# Unveiling neuroradiological and neurophysiological features in a novel proteolipid protein 1 (PLP1) related disorder

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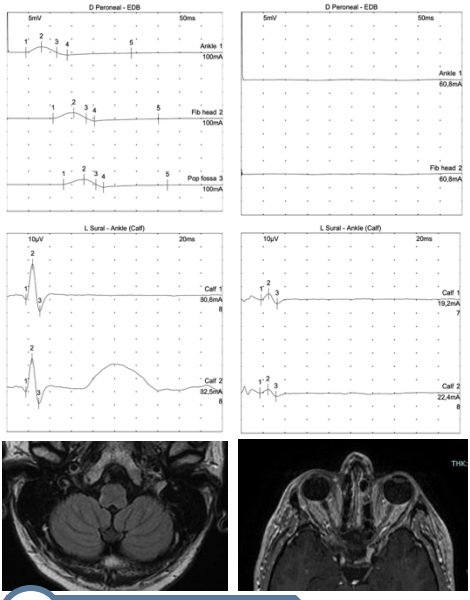
## 1 INTRODUCTION

Antibodies targeting **proteolipid protein-1 (PLP1)** and its peripheral isoform DM20 are predominantly associated with autoimmune demyelinating disorders, particularly MS and MOGAD[1,2], being reported as a negative predictor of disease progression. A recent study demonstrated that anti-PLP1 antibodies are primarily found in patients presenting with myelitis or encephalomyelitis accompanied by PNS involvement.[3]

To highlight possible common neuroradiological and neurophysiological findings, we report two patients presenting with acute motor and sensory axonal neuropathy (AMSAN) exhibiting atypical RM findings. To our knowledge, these are the first reported cases of PLP1 positivity demonstrating this specific neurophysiological and radiological pattern.




## 2 CASE PRESENTATION

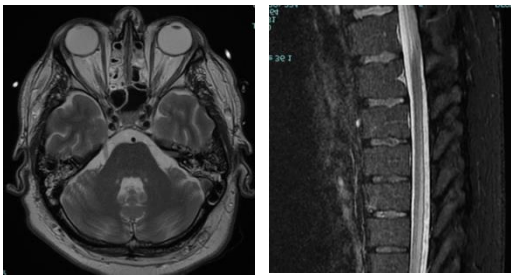
Patients were males aged 39 and 47 years, presenting with **rapidly worsening muscle weakness and cranial nerve involvement**; neither exhibited cognitive impairment or behavioral abnormalities. At onset, symptoms included fever, limb weakness, gait disturbance, and hearing loss.

Neurophysiological studies showed acute motor and sensory axonal neuropathy (**AMSAN**) with a non-length-dependent pattern and cranial nerves involvement, rapidly progressing; MEP and SEP revealed a combined involvement of peripheral and pyramidal efferences.

Neuroimaging showed **CNS involvement**: in one patient, RM detected contrast-enhancing hyperintensities in the optic nerve, left pons and right medulla, also affecting other cranial nerves, cauda equina, and margins of the conus medullaris. The other patient showed pontine signal hyperintensities extending to cerebellar peduncles and posterior cord, with contrast enhancement of both seventh cranial nerves and cauda equina roots.

We screened LCRs for **PLP-IgG** using a cell-based assay: both samples tested positive. All neuroimmunological and infectious assays performed on serum and LCR, including urinary porphyrin quantification, were negative.

Both patients received corticosteroid therapy, plasma exchange, and IVIg. Due to insufficient clinical improvement, one patient underwent additional treatment with Rituximab (1 gram, followed by a second 1-gram dose two weeks later, with cycles administered every 5 months).



## 3 DISCUSSION

Interestingly, despite demyelinating lesions involving CNS, both patients showed neurophysiological features of an Acute Motor and Sensory Axonal Neuropathy (AMSAN) without any evidence of partial or complete "reversible Conduction Failure" (RCF), as demonstrated by seriate electromyographic examinations. These observations raise the hypothesis that PLP1 antibodies may also contribute to axonal injury through mechanisms still to be clarified. The overlap of central and peripheral involvement underscores the importance of considering PLP1 testing in patients with atypical presentations not fitting into classical syndromes.

## 4 CONCLUSION

These cases expand the clinical spectrum of PLP1 autoimmunity to include combined central and peripheral nervous system involvement with axonal pathology and atypical imaging findings. The coexistence of specific demyelinating lesions and AMSAN may suggest a novel nosological entity, though marker specificity remains to be established Although the exact localization of PLP1 antigen has not been elucidated so far, our findings suggest that PLP1 antibodies may serve as biomarkers in autoimmune axonal neuropathies with CNS manifestations, highlighting the need for comprehensive immunological testing in atypical neuropathies to guide diagnosis and treatment.

*Greer JM, Pender MP. Myelin proteolipid protein: an effective autoantigen and target of autoimmunity in multiple sclerosis. J Autoimmun 2008;31(3):281-287.*

*Warren KG, Catz I. Relative frequency of autoantibodies to myelin basic protein and proteolipid protein in optic neuritis and multiple sclerosis cerebrospinal fluid. J Neurol Sci. 1994;121(1):66-73. Masciocchi S, Businaro P, Greco G, et al. Conformational Antibodies to Proteolipid Protein-1 and Its Peripheral Isoform DM20 in Patients With CNS Autoimmune Demyelinating Disorders. Neurol Neuroimmunol Neuroinflamm. 2025;12(3):e200389.*