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Case Report

Leighs disease: powerhouse failure

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Abstract:

Leigh disease, also known as juvenile sub acute necrotizing encephalomyelopathy, Leigh syndrome, infantile sub acute necrotizing encephalomyelopathy, and sub acute necrotizing encephalomyelopathy (SNEM), is a rare inherited neurometabolic disorder that affects the central nervous system. A five months old male child born out of non-consanguineous marriage was in regular follow up with a pediatrician in view of birth history of full term, low birth weight. Records showed steady weight gain with gross motor delay and central hypotonia. 15 days prior to admission, child had rhinorrhea, cough, hoarseness and intermittent stridor which were initially treated with oral medication. Subsequently the child developed fever for which he was admitted and treated with antibiotics. Complete blood count, C reactive protein, blood culture, CSF was normal. X-ray showed hyperinflation. The child then developed features of encephalopathy with myoclonic jerks. In view of history of developmental delay and clinically central hypotonia, with investigations pointing towards non-infective etiology, a possibility of metabolic, structural malformation of brain or mitochondropathy was entertained and accordingly investigated. MRI was suggestive of Leighs Disease and his CSF lactate levels were high. This case is presented to highlight that in case of absence of infection, metabolic encephalopathy or mitochondropathies can be thought as a cause of Encephalopathy

Key words: Leigh disease, necrotizing, infantile

Introduction:

Leigh disease (also known as sub acute necrotizing encephalomyelopathy (SNEM)) is a progressive neurodegenerative disorder and invariably leads to death in childhood. Necrosis and capillary proliferation occur in the basal ganglia, spinal cord and brain stem. Three clinical subtypes are recognized: An infantile form with symptoms onset during first 2 years of life, a juvenile form with disease manifestations in early childhood and an adult form with onset during fifth or sixth decade. An infantile form occurs with hypotonia, vomiting, seizures. Slow progression with death from respiratory failure is typical. The inheritance pattern may be either autosomal recessive or X linked. Leigh disease is one of many mitochondrial disorders, due to a wide variety of genetic mutations in mitochondrial DNA (mtDNA). Chronic energy deprivation leads to histological features such as: capillary proliferation, demyelination, neuronal loss & Gliosis. Here we present a rare case of Leighs Disease. [1-5]

Case Report:

A 5 months old male 1st issue of non consanguineous marriage presented to the Department of Pediatrics. He was a full term, IUGR; born from LSCS in view of transverse lie Developmentally, Gross motor delay present, with hypotonia. Fine motor, language, Social milestones & Anthropometry were normal. On the day of admission, he came with the complaints of cough and hoarseness of voice of 15 days, fever of 10 days, lethargy and decreased acceptance of feeds since 7 days. Myoclonic jerks and loss of consciousness was seen on 1st day. On examination No dysmorphisms, Pallor was present. Anterior fontanelle was open and central hypotonia (brisk DTR with hypotonia). Patient had progressive encephalopathy. On Investigating Complete Blood Count, C - reactive protein, Blood culture, Lumber Puncture were within normal limits. X ray suggestive of hyperinflation, Sr. ammonia and lactate levels were raised and CSF lactate was high.

Discussion:

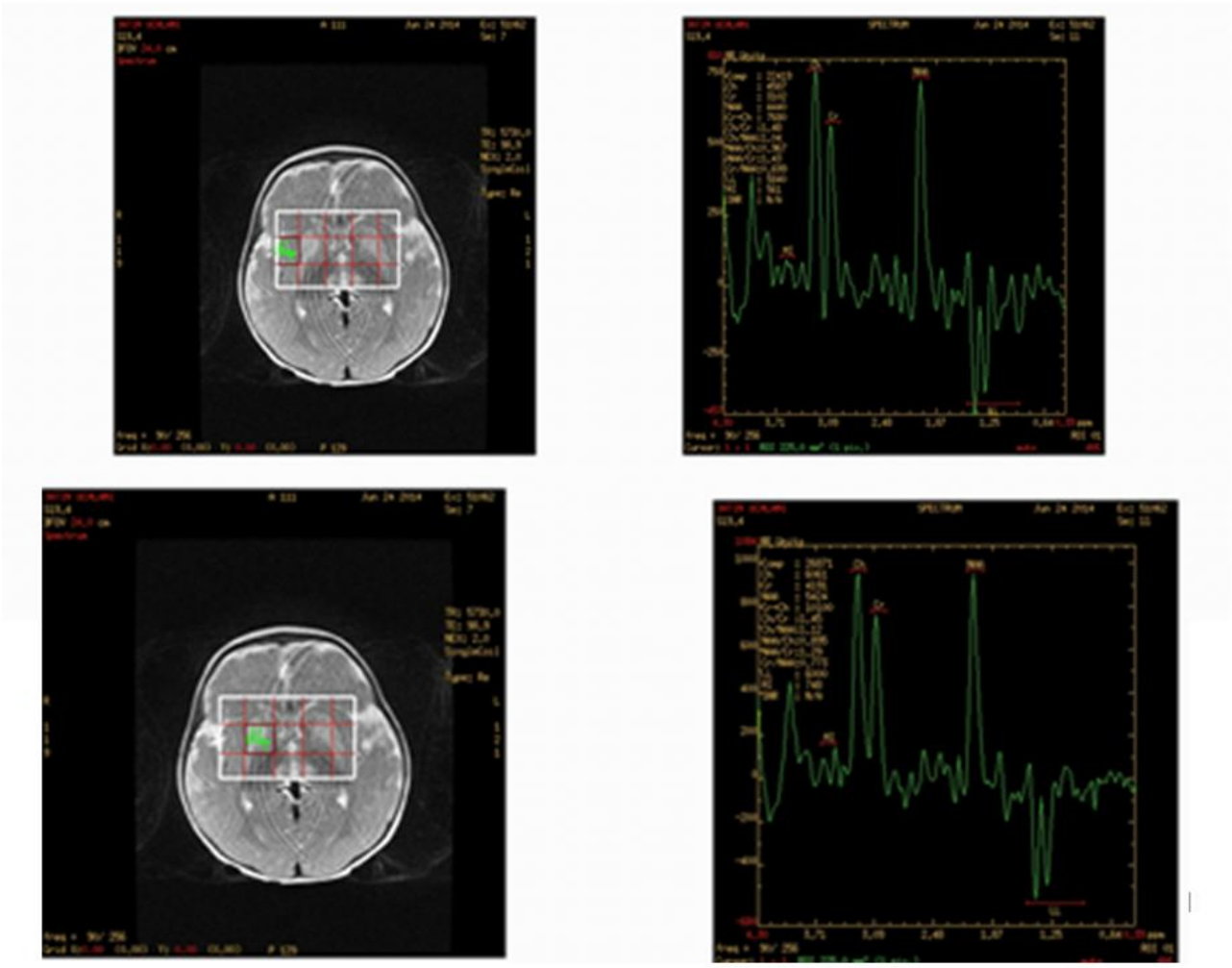
Leigh disease (also known as sub acute necrotizing encephalomyelopathy (SNEM)) is a progressive neurodegenerative disorder and invariably leads to death in childhood. Necrosis and capillary proliferation occur in the basal ganglia, spinal cord and brain stem. Three clinical subtypes are recognized. An infantile form with symptoms onset during first 2 years of life, a juvenile form with disease manifestations in early childhood and an adult form with onset during fifth or sixth decade. An infantile form occurs with hypotonia, vomiting, seizures. Slow progression with death from respiratory failure is typical. The inheritance pattern may be either autosomal recessive or X linked. Leigh disease is one of many mitochondrial disorders, due to a wide variety of genetic mutations in mitochondrial DNA (mtDNA). Chronic energy deprivation leads to histological features such as capillary proliferation demyelinationneuronal loss Gliosis Markers - CSF lactate may be elevated MRI - The distribution tends to be generally symmetrical. T2 characterized by high signal typically in: Brainstem Putamen. Other sites of T2 signal change include: remainder of the corpus striatum (globus pallidus and caudate nucleus (heads)) subthalamic nuclei substantia nigra thalami. [6-15]

Conclusion:

This case was taken to highlight that Leighs Disease although rare, is an important cause of progressive encephalopathy and in case of absence of infection metabolic encephalopathy or mitochondropathies can be thought as a differential diagnosis.

References:

1. Leigh D. Sub acute necrotizing encephalomyelopathy in an infant. J Neurol Neurosurg Psychiatry. 1951;14(3):216–21.
2. Genetics Home Reference. Leigh syndrome. 2011. [Accessed: Jun 2014]. Available from: http://ghr.nlm.nih.gov/condition/leigh-syndrome.
3. Carrozzo R, Dionisi-Vici C, Steuerwald U et al. SUCLA2 mutations are associated with mild methylmalonic aciduria, Leigh-like encephalomyopathy, dystonia and deafness. Brain. 2007;130(Pt 3):862–74.
4. Darin N, Oldfors A, Moslemi AR et al. The incidence of mitochondrial encephalomyopathies in childhood: clinical features and morphological, biochemical, and DNA abnormalities. Ann Neurol 2001;49(3):377–83.
5. Sofou K, De Coo IFM, Isohanni P et al. A multicenter study on Leigh syndrome: disease course and predictors of survival. Orphanet J Rare Dis. 2014;9(1):52.
6. Saneto RP, Singh KK. Illness-induced exacerbation of Leigh syndrome in a patient with the MTATP6 mutation, m 9185 T.C. Mitochondrion. 2010;10(5):567–572
7. Koene S, Rodenburg RJ, van der Knaap MS et al. Natural disease course and genotype-phenotype correlations in Complex I deficiency caused by nuclear gene defects: what we learned from 130 cases. J Inherit Metab Dis. 2012;35(5):737–747.
8. Patel KP, O'Brien TW, Subramony SH, Shuster J, Stacpoole PW. The spectrum of pyruvate dehydrogenase complex deficiency: clinical, biochemical and genetic features in 371 patients. Mol Genet Metab. 2012;105(1):34–43
9. Santorelli FM, Shanske S, Macaya A, DeVivo DC, DiMauro S. The mutation at nt 8993 of mitochondrial DNA is a common cause of Leigh's syndrome. Ann Neurol. 1993;34(6):827–834.
10. Chol M, Lebon S, Bénit P, et al. The mitochondrial DNA G13513A MELAS mutation in the NADH dehydrogenase 5 gene is a frequent cause of Leigh-like syndrome with isolated complex I deficiency. J Med Genet. 2003;40(3):188–191.
11. Tsuji M, Kuroki S, Maeda H, et al. Leigh syndrome associated with West syndrome. Brain Dev. 2003;25(4):245–250.
12. Rahman S, Blok RB, Dahl HHM, et al. Leigh syndrome: clinical features and biochemical and DNA abnormalities. Ann Neurol. 1996;39(3):343–351.
13. Cavanagh JB, Harding BN. Pathogenic factors underlying the lesions in Leigh's disease. Tissue responses to cellular energy deprivation and their clinico-pathological consequences.Brain. 1994;117(Pt 6):1357–1376.
14. Haack TB, Gorza M, Danhauser K, et al. Phenotypic spectrum of eleven patients and five novel MTFMT mutations identified by exome sequencing and candidate gene screening. Mol Genet Metab. 2014;111(3):342–352.
15. Calvo SE, Compton AG, Hershman SG, et al. Molecular diagnosis of infantile mitochondrial disease with targeted next-generation sequencing. SciTransl Med. 2012;4(118)



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