A novel peripherin mutation in young Indian male with sporadic amyotrophic lateral sclerosis

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Case history

- 33-year-old male
- Insidious onset gradually progressive
- Right upper limb weakness - 2.5 years
- Dysarthria, left upper limb weakness-1.5 years
- No h/o LL weakness, diplopia, dysphagia, regurgitation of feeds
- No sensory/bowel/bladder complaints

Examination

- General examination normal
- Neurologic examination
  - HMF normal
  - Tongue wasting, fasciculations+
  - Hyponasal dysarthria, gag normal, palatal arches equal and normal
  - Normal tone all 4 limbs
  - R>L hand muscle wasting
  - Hyperreflexia in UL, Hyporeflexia in LL
  - Normal sensations, no cerebellar signs
  - ALSFRSR score- 31

Investigations

- *NCS*-normal
- No decremental response in RNST
- *EMG*- denervation and chronic reinnervation in cervical, lumbosacral, and bulbar myotomes- definite ALS
- *MRI brain +C spine*- normal
- *Whole exome sequencing* -novel heterozygous missense mutation in exon 1 of the *PRPH* gene (c.490C>T; p.Arg164Trp)
- Mutation confirmed on *Sanger sequencing*
- Segregation analysis revealed a similar mutation in the mother

- 3-month *follow-up*- ALSFRS-R remained stable

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Discussion

- ALS- progressive neurodegenerative disease affecting upper and lower motor neurons
- Mostly sporadic; ~5–10% familial (SOD1, TARDBP, FUS, C9orf72 mutations)
- **Role of peripherin**
  - Type III intermediate filament protein in motor neurons
  - Maintains axonal architecture and regeneration
  - Aggregates found in ALS motor neurons; linked to cytoskeletal disorganization
- **Present case**
  - Novel heterozygous missense *PRPH* mutation (c.490C>T; p.Arg164Trp)
  - Located in conserved rod domain—critical for filament assembly
  - Also found in asymptomatic mother → possible incomplete penetrance
  - Previous studies have reported rare *PRPH* variants (e.g., p.Ser301Cys, p.Asn52Ser) in sporadic ALS, though their pathogenicity remains uncertain
- **Significance**
  - Expands spectrum of *PRPH* variants associated with sporadic ALS
  - Suggests potential modifier or risk factor role in pathogenesis

Conclusion

- We present a novel *PRPH* mutation in a young Indian male with sporadic ALS.
- Further studies are needed to understand the pathogenic role of *PRPH* in ALS progression.