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FATTY ACID HYDROXYLASE ASSOCIATED NEURODEGENERATION (FAHN)

A case report from India highlighting its heterogenous nature

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INTRODUCTION

Fatty Acid Hydroxylase associated Neurodegeneration (FAHN) is a rare autosomal recessive disorder

A subtype of Neurodegeneration With Brain Iron Accumulation (NBIA)

Progressive disease with childhood onset

Presents with spasticity, movement and eye abnormality

Later impaired cognition, seizures

Diagnosed on clinical + neuroimaging findings

Confirmed by molecular testing

CASE REPORT

Presenting Complaints

6-year-old female came with

Change in the gait since past 6 months (Video 1 , Video 2 after 6 months) - Slowing, waddling, difficulty in climbing up stairs, climbing one step at a time

Some slowing in reciting of poems

No history of –

- exercise Intolerance, Fatigue, Atrophy
- cramps, contractures, muscle hypertrophy, myalgia, myoglobinuria, stiffness
- Proximal / Neck muscle involvement
- ptosis or symptoms suggestive of other cranial involvement

Birth history, cognition and development – Age appropriate

EVALUATION

General examination – Normal

Neurological examination

Normal Higher functions, Speech, behavior
(father felt that her processing speed and speech had slowed)
Cranial Nerves; Ophthalmological Exam N
Motor System
Power- UL- N, LL- Hip –Flexors and Adductors- 3, Extensors, Abductors -2+; Knees-Flexors and Extensors 3-4; Ankle- 3-4
Tone- Normal except TA tightness
Reflexes- UL- N; KJ and AK- brisk, plantars-equivocal
Sensory system-N, Vibration Sense- Could not be tested,
No cerebellar signs, Gowers's negative,

Gait
Waddling gait as well as high stepping gait
Drags her right foot

Rest systemic examination – normal

INVESTIGATION

Basic + metabolic blood investigation, EMG / NCV - NORMAL

Ophthalmic evaluation

- bilateral intermittent exotropia
- myopic astigmatism
- Central vision impairment

NEUROIMAGING

Increasing Periventricular White matter signal predominantly posterior (A >C)

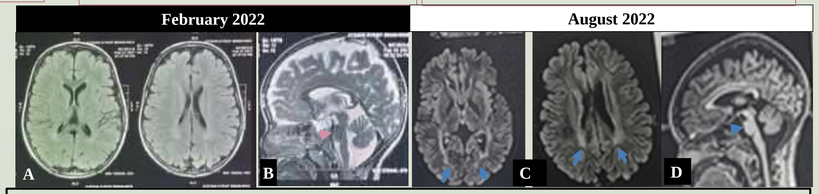
Thinning of Corpus Callosum

Cerebellar atrophy

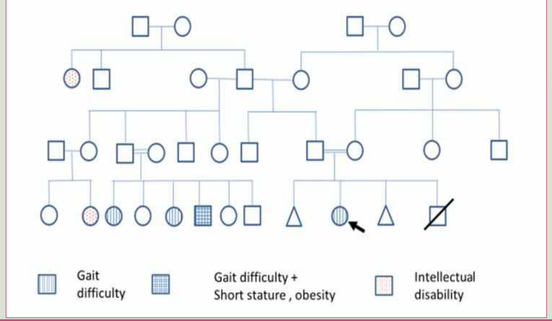
Increased Pontine volume loss (B>D)

Prominent cisterns in the posterior fossa

Spinal cord sparing



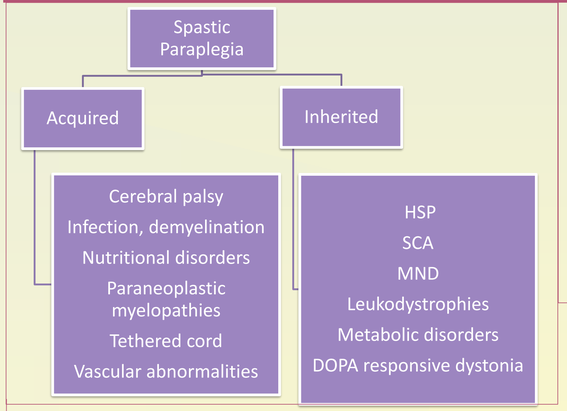
Family History

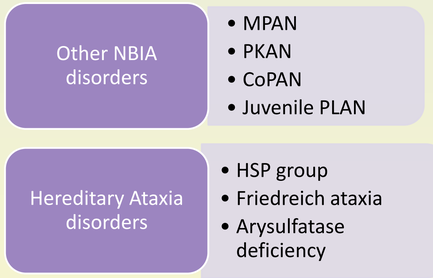


GENETIC TEST (Whole exome sequencing in child + sanger sequencing in parents)

Gene	Chromosome position	Variant	Zygosity	OMIM Phenotype	Inheritance	Clinical significance	Variant in Mother	Variant in Father
FA2H	Chr16:74718990-74718993	c.781_784delinsA p.H261del	Homozygous	Spastic Paraplegia 35, FAHN	Autosomal Recessive	Likely pathogenic	Heterozygous delGTG	Heterozygous delGTG

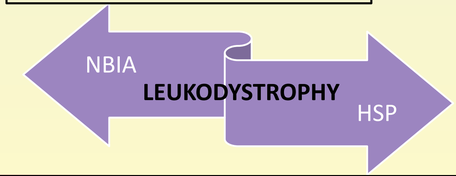
DISCUSSION





- Initially 3 different phenotypes
- Now considered a single disorder with evolving phenotype
- The severity can be variable, progression can be intermittent

CLINICAL HETEROGENITY



LITERATURE REVIEW

Reported features	Features in our Patient
Age of onset: <5 yr onwards	~ 5 yrs
Spasticity , Gait abnormality	+ presenting complaints
Dysarthria	Slowing of speech
Eye abnormality – Exotropia, OPTIC atrophy	Intermittent exotropia + Central vision impairment
Cognitive defects, seizures (later onset)	Absent
Ataxia, Dystonia, truncal abnormality	
MRI abnormality White matter abnormality PONS, Cerebellar atrophy Basal ganglia hypointensity (iron dep) Thin corpus callosum	Bilateral symmetrical periventricular white matter changes – posterior predominant, increasing Cerebellar and PONS atrophy Thinning of corpus callosum ? Subtle globus pallidus hypointensity

Genetics of FAHN

1. Generally Loss of function variants in FA2H
2. Causes deficiency of fatty acid 2-hydroxylase enzyme of endoplasmic reticulum
3. Truncating and missense variants reported so far
4. Most are novel since so far <100 reported cases worldwide
5. **Variant in our proband is novel and causes protein truncation**
6. **Similar variant (C.782_783insA / p.H261Qfs*52) close to ours reported previously in FAHN**

TAKE HOME MESSAGE

Rare disorder with evolving phenotype - 1st reported case of Indian origin

Suspect in presence of progressive spasticity with suggestive MRI findings, Molecular testing is confirmatory

Need for studies on natural history and neuropathology required

REFERENCES

1. Gregory A, Venkateswaran S, HayflickSJ. Fatty Acid Hydroxylase-Associated Neurodegeneration. 2011 Jun 28 [Updated 2018 Sep 27]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. 2. Rattay TW, Lindig T, Baets J, et al. FAHN/SPG35: a narrow phenotypic spectrum across disease classifications. BRAIN 2019: 142; 1561–1572. 3. Jain V, Bijarnia-Mahay S, Ramprasad VL, et al. Fatty Acid Hydroxylase- Associated Neurodegeneration - A Rare Case of Neurodegeneration with Brain Iron Accumulation (NBIA). Genetic Clinics. 2018: Oct-Dec;11:6-9. 4. Incecik F, Besen S, Bozdogan ST. Hereditary Spastic Paraplegia Type 35 with a Novel Mutation in Fatty Acid 2-Hydroxylase Gene and Literature Review of the Clinical Features. Ann Indian Acad Neurol. 2018 Oct-Dec;21(4):335-339.

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Thank the patient and her family for their permission to share the details of their family and to cooperate through this difficult medical journey