CASE REPORT

JIACM 2025; 26 (4): 240-43

Autoimmune Nodopathy Masquerading as Guillain-Barré Syndrome

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Abstract

Autoimmune Nodopathies are characterised by antibody-mediated damage of the nodes of Ranvier, thereby affecting the propagation of action potential. We present the case of a 42-year-old woman who initially presented with acute flaccid quadriparesis. Based on clinical and electrophysiological findings, a diagnosis of Guillain-Barré Syndrome (GBS) was made, and the patient was started on intravenous immunoglobulin therapy. However, her condition worsened, and the patient developed bilateral Lower Motor Neuron facial paresis and bulbar weakness, prompting a diagnostic reevaluation. Repeat nerve conduction studies showed absent responses, and cerebrospinal fluid analysis revealed a rising protein level. A nodopathy panel revealed anti-neurofascin-140 antibody positivity, confirming autoimmune nodopathy. The patient responded dramatically to plasmapheresis and was subsequently maintained on rituximab therapy with sustained clinical remission. This case highlights the importance of considering autoimmune nodopathies in patients with atypical or treatment-resistant GBS-like presentations.

Key words: Bulbar palsy, ascending flaccid paralysis, neurofascin, autoimmune nodopathy, Guillain-Barré syndrome.

Introduction

The nodes of Ranvier are specialised unmyelinated segments of axons essential for the rapid conduction of action potentials via saltatory conduction. Flanked by paranodes, these nodes are densely populated with voltage-gated sodium channels and anchoring proteins that stabilise the membrane and secure the membrane protein to the underlying cytoskeleton[1]. One such anchoring protein is Neurofascin[2]. Autoantibodies directed against anchoring proteins such as Contactin, Neurofascin and Gliomedin disrupt the structural and functional integrity of nodes, impairing action potential conduction[3]. Over time, Neurofascin antibodies have been implicated in atypical presentations of Guillain-Barré Syndrome and Chronic Inflammatory Demyelinating Polyneuropathy[4]. Although initially thought to represent a variant of chronic inflammatory demyelinating polyneuropathy, autoimmune nodopathy is now recognised as a distinct entity due to its unique pathophysiology[5].

We present the case of a 42-year-old woman who developed acute-onset flaccid quadriparesis. A provisional diagnosis of Guillain-Barré Syndrome was made based on clinical findings and supporting evidence from nerve conduction studies and cerebrospinal fluid analysis, which showed albuminocytological dissociation. The patient was treated with intravenous immunoglobulin at 2 g/kg. However she deteriorated, and developed bilateral lower motor neuron facial palsy and bulbar weakness. The Nerve Conduction Study showed further worsening. Repeat Cerebrospinal fluid analysis showed an elevated protein level despite completion of the Intravenous immunoglobulin course. Given her treatment-resistant course, the possibility of autoimmune nodopathy was suspected. A Nodopathy antibody panel revealed positive neurofascin - 140 IgG antibodies, confirming the diagnosis. The patient responded dramatically to plasmapheresis and was subsequently maintained on rituximab therapy (every 6 months), achieving sustained remission. She currently performs all activities of daily living independently. This case underscores the importance of early reconsideration of diagnosis in patients with atypical or treatment-refractory Guillain-Barré syndrome presentations.

Case Presentation

A 42-year-old woman with no known co-morbidities presented with a history of difficulty walking for two days and weakness in both upper limbs for one day before admission. She was admitted to the ward with the above complaints.

On examination, hypotonia was present in all four limbs. Muscle power was Medical Research Council (MRC) grade III in the proximal and distal muscles of both lower limbs.

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On examination, hypotonia was present in all four limbs. Muscle power was Medical Research Council (MRC) grade III in the proximal and distal muscles of both lower limbs. Muscle power was MRC grade IV in both upper limbs. Generalised areflexia was noted. Sensory examination revealed absent joint position and vibration sense, with intact pain and temperature sensation. Based on these findings, a provisional diagnosis of polyradiculoneuropathy was considered. Nerve conduction studies (NCS) of all four limbs and cerebrospinal fluid (CSF) analysis were planned to assess for albumino-cytological dissociation. On the second day of admission, the patient's weakness worsened in all four limbs, accompanied by flaccid dysarthria and bilateral lower motor neuron (LMN) facial paresis. Given the progressive course, she was transferred to the medical ICU. The initial NCS showed generalised demyelinating polyradiculoneuropathy with conduction block (Table I).

Table I: Nerve conduction study prior to Intravenous immunoglobulin.

Nerve	Latency (ms)	Amplitude (mV)	Conduction Velocity (m/s)	Interpretation
Left Median (Wrist)	11.25	2.5	54.92	Demyelinating changes with conduction block
Left Median (Elbow)	15.63	1.5	–	Demyelinating changes with conduction block
Left Ulnar (Wrist)	5.31	4.0	58.55	Demyelinating changes with conduction block
Left Ulnar (Elbow)	9.58	3.7	—	Demyelinating changes with conduction block
Right Peroneal (Ankle)	14.27	2.3	35.18	Demyelinating changes with conduction block
Right Peroneal (Knee)	23.65	0.5	—	Demyelinating changes with conduction block
Left Peroneal (Ankle)	21.04	1.9	32.64	Demyelinating changes with conduction block
Left Peroneal (Knee)	31.15	1.0	—	Demyelinating changes with conduction block
Right Tibial (Ankle)	11.56	3.1	35.35	Demyelinating changes with conduction block
Right Tibial (Knee)	21.46	0.8	—	Demyelinating changes with conduction block
Left Tibial (Ankle)	8.65	4.1	—	Demyelinating changes with conduction block

Abbreviations: ms = Milliseconds, mV = Millivolts, m/s = Meters per second.*

CSF analysis revealed elevated protein (84 mg/dL) with no cells, consistent with albumino-cytological dissociation.

A diagnosis of Guillain-Barré syndrome (GBS) was made, and intravenous immunoglobulin (IVIG) was initiated at 400 mg/kg/day for five days. On the third day of admission, the patient developed dysphagia to liquids and solids, along with orthopnoea. She was electively intubated for bulbar symptoms. Supportive measures included physiotherapy, a high-protein diet, and symptomatic medications. Despite completing the IVIG course, no significant clinical improvement was noted. She remained on invasive ventilation and subsequently underwent tracheostomy for prolonged airway support. Repeat NCS performed 10 days after completing IVIG course demonstrated worsening with no recordable potentials in all four limbs (Table II).

Table II: Nerve conduction study post-intravenous immunoglobulin.

Nerve	Latency (ms)	Amplitude (mV)	Conduction Velocity (m/s)	Interpretation
Left Median (Wrist)	–	NR	–	No recordable response
Left Median (Elbow)	–	NR	–	No recordable response
Left Ulnar (Wrist)	–	NR	–	No recordable response
Left Ulnar (Elbow)	–	NR	–	No recordable response
Right Peroneal (Ankle)	–	NR	–	No recordable response
Right Peroneal (Knee)	–	NR	–	No recordable response
Left Peroneal (Ankle)	–	NR	–	No recordable response
Left Peroneal (Knee)	–	NR	–	No recordable response
Right Tibial (Ankle)	–	NR	–	No recordable response
Right Tibial (Knee)	–	NR	–	No recordable response
Left Tibial (Ankle)	–	NR	–	No recordable response

Abbreviations: ms = Milliseconds, mV = Millivolts, m/s = Meters per second.*

Repeat CSF analysis showed a further increase in protein concentration to 270 mg/dL, with no cells present.

Given the patient's rapidly progressive course and poor response to IVIG, the possibility of nodopathy was considered. A CSF nodopathy antibody test was sent, and plasma exchange (PLEX) was initiated, with five cycles on alternate days. Following the initiation of PLEX, gradual improvement was observed in both limb weakness and bulbar symptoms. The patient was subsequently weaned from ventilatory support and initiated on oral feeding. The CSF nodopathy test result was positive for neurofascin - 140 antibodies (Table III).

Table III: Neurofascin 140 antibody - ELISA method.

Test	Result	Reference range	Unit
Neurofascin 140 IgG antibody (ELISA)	342	0 - 233	ng/mL

**Abbreviations: ELISA = Enzyme-linked immunosorbent assay.*

Based on these findings, Rituximab 375 mg/m^2 (two doses, 15 days apart) was initiated. By three weeks of admission, the patient was walking with minimal support. The

tracheostomy was decannulated at an outpatient follow-up. At her most recent visit, she remained functionally independent in daily activities while on a 6-monthly rituximab maintenance course.

Discussion

This case highlights a presentation of autoimmune nodopathy, initially thought to be Guillain-Barré syndrome, due to overlapping clinical features. The patient, a 42-year-old woman, exhibited classical signs of acute inflammatory demyelinating polyneuropathy, including bilateral lower limb weakness, leading to the initial suspicion of GBS. Initially, the NCS suggested generalised demyelinating polyradiculoneuropathy, consistent with GBS, while the CSF analysis revealed albumino-cytological dissociation, a hallmark of this syndrome. However, the absence of response to intravenous immunoglobulin therapy and the subsequent worsening of neurological deficits, as evidenced by deterioration in the nerve conduction study, prompted a re-evaluation of the diagnosis. The increasing trend of CSF proteins and bulbar features further strengthened the suspicion of widespread damage beyond typical GBS[6,7]. Hence a possibility of autoimmune nodopathy was considered. In autoimmune nodopathy, antibody-mediated damage to the nodes of Ranvier results in destruction and detachment of the ion channels, thereby disrupting the depolarisation of the successive nodes. Neurofascin, a critical cell adhesion molecule at the nodes of Ranvier, plays a vital role in stabilising sodium channels essential for proper nerve conduction[8,9].

The nodal and paranodal antibodies primarily belong to the IgG4 class of immunoglobulins, which have a poor affinity for Fc receptors and thus are unable to activate complement[7]. Hence, the patient showed no improvement following the completion of the IVIG course.

The discovery of autoantibodies targeting neurofascin highlights a distinct autoimmune process that can lead to neuropathy with features similar to GBS and CIDP, but diverges in pathophysiology and treatment response[10]. Earlier, autoimmune nodopathy was thought to be a variant of CIDP. However, the acute onset and rapid progression of the disease, coupled with lack of inflammation and macrophage-mediated demyelination, led to the conclusion of Autoimmune nodopathy being a different entity[11].

In this patient's case, after transitioning to plasmapheresis therapy, we observed a significant clinical improvement. The gradual recovery of limb and bulbar strength following plasmapheresis underscores the critical role of timely and appropriate therapeutic interventions in improving outcomes for patients with autoimmune-mediated nerve injuries[9].

The identification of specific autoantibodies can further guide management strategies and provide insight into prognosis. In this case, the follow-up treatment plan included consideration for Rituximab therapy. Rituximab is a chimeric monoclonal antibody against the CD20 antigen primarily found on pre-B and mature B lymphocytes[12]. In patients with nodopathy associated with IgG4 autoantibodies, rituximab has emerged as an effective approach to achieve remission. Rituximab depletes these CD20+ B cells, thereby interrupting the generation of new plasmablasts and reducing the production of IgG4 antibodies[13]. This mechanism is particularly relevant since IgG4 antibodies are functionally monovalent, do not activate complement, and tend to exert pathogenicity via disruption of the paranodal axo-glial junctions, rather than through inflammatory demyelination[13].

This case highlights how early diagnostic reconsideration, particularly in patients presenting with atypical or treatment-resistant forms of demyelinating polyradiculoneuropathy, can lead to a significant shift in management and markedly improved patient outcomes.

Conclusions

Autoimmune Nodopathies are rare, yet important differential diagnoses in patients with atypical or treatment-refractory presentations of Guillain Barré Syndrome. This case highlights the need for timely reconsideration of diagnosis, especially when traditional management fails. Early identification of Autoimmune Nodopathies can significantly influence treatment decisions and underscores the importance of long-term immunotherapy planning to achieve sustained remission.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the consent form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity; however, anonymity cannot be guaranteed.

References

1. Grider MH, Belcea CQ, Covington BP *et al*. Neuroanatomy, nodes of Ranvier. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 (updated 2023 Jul 24).
2. Zhang A, Desmaziere A, Zonta B *et al*. Neurofascin 140 is an embryonic neuronal neurofascin isoform that promotes the assembly of the node of Ranvier. *J Neurosci* 2015; 35 (4): 2246-54.
3. Burnor E, Yang L, Zhou H *et al*. Neurofascin antibodies in autoimmune, genetic, and idiopathic neuropathies. *Neurology* 2018; 90 (2): 31-8.

4. Devaux JJ, Odaka M, Yuki N. Nodal proteins are target antigens in Guillain-Barré syndrome. *J Peripher Nerv Syst* 2012; 17: 62-71.
5. Liu B, Zhou L, Sun C *et al*. Clinical profile of autoimmune nodopathy with anti-neurofascin 186 antibody. *Ann Clin Transl Neurol* 2023; 10: 944-52.
6. Martín-Aguilar L, Lleixà C, Pascual-Goñi E. Autoimmune nodopathies, an emerging diagnostic category. *Curr Opin Neurol* 2022; 35: 579-85.
7. Appeltshauser L, Junghöfer H, Messinger J *et al*. Anti-pan-neurofascin antibodies induce subclass-related complement activation and nodo-paranodal damage. *Brain* 2023; 146 (5): 1932-49.
8. Khadilkar SV, Kamat S, Patel R. Nodo-paranodopathies: concepts, clinical implications, and management. *Ann Indian Acad Neurol* 2022; 25: 1001-08.
9. Van den Bergh PYK, van Doorn PA, Hadden RDM *et al*. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: second revision. *J Peripher Nerv Syst* 2021; 26: e12455.
10. Sharma R, Bellacicco NJ, Husar WG. Pearls and Oy-sters: Breaking Bad CIDP: Recognition of Anti-NF155 Autoimmune Nodopathy in Refractory CIDP. *Neurology* 2024; 103 (10): e209848.
11. Kira J-i. Anti-neurofascin 155 antibody-positive chronic inflammatory demyelinating polyneuropathy/combined central and peripheral demyelination: strategies for diagnosis and treatment based on the disease mechanism. *Front Neurol* 2021; 12: 665136.
12. Kmezic I, Press R, Glenewinkel H *et al*. Low-dose rituximab treatment in a patient with anti-neurofascin-155 IgG4 autoimmune nodopathy. *J Neuroimmunol* 2024; 15: 578326.
13. Martín-Aguilar L, Lleixà C, Pascual-Goñi E. Clinical and laboratory features in anti-NF155 autoimmune nodopathy. *Neurol Neuroimmunol Neuroinflamm* 2022; 9 (1): e1098..