Case Report On L2 HydroxyGlutaricAciduria :A Disorder Of Protein and Amino Acid Metabolism

*Ms.Priyalatha.G, **Prof.Rajeswari.S& ***Ms.Saranya.S

Abstract:

Inborn errors of metabolism are a large group of hereditary biochemical disease in which specific gene mutations cause abnormal (or) missing proteins that lead to alter function. Inborn error of metabolism occurs from a group a rare genetic disorder in which the body cannot metabolize food components normally. Here we report a case of L_2Hydroxyglutaricaciduria, a rare inherited genetic disorder that affects TCA cycle and the child presented with typical symptoms such as seizure, hypotonia and global developmental delay.[1]

Key disorder: *Inborn error of metabolism, Tricyclic acid(TCA), L_2hydroxyglutaricAciduria.*

CASE REPORT

A 9 years old male child got admitted in Paediatric Medical Ward, with a known case of seizure disorder and global developmental delay such as hypotonia, lack of coordination of upper and lower extremities, walking, delayed speech from 6 months of age. The child was on continuous treatment with Anti-convulsant treatment with T. Lorazepam (20mg/bd) and Sodium valproate 20mg(0.5mg/bd). The child had got admitted for the complaints of recurrent generalized seizure and to rule out the cause by MRI and EEG. The child was diagnosed as **L_2 hydroxyglutaricaciduria** with typical clinical symptoms and MRI findings. The child was advised to continue the same anti-convulsant therapy and added with T. CoE(100mg/od) to prevent further nerve damage.

The child was hospitalised for 5 days and parents were counselled regarding the disease condition, treatment and appropriate rehabilitative care.

History Collection

Child parents had consanguineous marriage,**degree of consanguinity was second degree.** The order of birth was second. Their first son had the same global developmental delay with seizure disorder from 6 months of age.

(ORGANIC ACIDURIA- L_2 hydroxyglutaricaciduria)

Inborn errors of metabolism (IEM):

Inborn errors of metabolism (IEM) are conditions caused by genetic defects related to synthesis, metabolism, transport or storage of biochemical compounds.

*Tutor, **Asso.Prof,**& *Tutor, Kasturba Gandhi Nursing College, Sri BalajiVidyapeeth , Puducherry, India.

The term "organic acidaemia" or "organic aciduria" (OA) applies to a group of disorders characterised by the excretion of non-amino acids in urine. This group of disorders results from enzyme deficiencies in pathways of amino acids degradation.

Defects in the metabolism of the branched chain amino acids (leurine, isoleurine, valine, tryrosine, homocysteine, lysine, hydroxy lysine and tryptophan) are responsible for this disorder.

TWO TYPE OF CLINICAL PRESENTATIONS.

L_2 hydroxyglutaricaciduria- A disorder of Protein and amino acid metabolism

Definition:

L_2hydroxyglutaricaciduria is an inherited metabolic condition due to accumulation of toxic L_2 hydroxyglutaric acid characterized by progressive brain damage that results in psychomotor retardation, cerebellar ataxia ,hypotonia and epilepsy.

Incidence:

- L_2-hydroxyglutaric aciduria is a rare disorder.
- D-2-HGA and L-2-HGA have each been reported to affect fewer than 150 individuals worldwide. Combined L-2-HGA appears to be even rarer, with only about a dozen reported cases.

Causes:

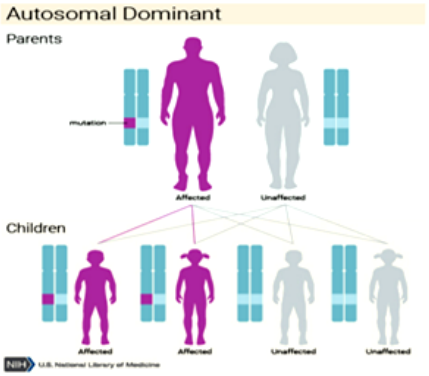
Genetic changes:

L2 – HGA results from **mutations in the L2 HGDH gene**(normally that helps in TCA cycle)

L2 – hydroxyglutaric and D2 – hydroxyglutaric acids are products of the tricyclic acid (TCA cycle). (They are the waste / end products without any metabolic functions and accumulation of these products has toxic effects.)[3]

Normally	**Deficit / mutation in L2 HGDA genes**
L2- hydroxyglutaric and D2 hydroxyglutaric acid genes (chromosome 14q 22.1) Instructions for making enzymes in mitochondria ↓ Secret functional enzymes & breaks ↓ D2 – hydroxy glutamate and L2 – hydroxy glutamate ↓ To produce energy for cell activities	Shortage of functional enzymes to break D2 – hydroxy glutamate and L2 – hydroxy glutamate ↓ Accumulation of Toxic /L2HGA ↓ Damage brain cells and other cells leads to death of cells.

The two sub types are distinguished by their genetic cause and pattern of inheritance, although they also have some difference in signs and symptoms.2

TYPE I	***TYPE II***
An autosomal recessive pattern of inheritance	An autosomal dominant pattern of inheritance
Parents have a copy of mutated gene but do not show signs and symptoms of the condition.	People with no history of the condition in their family. 
Type I tends to begin late.	Type II tends to begin earlier and often causes more severe health problems.
Weakened and enlarged heart is not found in type I	Type II may also be associated with a weakened and enlarged heart.

CLINICAL MANIFESTATION:

The child had type II L_2 hydroxyglutaricaciduria with autosomal dominant type

BOOK PICTURE	CHILD PICTURE
• Onset is usually in late infancy with slow evolution • No symptoms within first 6months **Second 6 months, non-specific developmental delay.** • Muscular hypotonia • Delayed unsupported walking • Delayed speech **At 3 years of age** • Gait ataxia • Other cerebellar symptoms: • Hand dysmetria • Dysarthria • One half of the child have seizures (generalized type) • The disease is slowly progressive and loss of verbal and non-verbal intelligence has been recorded. • Macrocephaly	The child had poor head control and head control achieved by one year. No symptoms up to first six months. The child has hypotonia and presence of seizure episodes. The child has delayed speech. Muscle strength was 3/5(moves against gravity with no resistance) and hypotonia in all extremities. The child was not able to walk, and had Unsteady gait ataxia, dysarthria, hand dysmentria and generalized seizure.
Diagnostic evaluation	
History collection:	History collection. Parents had consanguineous marriage with second degree of consanguinity. Both of their children had Organic aciduria.
Physical examination	The child has delayed speech and motor development. Presence of hemiparesis and hypotonia with Muscle strength of 3/5 in all extremities.
Biochemical markers elevation of glutaric acid, glutaric acid, 3 – hydroxyglutaric acid	Blood investigation are not carried out.
Magnetic Resonance Imaging (Brain)	MRI report reveals that subcortical encephalopathy affecting the nerve fibres and sparing the central nervous system and white matter.

Urine findings: Increased excretion 2-hydroxy glutaric acid	Not done
Prenatal diagnosis: Measuring L2 HGA in amniotic fluid	Not done
Treatment: No definitive management for L2 – HGA Supportive and conservative management • Anti-seizure medications • Administration of vitamin supplements • Physical therapy	The child is on regular antiseizure medications T-Sodium Valproate 20mg/bd T-Lorazepam 0.5 mg/bd T-CoE 10 -100mg/od (coenzyme Q10- to prevent accumulation of toxic metabolites and to improve nerve damage)
Complication: The condition progresses and worsen by the age. The quality of life is 2 decades. • Brain tumor (Glioma) • Motor deficits	The child has motor deficits.
Nursing care & rehabilitation : **To maximize the mobility with absence of contracture and injury**. ✓ Facilitate activities in using fine and gross motor skills. (holding the cup, ball etc. ✓ Allow the child to do activities(or) routine care at his own pace. ✓ Encourage the parent to participate in passive range of motion exercise. ✓ Encourage the child to take rest between activities. ✓ Refer and educate the family to use assistive devices such as ankle foot orthosis etc. **Dietary management:** ✓ No dietary restriction. ✓ Educate the parent to avoid fasting to the child by providing food on proper time.	Encourage the child to do mild activities such as holding the cup and spoon etc. ✓ Encouraged the child to take rest in between activities. ✓ Encouraged the parent to participate in providing passive range of motion exercise. ✓ Counselled the family for special schools and to use of assistive devices. ✓ The child is going to private special school at nearby their home town. ✓ Educated the parent to come regular follow up and strictly adhere to medical treatment ✓ Educated the parents to avoid fasting to the child.

Conclusion:

The goals of treatment for children with inborn errors of metabolism(IBM) are prevention of further accumulation of harmful substances and elimination of toxic metabolites.

Appropriate genetic counselling and prenatal diagnosis helps in early identification and prevention of inborn error of metabolism. [4,5.]

References:

1. Suraj Gupta, "The Short Text on Pediatric Nursing",9th Edition, 2014, Published by Jaypee Brothers Medical Publishers(p) Ltd, New Delhi.pg no.226-28.
2. Kleigman Nelson et.al, "Textbook of Pediatrics" 17th edition, 2004, published by Elsevier, a Division of reed Elsevier India(P)Ltd. New Delhi. Pg. no.1756-60.
3. Robert E. Nickel& Larry W.Derch, " ThePhysican's Guide to caring for children and chronic condition" 1st edition, 2000.Published by Paul Brokes publishing company, Maryland. Pg no. 289-91.
4. Struys EA, Salomons GS, Achouri Y, Van Schaftingen E, Grosso S, Craigen WJ, Verhoeven NM, Jakobs C (Jan 2005). "Mutations in the D-2-hydroxyglutarate dehydrogenase gene cause D-2-hydroxy glutaric aciduria".HumGenet. 76 (2):358–60. doi:10.1086/427890. PMC 1196381. PMID 15609246
5. Genetic Home reference, "your guide to understanding genetic condition", published by NIH, U.S.National Library of Medicine, December 2017. Available at URL : https://ghr.nlm.nih.gov/condition/2-hydroxyglutaric-aciduria#statistics.