Original Research Paper

Volume - 16 | Issue - 05 | May - 2026 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Neurology

# A HOMOZYGOUS SORD MUTATION CAUSING AUTOSOMAL RECESSIVE DISTAL HEREDITARY MOTOR NEUROPATHY IN AN INDIAN ADOLESCENT: A CASE REPORT


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**ABSTRACT** **Background:** Distal hereditary motor neuropathies (dHMN) are genetically heterogeneous disorders characterized by progressive distal motor weakness with sparing of sensation. Mutations in the SORD gene, encoding sorbitol dehydrogenase, have recently been identified as a common cause of recessive dHMN. **Case Presentation:** We report a 17-year-old boy who presented with 4 years of progressive, symmetrical distal weakness of both lower limbs associated with calf wasting and frequent tripping. There were no upper limb, sensory, bulbar, or autonomic complaints. Neurological examination revealed distal weakness of ankle dorsiflexion and plantarflexion (3/5 bilaterally) with preserved proximal strength, reduced ankle reflexes, and normal sensory findings. Nerve conduction studies showed reduced CMAP amplitudes in peroneal and tibial nerves with preserved velocities and normal sensory responses, consistent with a pure motor axonal neuropathy. Genetic analysis revealed a homozygous SORD c.757delG (p.Ala253GlnfsTer27) pathogenic variant, confirming the diagnosis of autosomal recessive dHMN-8. **Conclusion:** This case highlights the importance of screening for SORD mutations in adolescent-onset pure motor axonal neuropathy, as early genetic diagnosis carries therapeutic implications given ongoing trials of aldose reductase inhibitors.


**KEYWORDS :**

## BACKGROUND

Distal hereditary motor neuropathies (dHMN) are inherited disorders presenting with slowly progressive distal motor weakness and wasting, usually with minimal or no sensory involvement. Over 30 causative genes have been identified, yet a significant proportion of patients remain genetically undiagnosed.

Mutations in the SORD gene, encoding sorbitol dehydrogenase, were first described in 2020 as a frequent cause of autosomal recessive dHMN and Charcot–Marie–Tooth disease type 2 (CMT2). The pathophysiology involves impaired conversion of sorbitol to fructose, leading to toxic accumulation of sorbitol and axonal damage.

We present a case of genetically confirmed SORD-related dHMN in an Indian adolescent with pure lower limb involvement.

## Case Presentation

A 17-year-old left-handed male, born of non-consanguineous parentage, presented with a 4-year history of progressive, symmetrical distal weakness of both lower limbs. He developed tripping, difficulty running, and calf wasting. There were no upper limb complaints, sensory symptoms, cranial nerve involvement, bulbar features, bladder/bowel disturbances, or family history of similar illness.

## Investigations

Examination: The patient was alert, oriented, with normal higher functions. Bilateral calf wasting was noted with preserved extensor digitorum brevis bulk. Motor testing revealed weakness in ankle dorsiflexion and plantarflexion (3/5 bilaterally), while proximal lower limb and upper limb strength were preserved (5/5). Deep tendon reflexes were reduced at the ankles but normal elsewhere. Plantars were flexor. Sensory, cranial nerve, and cerebellar examinations were normal.

Routine labs: CBC, electrolytes, liver and renal function — normal. MRI lumbosacral spine: only mild disc bulges (L4–5, L5–S1), no significant pathology.

NCS/EMG:
- Motor: reduced CMAP amplitudes in peroneal and tibial nerves with preserved conduction velocities. Median and ulnar motor nerves normal.
- Sensory: normal sural and superficial peroneal SNAPs.
- EMG: chronic denervation in distal lower limb muscles.

**Table 1. Nerve Conduction Study Findings in Our Patient Compared with Previously Reported SORD Neuropathy Cases**

| Nerve | Latency (ms) | Amplitude (mV/μV) | Conduction Velocity (m/s) | Our Patient Remarks | Previously Reported SORD cases |
|---|---|---|---|---|---|
| R Peroneal - EDB | 2.38 | 2.0 | 42.6 | Reduced CMAP | Reduced CMAP, preserved CV |
| L Peroneal - EDB | 4.46 | 1.2 | 33.3 | Reduced CMAP | Reduced CMAP, preserved CV |
| R Tibial - AH | 3.52 | 4.5 | 47.7 | Reduced CMAP | Reduced CMAP, preserved CV |
| L Tibial - AH | 4.63 | 6.5 | 52.3 | Reduced CMAP | Reduced CMAP, preserved CV |
| Median (motor) | 3.21 | 16.7 | 56.3 | Preserved | Normal/ Preserved |
| Ulnar (motor) | 3.00 | 11.1 | 54.6 | Preserved | Normal/ Preserved |
| Sural (sensory) | 2.00 | 11.0 | 53.0 | Normal | Normal |
| Superficial Peroneal (sensory) | 2.70 | 5.9 | 51.0 | Normal | Normal |

**Genetic Results**

Clinical exome sequencing revealed a homozygous SORD c.757delG (p.Ala253GlnfsTer27) pathogenic variant, consistent with autosomal recessive dHMN-8.

## DISCUSSION

This case highlights the classical SORD neuropathy phenotype: adolescent-onset, slowly progressive, distal weakness confined to the lower limbs, with sparing of sensation and cranial nerves. Electrophysiology revealed a pure motor axonal neuropathy, matching published descriptions.

The c.757delG variant is the most frequently reported mutation in SORD neuropathy worldwide. Literature indicates that over 70% of genetically confirmed patients carry this homozygous deletion.

Importantly, SORD neuropathy is potentially treatable. Aldose reductase inhibitors such as govorestat (AT-007) are under investigation and have shown promise in reducing sorbitol accumulation, raising hopes for disease modification. Early genetic diagnosis is therefore clinically meaningful.

## CONCLUSION

We report a genetically confirmed case of autosomal recessive dHMN due to SORD c.757delG mutation in an Indian adolescent with pure lower limb involvement. This case expands clinical recognition of SORD neuropathy in South Asia and underscores the importance of genetic testing in unexplained distal motor neuropathies.

**Patient Perspective**

The patient and his family expressed relief at having a definitive genetic diagnosis after years of uncertainty. They were reassured about the non-life-threatening nature of the disorder and expressed willingness to participate in future clinical trials.

**Learning Points**

- SORD mutations are among the most common causes of recessive distal hereditary motor neuropathies.
- Typical phenotype: adolescent-onset, distal motor weakness of lower limbs, sensory sparing.
- NCS shows reduced distal CMAPs with preserved conduction velocities and sensory responses.
- Genetic confirmation is vital due to overlap with CMT2 and other motor neuropathies.
- Disease-modifying therapies (aldose reductase inhibitors) are under development.

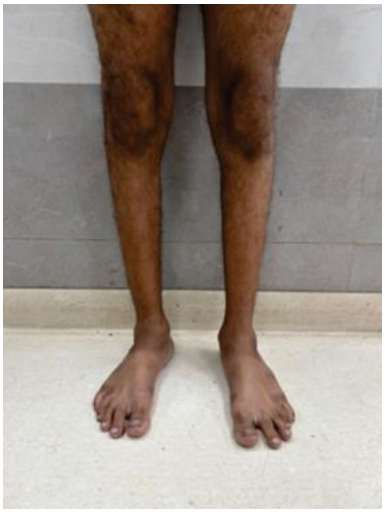

**Figure 1a: Clinical Photograph Showing Bilateral Calf Muscle Wasting.**

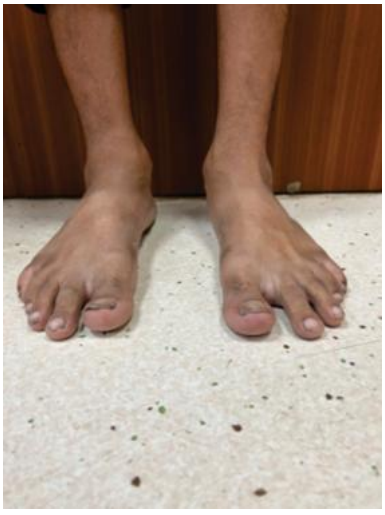

**Figure 1b: Clinical Photograph Showing Bilateral Pes Planus Deformity.**

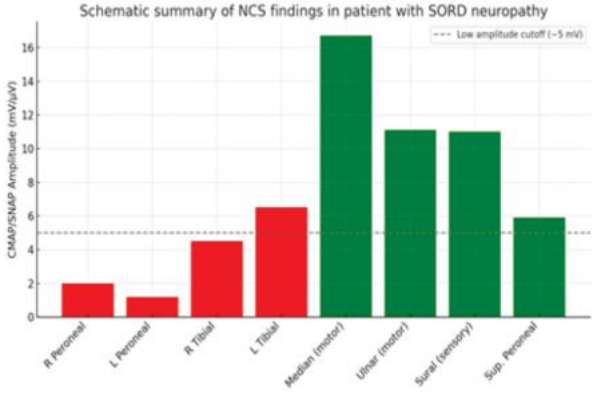


**Figure 2: Schematic Representation of NCS Findings in the Patient Showing Reduced CMAPs in Distal Lower Limb Motor Nerves (Red) with Preserved Upper Limb Motor and Sensory Responses (Green).**

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