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Leigh's Disease: A Diagnostic Probability on Serial Neuroimagings

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Abstract

We report a case of 3 year old male child presented with regressed milestone in form of motor, language and cognition after the age of one year. The initial detail work up including neuroimagings and genetic studies for leukodystrophy, mitochondrial disorders, congenital muscular dystrophy, congenital myopathy, Wilson disease and metabolic disorders were normal. However serial neuroimagings were helpful to reach the diagnosis of mitochondrial disease (leighs disease).

Keywords: *Leigh's disease; 3Tesla MRI; Mitochondrial disease; MR spectroscopy; Basal ganglia.*

Introduction

Leigh syndrome is a progressive neurodegenerative disorder of infancy and early childhood. It has considerably variable clinical signs, symptoms, onset time, and disease course and non specific clinical presentations such as developmental regression, hypotonia, ataxia, dystonia, swallowing difficulties and brainstem dysfunction. It is caused by defects of mitochondrial enzymes, including pyruvate dehydrogenase complex, and respiratory chain complexes I, II, IV, and V[1]. MRI demonstrates progressive signal abnormalities, most frequency in the basal ganglia, but abnormalities involving the thalamus, periaquiductal gray, brainstem tegmentum, and dentate nuclei can be seen[2]. Magnetic resonance spectroscopy (MRS) studies of the brain revealed elevated lactate levels in the basal ganglia region , the brainstem and in the occipital cortex[3].

Case report

A 3 year old female baby with normal birth and development till the age of one year without any remarkable positive family history or any significant drug or toxin exposure in utero and infantile period presented with regressed milestone in form of of speech, motor, as well as cognitive involvement. Patient did not have history of fever, seizure, altered sensorium, visual disturbance, and abnormal involuntary movement. Patient attended department of pediatric neurology in tertiary hospital. Patient was evaluated for leukodystrophy, mitochondrial disorders, congenital muscular dystrophy, congenital myopathy, Wilson

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disease and metabolic disorders with different investigations like neuroimaging (MRI brain,Figure A),enzyme studies, arylsulphatase for metachromatic leucodystrophy, galactocerebrosidase (krabbe disease), metabolic profile, Visual evoked potential(VEP), Brainstem auditory evoked response(BAER), Electroencephalogram(EEG) and profile for Wilson disease, mitochondrial deletion/duplication analysis of mitochondrial DNA. However the above mentioned investigation did not revealed any diagnosis.

At 18 months of age, patient was reviewed with neuroimaging of brain. MRI brain in FLAIR images(Figure B) showed subtle hyperintensities involving head of bilateral caudate nucleus suggestive of non specific neurodegenerative disease. However the above mentioned enzyme studies, VEP, EEG did not coroborate the imaging diagnosis.

The patient was sent to us for muscle biopsy to exclude congenital myopathy or any dystrophic disorders. After reviewing the case with detail history and clinical examination patient was reinvestigated with neuroimaging (MRI of brain), MR spectroscopy, serum CPK, lactate, ammonia, VEP, NCV, and other routine investigation with detail opthalmological examination. serum lactate level was persistently high in repeated studies. T2 weighted image (3 Tesla MRI) showed symmetrical hyperintensties in b/l basal ganglia (caudate and putamen) and dorsomedial thalami sugessitive of Leigh's disease(figure C) and MR spectroscopy(figure D) showed lactate peak in corresponding brain lesion that support the diagnosis. Patient was advised with thiamine, l-carnitine,

Figure A

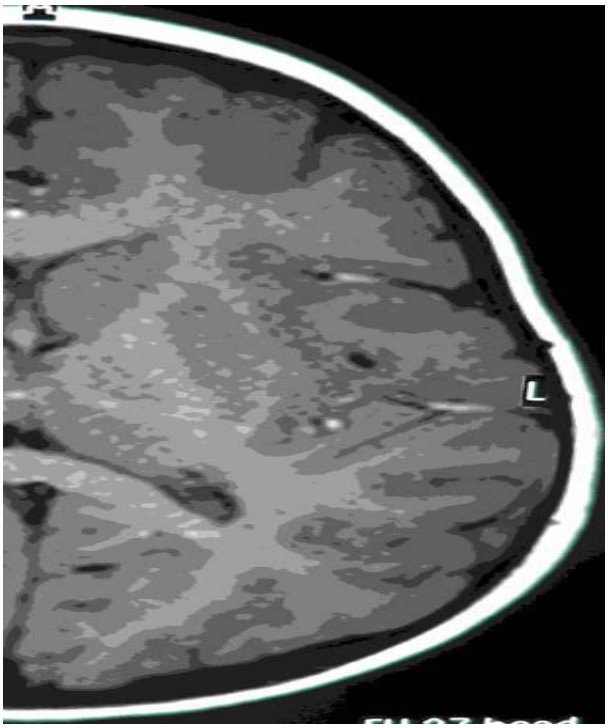


Figure B

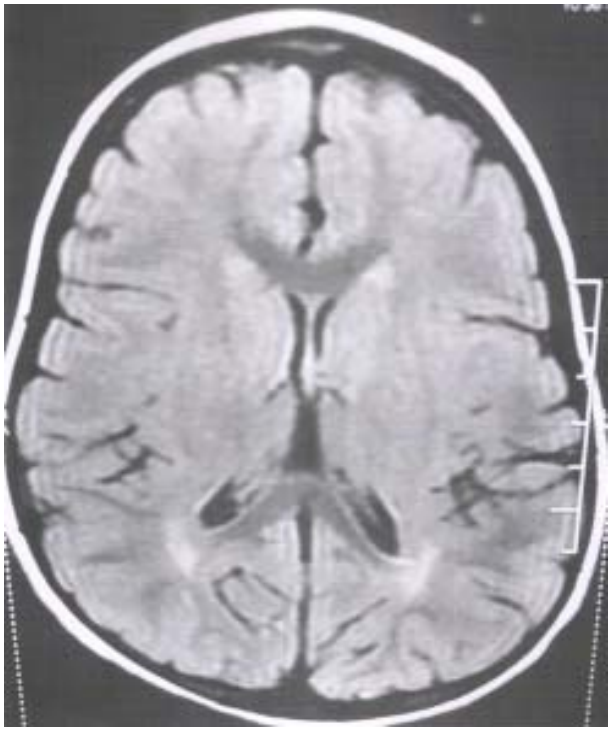


Figure C

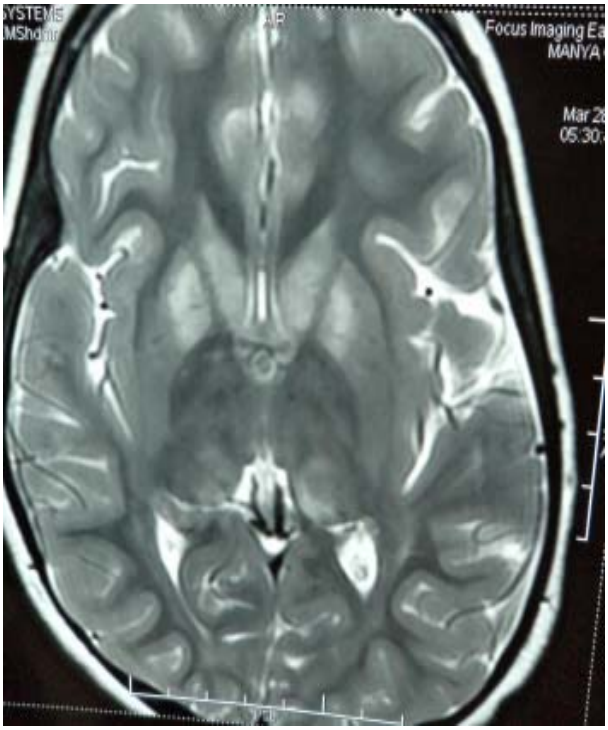
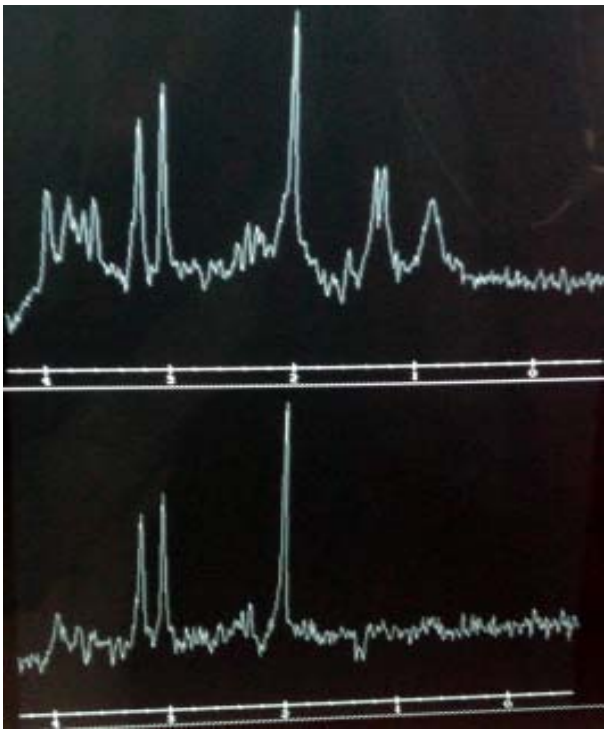


Figure D



Co Q, high fat and low carbohydrate diet with regular follow up.

Disscussion

Leigh's syndrome is a fatal rapidly progressive neurodegenerative condition of infancy and childhood. The clinical presentation and course can vary but symptoms commonly include features of brainstem or basal-ganglia dysfunction. The common manifestation include developmental delay particularly developmental regression. Other clinical features are nystagmus, ataxia, dystonia, hypotonia, optic atrophy and respiratory abnormalities[4]. The lesions in MRI of brain are symmetric and commonly affect putamen, globous pallidus ,caudate ,thalami, substantia nigra, inferior olivary nuclei, periaqueductal grey matter and brain stem tegmentum[4]. MRS scan reveals decreased N-acetylaspartate(NAA) and increased lactate in bilateral basal ganglia and thalami affecting energy metabolism in Leigh disease[3]. The clinical course follows either a stepwise deterioration or a slowly progressive decline.

Leigh's syndrome is a mitochondrial disorder resulted from various biochemical and molecular defects due to failure of oxidative metabolism within the developing brain. Inheritance pattern can be X-linked recessive, autosomal recessive, or maternal in heritance. Point mutations in the ATPase 6 gene are the most common but several mutations in mtDNA have also been described[5].

There is an important role of serial neuroimagings considering diagnosis of this syndrome which may manifest over time progression. In our case though initial neuro imagings were inconclusive but subsequent imaging and MR spectroscopic studies helped in reaching the probable diagnosis of the disease. Due to poor socioeconomic status, un affordability along with unavailability for detail mitochondrial work up even in various tertiary care center the disease still remains under diagnosed. Serial Magnetic resonance imaging of brain along with clinical correlation may be taken as a consideration

for valuable diagnostic support in leigh's syndrome.

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