delay and hypotonia.

IMAGING:

MRI brain plain was done and showed findings of T2 & FLAIR weighted images show extensive T2 hyperintensity in the corpus callosum, periventricular and deep cerebral white matter.

Axial ADC images shows reduced ADC values in the corpus callosum and corticospinal tracts but increased diffusivity (hyperintensity) in the deep cerebral white matter.

MR spectroscopy in the frontal white matter shows a large singlet at 2.4 ppm representing Succinate (Su) along with inverted lactate peak.

Based on the imaging findings we conclude that it's a mitochondrial disorder with features of Leigh syndrome due to Complex II deficiency.

Fig 1) T2 axial and coronal images show confluent hyperintense areas in the fronto-parietal white matter and corpus callosum (arrows)

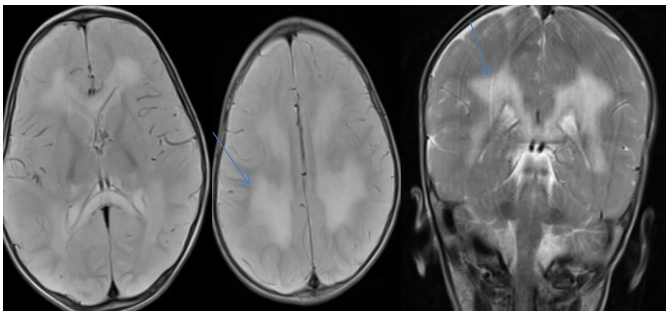


Fig 2) FLAIR axial images show confluent symmetrical hyperintense areas in the fronto-parietal white matter and corpus callosum (arrows)

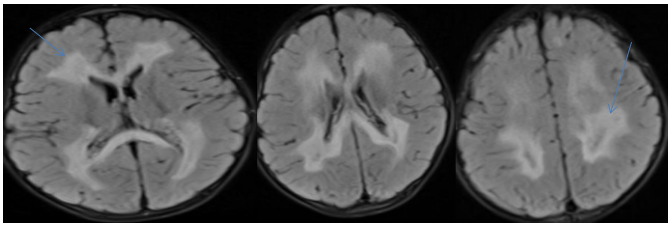


Fig 3) DWI axial images show confluent symmetrical hyperintense areas in the fronto-parietal white matter and corpus callosum

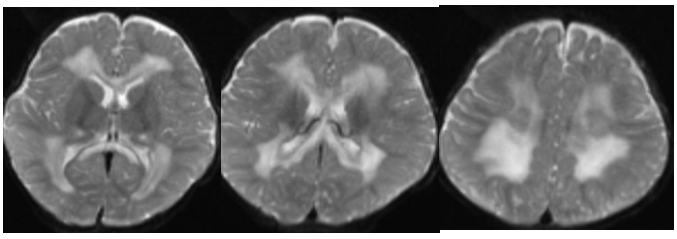


Fig 4) ADC axial images show confluent symmetrical hypointense areas with peripheral hyperintense areas in the fronto-parietal white matter and corpus callosum

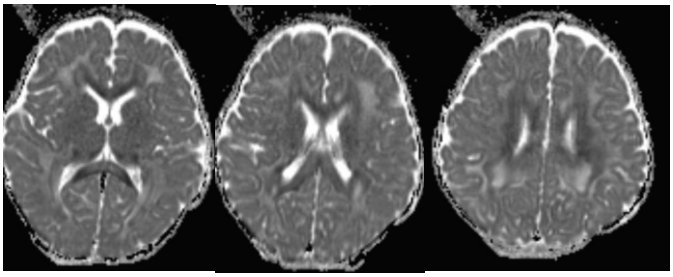
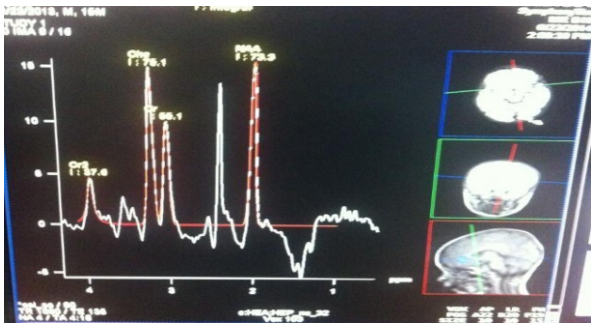


Fig.5) Multi voxel proton MR Spectroscopy from the frontal white matter shows a large singlet at 2.4 ppm representing Succinate (Su) (blue arrow) along with inverted lactate peak (red arrow).



Discussion

Leigh's syndrome is a rare progressive neurological disorder of the childhood. It is usually inherited in an autosomal recessive fashion, and the underlying defect can be at any of a number of sites in the enzyme pathway for respiratory metabolism. Associated mitochondrial enzyme deficiencies are pyruvate carboxylase, pyruvate dehydrogenase (complex II deficiency), cytochrome C oxidase, and Complex I (NAD-Coenzyme Q Reductase) deficiencies. The pathology of Leigh's syndrome is characterized by capillary proliferation with bilaterally symmetric grey and white matter necrosis, spongiform degeneration or vacuolization and demyelination.

Neuroimaging plays an important role in diagnosis of patients with Leigh syndrome. The most characteristic neuro-radiological findings are bilateral, symmetric focal hyperintensities in the basal ganglia, thalamus,substantia nigra, and brainstem nuclei at various levels on T2-weighted MRI. These high T2 signals on MRI reflect the spongiform changes and vacuolation in the affected brain structures. In the basal ganglia, the putamen is particularly involved. However apart from the classic imaging findings, the imaging findings can vary depending on the cause of the Leigh's syndrome.

In complex II deficiency which accounts for 2% of mitochondrial encephalopathies, leukodystrophy and Leigh's syndrome have been among wide range of presentation. Succinate dehydrogenase deficiency can present with any these phenotypes. Patients typically present with acute neuromotor deterioration in the first or early second year of life. MRI shows either basal ganglia disease typical of Leigh's syndrome or T2 & FLAIR hyperintensity of the periventricular and deep cerebral white matter. Diffusivity is reduced in the actively involved areas.

Diagnosis can be confirmed by MR spectroscopy, which shows a large singlet (succinate) at 2.4 ppm in the white matter.

In our case series, we discuss the MRI findings in the rare complex I and complex II deficiency. With respect to case I, few reports are available regarding the neuroimaging findings in this disorder. Most of the reports suggest cavitation in the corpus callosum, periventricular and deep white matter to be common together with high lactate peak on proton MR spectroscopy

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