Headache with hidden roots – Revealing MEROSINOPATHY

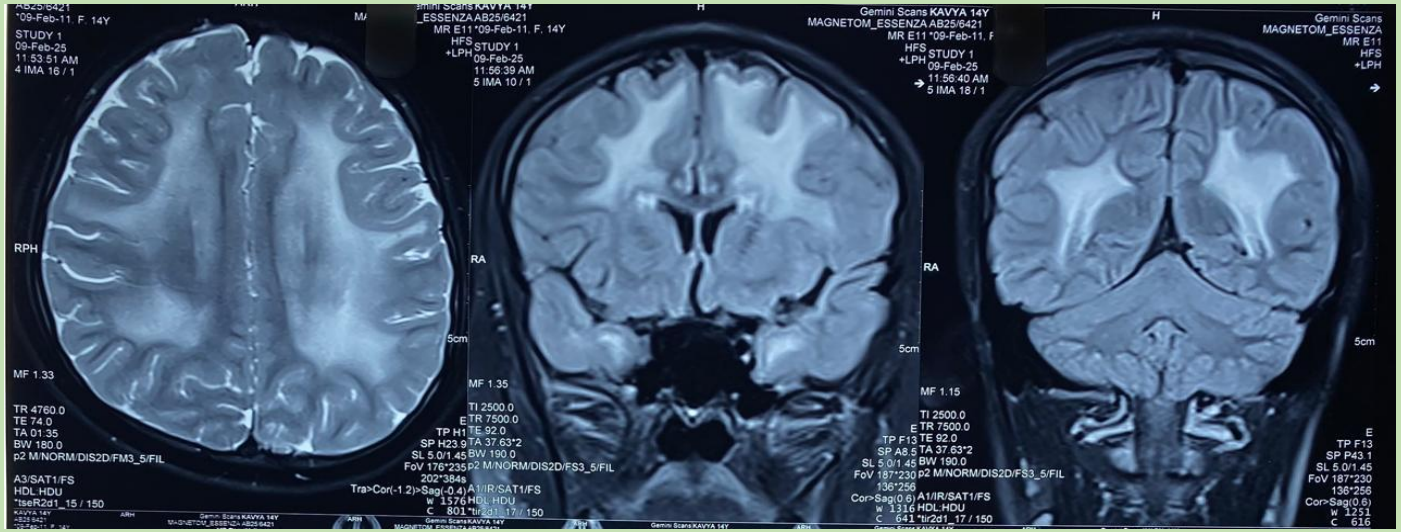
Presenting Author- DR. PRASANTHI CHILAKA[1], DR. P.R. SOWMINI[2], DR.K. MALCOLM JEYARAJ[2] DR. S. SAKTHI VELAYUTHAM[2], DR. KRISHNA KUMAR[2], DR. V. KANNAN[3], DR. S. VELUSAMY[3], DEPARTMENT OF NEUROLOGY, STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI.
1-Resident, 2-Assistant Professor, 3-Professor

Case history :

- A 14 year old female patient, born out of non consanguineous marriage, with normal birth history , presented to OPD with history of headache since two years, which is of migranous character. She was kept on migraine prophylactics and headache partially subsided. Neuroimaging was done and it showed white matter changes.
- When retrospectively questioned , her motor milestones were normal till age of one year, later, while standing, her mother noticed that she is using her right lower limb more, and supporting on right lower limb while getting up, and she was walking, and she was running normally, and her language and social milestones were normal. But when compared to her sister, mother observed that she is running a little bit slow, but that is not affecting her activities, so they didn't seek medical attention.
- By 12 years of age , she used to climb two stairs when she found difficulty in climbing stairs, due to had pain in the thighs , she also noticed that she had difficulty in getting up from squatting position as she is having pain in the back of thigh.
- By 13 years, she used to climb three stairs where she notice difficulty due to pain in the thighs but able to manage by climbing slowly. She also noticed difficulty in lifting her schoolbag, but she was able to carry her bag. She also noticed that she had pain in both upper limbs when she carries textbooks in hands.

Examination

- MMSE- 25/30
- Cranial nerve examination- normal
- Fundus examination - normal
- Spinomotor system
- Mild left calf atrophy
- Tone – normal
- Power- 4/5 around shoulder and hip mucles
- DTR- biceps and knee- diminished
- Plantar- flexors
- Sensory – normal
- Cerebellar examination - normal

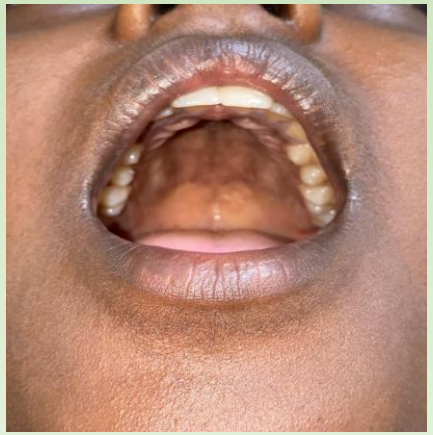


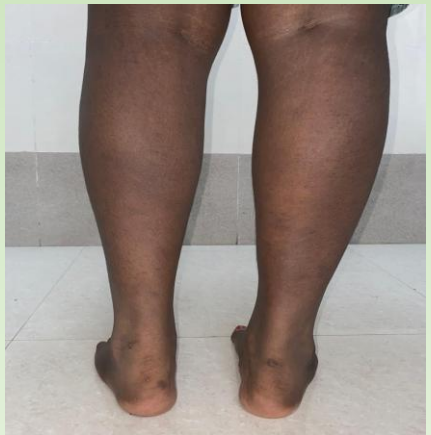
Summary of Variants

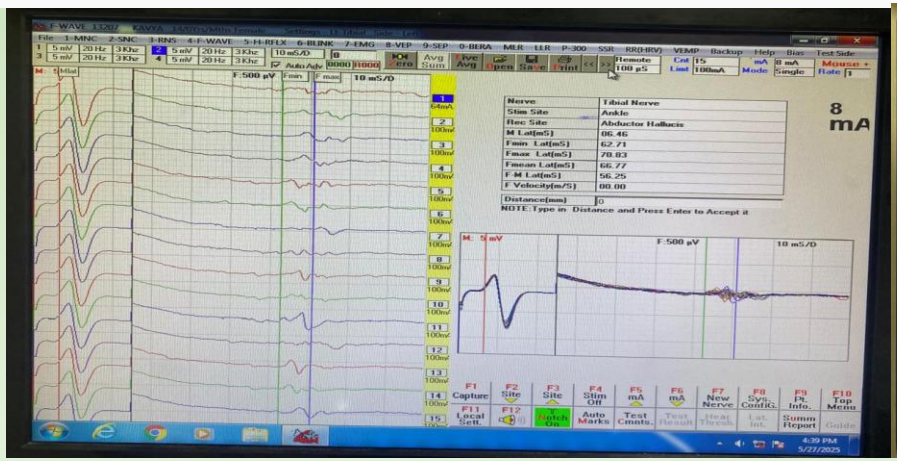
Gene and Transcript	Exon/Intron Number	Variant Nomenclature [Variant depth/ Total depth]	Zygosity	Classification	OMIM Phenotype	Inheritance
LAMA2 (NM_000426.4)	Intron 19	c.2749+1G>A [104X/104X]	Homozygous	Pathogenic	Muscular dystrophy, congenital, merosin deficient or partially deficient	Autosomal recessive

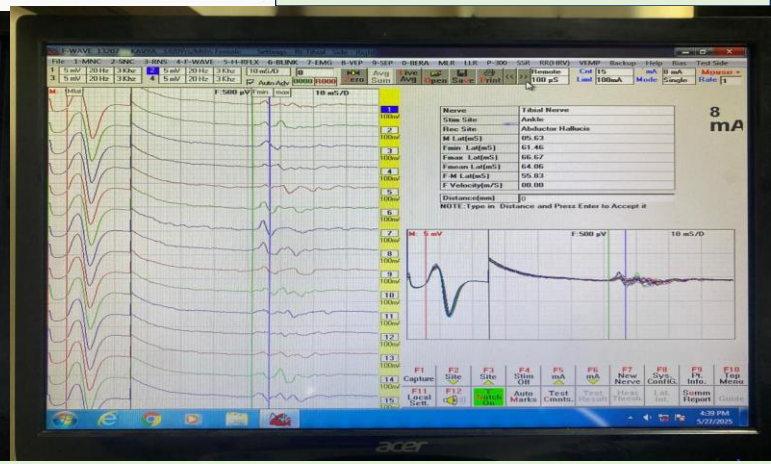
Investigations

Haemoglobin – 12
Tot count 7800
Serum CPK – 401
TSH- 2.4
LIVER FUNCTION- NORMAL
RENAL FUNCTON- NORMAL
ECHO- NORMAL
MRI BRAIN – DIFFUSE WHITE MATTTER CHANGES
NCS- DEMYELINATING CHANGES
GENETIC TESTING- LAMA2 MUTATION



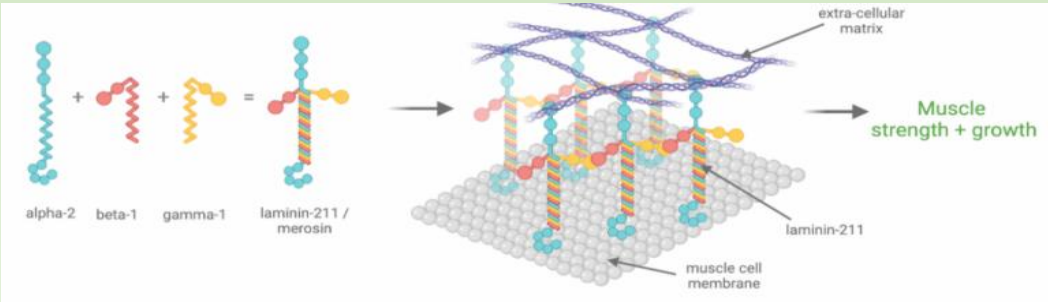






Discussion

- ✓ Merosin" refers to laminin α-2 chain, part of laminin-211 (also called laminin-2). Mutations in **LAMA2** lead to merosin deficiency, giving rise to what was earlier called merosin-deficient congenital muscular dystrophy (MDC1A)[1]
- ✓ Features include congenital or early infancy onset hypotonia, muscle weakness, delayed gross motor milestones, contractures, sometimes scoliosis, respiratory compromise.[2]
- ✓ A striking feature, often considered "extramuscular," is **cerebral white matter abnormalities** on brain MRI. Many patients > 6 months show symmetric T2 hyperintensities in cerebral white matter (especially periventricular) while the cortex is relatively spared. Seizures seen in a minority (~6-8 %) of cases[2,3].
- ✓ Respiratory muscle involvement may lead to nocturnal hypoventilation; this can manifest by **morning headaches** in neuromuscular disease,due to hypercapnia / hypoxia during sleep.[4]



Conclusion

Merosin-deficient congenital muscular dystrophy (LAMA2-related dystrophy) is classically recognized for early hypotonia, muscle weakness, and delayed motor milestones. However, our case emphasizes that **headache may occasionally be the initial and predominant presentation**, which is atypical and easily overlooked. The pathophysiology of headache in this context may be multifactorial—ranging from **respiratory hypoventilation leading to morning headaches**, to **white matter abnormalities and CNS involvement**, or a combination of these "hidden roots." This case highlights the importance of considering neuromuscular disorders with central nervous system manifestations in the differential diagnosis of unexplained headache. Early recognition of such unusual presentations can prevent diagnostic delay, guide appropriate genetic testing and respiratory monitoring, and improve patient outcomes.

References

1.Ip JJ, Hui PK, Chau MT, Lam WW. Merosin-deficient congenital muscular dystrophy (MDCMD): a case report with MRI, MRS and DTI findings. J Radiol Case Rep. 2012 Aug;6(8):1-7. doi: 10.3941/jrcr.v6i8.997. Epub 2012 Aug 1. PMID: 23365711; PMCID: PMC3558266.

2. Mercuri E, Muntoni F. The ever-expanding spectrum of congenital muscular dystrophies. *Ann Neurol.* 2012;72(1):9-17.

3. Geranmayeh F, Clement E, Feng LH, Sewry C, Pagan J, Mein R, et al. Genotype–phenotype correlation in a large population of muscular dystrophy patients with LAMA2 mutations. *Neurology.* 2010;74(8):727-735.

4. Quijano-Roy S, Sparks S, Rutkowski A. LAMA2-related muscular dystrophy. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. *GeneReviews® [Internet].* Seattle (WA): University of Washington, Seattle; 2005–2023.

Dr Prasanthi, prasanthi.chilaka123@gmail.com, 8333858119