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CASE REPORT

A pediatric case of multifocal motor neuropathy with the conduction block

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ABSTRACT

Background: Multifocal motor neuropathy with conduction block (MMNCB) is a rare immune-mediated motor neuropathy, predominantly seen in adults, with few pediatric cases reported. It presents as asymmetric distal limb weakness without sensory loss. Diagnosis is based on clinical features, nerve conduction studies (NCS), and occasionally anti-ganglioside antibodies, which are less frequently positive in children. Intravenous immunoglobulins (IVIG) are the primary treatment, with corticosteroids and plasmapheresis being ineffective.

Case presentation: We report the case of a 14-year-old boy presenting with progressive, asymmetric limb weakness over one year, beginning with the left foot and later involving all limbs. The weakness affected distal muscles more severely, impairing his mobility and daily activities. Neurological examination revealed reduced muscle tone, generalized areflexia, and preserved sensory function. NCS demonstrated conduction block with temporal dispersion in multiple motor nerves, consistent with MMNCB. Anti-GM1 antibodies were negative, but anti-GM3 and GD1b antibodies were positive. Cerebrospinal fluid analysis showed elevated protein levels without pleocytosis. The patient was treated with IVIG (0.4 g/kg/day for five days) and initiated on occupational and physiotherapy. Significant improvement in muscle strength was observed within three months, with only mild residual weakness.

Conclusion: This rare case highlights the diagnostic challenges of MMNCB in pediatric patients and highlights the importance of clinical and electrophysiological correlation, even in the absence of anti-GM1 antibodies. Early recognition and timely IVIG therapy can lead to remarkable recovery, emphasizing the need for increased awareness of this rare pediatric condition.

Keywords: Multifocal Neuropathy (MeSH); Paraneoplastic Polyneuropathy (MeSH); Demyelination (MeSH); Demyelinating Diseases (MeSH); Intravenous Immunoglobulins (MeSH); Immunoglobulins, Intravenous (MeSH); Child (MeSH); Antiganglioside antibodies (MeSH); Antibodies (MeSH).

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INTRODUCTION

Multifocal motor neuropathy with conduction block (MMNCB) is a rare, acquired motor neuropathy first described in 1986.[1] The prevalence of MMNCB is approximately 0.6 per 100,000 population, with men being more frequently affected than women. The condition primarily manifests in adults. Diagnosing neuropathic processes in children is challenging, and recognizing potentially reversible underlying pathologies is crucial due to their significant therapeutic implications.[2,3]

MMNCB typically presents as asymmetric limb weakness without sensory loss, with the upper limbs more commonly affected than the lower limbs. Distal muscle weakness is more frequent compared to proximal. Patients may experience muscle cramps, fatigability, twitching, or fasciculations, while bulbar or respiratory involvement is rare. Sensory symptoms are minimal or absent. As an immune-mediated neuropathy, the pathophysiological mechanism involves the formation of anti-ganglioside antibodies (GM1) targeting the myelin sheath, causing delayed saltatory conduction and resulting in limb weakness.

Diagnosis is based on core clinical features outlined by the European Federation of Neurology Task Force,[3] as detailed later in this article. Supporting diagnostic findings include conduction block at non-compressible sites on nerve conduction studies (NCS) and the presence of antiganglioside antibodies. Pediatric and adult MMNCB cases show slight variability. Literature indicates that approximately 43% of adult MMNCB cases test positive for anti-GM1 antibodies, while most pediatric cases rely on clinical evaluation, with only one reported instance of anti-GM1 antibody positivity.[4,5]

Management involves intravenous immunoglobulins (IVIG), as corticosteroids and plasmapheresis are ineffective in MMNCB but are treatments of choice for other inflammatory demyelinating neuropathies. For resistant cases, immunomodulators such as Azathioprine, Rituximab, Eculizumab, and Cyclophosphamide may be considered.[6]

CASE REPORT

A 14-year-old boy presented with progressive, asymmetric weakness in all four limbs over the past year. The weakness initially affected his left foot, noticeable by a high-steppage gait. After four months, similar symptoms developed in his right foot, followed by weakness in both hands a month later, leading to difficulty writing and buttoning his shirt. There was no history of preceding fever, diarrhea, or respiratory infections. The family reported increasing fatigue and recurrent falls. The patient was born full-term with an unremarkable birth history, achieved all developmental milestones, and had age-appropriate cognitive abilities. He was currently an

8th-grade student. There was no significant family history of similar illness.

A detailed neurological examination revealed normal higher mental functions and cranial nerve assessments. Motor examination showed normal muscle bulk, no wasting or fasciculation, reduced tone, and power graded using the Medical Research Council (MRC) scale, as shown in Table I.

Sensory examination indicated intact joint position and vibration sensations with no dermatomal sensory loss. Reflexes were absent (generalized areflexia), and plantar responses were flexor. Cerebellar signs were not assessed due to weakness.

The patient was referred to a neurophysiology lab for nerve conduction studies (NCS) and electromyography (EMG), alongside baseline laboratory evaluations. The detailed findings from NCS and EMG are presented in Tables II and III, respectively. NCS/EMG findings revealed conduction block with temporal dispersion at non-entrapment sites in the bilateral ulnar and left median nerves. These nerves also exhibited slowed conduction velocities and either non-recordable or prolonged F-wave responses. Motor nerves in the lower limbs showed prolonged distal latencies and markedly low CMAP amplitudes (normal peroneal CMAP > 3 mV). Sensory responses were normal in all four limbs. These findings were consistent with multifocal motor neuropathy with the conduction block.

Baseline laboratory investigations, including CBC, urea, creatinine, electrolytes, calcium, magnesium, albumin, TSH, and vitamin B12 levels, were all within normal limits. Lumbar puncture revealed a CSF profile of glucose 67 mg/dL (normal range: 60–80), protein 219 mg/dL (normal range: 15–40), and 5 cells/mm^3 (normal up to 5). Although anti-GM1 antibodies were negative, anti-GM 3 and GD1b antibodies were positive.

The diagnosis of MMNCB was established based on EMG/NCS findings and clinical correlation. The patient was treated with five doses of intravenous immunoglobulin (IVIG) at a dose of 0.4 g/kg/day. Occupational and physiotherapy were initiated alongside IVIG therapy. The patient showed remarkable improvement over three months, regaining nearly full strength with only mild residual weakness. The family was counseled about the potential need for repeat IVIG doses in the event of symptom recurrence.

DISCUSSION

Multifocal motor neuropathy with conduction block is one of the acquired neuropathies which are reversible on the appropriate management. Our case emphasizes the significance of identifying this uncommon disease within a young population. It has been rarely reported in children. The table below (Table III) discusses a total of five reported cases, and our case constitutes the sixth instance of this rare diagnosis.[1,2,7-9] Patients with MMNCB typically present with asymmetrical muscle weakness, which follows a subacute to chronic course, similar to our observed scenario. The initial complaints may include wrist drop or foot drop. During clinical examination, certain characteristic features become evident, such as distal muscles being more affected than proximal muscles. Interestingly, individual nerves within the same myotome might be involved, with some nerves showing sparing.[10,11] Our case fulfilled the core clinical criteria made by European Federation of neurological societies and task force for the diagnosis of MMNCB.[3] This includes slowly progressive or stepwise progressive, focal, asymmetric limb weakness, that is, motor involvement in the motor nerve distribution of at least two nerves, for more than 1 month with no objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs. features which are considered as supportive for diagnosis are nerve conduction study and electromyography with the focus on conduction block at non-compressible sites. Conduction block is defined as a more than 50% reduction in compound muscle action potential (CMAP) amplitude or area between proximal and distal nerve stimulation site. The other factor includes elevated IgM anti-ganglioside GM1 antibodies-Anti-GM1 antibodies and increased cerebrospinal fluid protein (< 1 g/l).[3]

Gangliosides are a type of glycosphingolipid that contain sialic acid residues and are present on the cell membrane surface of various tissues, particularly nerve cells. In certain neuropathic conditions, antibodies mistakenly target gangliosides present on nerve cells, leading to inflammatory responses and damage to the peripheral nerves. These antibodies are

Table I: The medical research council grading for muscle power of the subject

Site		Right	Left
Upper Limb	Deltoid	5/5	5/5
	Biceps	5/5	5/5
	Triceps	5/5	5/5
	Extensor Carpi Radialis	4/5	4/5
	Flexor Carpi Radialis	0/5	0/5
	Palmar & Dorsal Interossei	0/5	0/5
Lower Limb	Glutei	5/5	5/5
	Hamstring	5/5	5/5
	Quadriceps	5/5	5/5
	Tibialis Anterior	0/5	0/5
	Gastrocnemius	2/5	2/5

Table II: Motor nerve conduction studies of the subject

Nerve-Muscles		Latency (ms)	Distance (cm)	Amplitude (mv)	NCV (ms)	F.LAT.(ms)
Post. tibial AH* (L)	Ankle	No Response				
	Knee					
Peroneal EDB* (L)	A					
	DK					
	PK					
Peroneal TA* (L)	DK	8.0	10.0	140uv		
	PK	11.8	10.0	100uv		
Post. tibial AH (R)	A	No Response				
	K					
Peroneal EDB* (R)	A					
	DK					
	PK					
Peroneal TA (R)	DK	7.8	10.0	200uv	-	-
	PK	11.4	10.0	110uv	27.8	-
Median APB* (R)	W	4.9	7.0	5.2	-	NR
	E	13.8	20.0	5.2	24.2	-
Ulnar ADQ* (R)	W*	4.2	7.0	3.0	-	NR
	DE*	12.0	18.0	270uv	20.8	-
	PE*	16.9	10.0	130uv	23.8	-
Median APB (L)	W	4.7	7.0	5.9	-	32.3
	E	13.3	21.0	1.7	24.0	-
Ulnar ADQ (L)	W	4.0	7.0	3.2	-	NR
	DE	12.5	18.0	490uv	21.2	-
	PE	16.0	10.0	150uv	22.0	-
Radial EIP (R)	F.A	2.7	10.0	3.5	-	-
	Triceps	7.2	15.0	2.0	33.0	-
Radial EIP (L)	F.A	2.7	10.0	3.8	-	-
	Triceps	6.3	15.0	2.2	42.3	-

*AH: abductor halluces; TA: Tibialis anterior; EDB: extensor digitorum brevis; APB: abductor pollicis brevis; ADQ: adductor digiti quinti; EIP: extensor indicisproprius; FA: forearm; W: wrist; DE: distal elbow; PE: proximal elbow

collectively called anti-ganglioside antibodies. Anti GD1 b and anti GM 3 found to be associated with ataxic sensory variants of GBS. These antibodies are not specific to GBS and they are found in limited cases.[12] In our described case, anti GD1b and GM3 were present but the long clinical course and pure motor weakness is against the diagnosis of any acute neuropathy like GBS. We think further case series are required to study the role of pathogenic antibodies other than antiGM1 in the pediatric population of MMNCB.

IV immunoglobulins remained the main pharmacological treatment for patients

Table III: Electromyography of the subject

Muscles	Spontaneous Activity			Motor Units			
	Fibs*	PSW*	Others	Amp	Duration	Polys	Recruit
Rt. APB	Nil	Nil	None	High	Broad	No	Decreased
Rt. Deltoid	Nil	Nil	RFR*	High	Broad	+	Decreased
Rt. Gastroc	Nil	Nil	RFR	High	Broad	+	Decreased
Rt. TA*	++	++	RFR	High	Broad	+	Decreased
Rt. VM*	+	+	RFR	High	Broad	+	Decreased
Lt. Gastroc	++	++	RFR	High	Broad	+	Decreased
Lt. TA	+	+	RFR	High	Broad	+	Decreased
Lt. VM	+	+	RFR	High	Broad	+	Decreased
Lt. FDI	Nil	Nil	RFR	High	Broad	+	Decreased
Lt. Biceps	Nil	Nil	RFR	High	Broad	+	Decreased
Lt. EDC*	++	++	RFR	High	Broad	+	Decreased
Lt. APB*	++	++	RFR	High	Broad	+	Decreased
Lt. FDI*	++	++	RFR	High	Broad	+	Decreased
Lt. Deltoid	Nil	Nil	None	Normal	Normal	No	Normal
Rt. EDC	++	++	RFR	High	Broad	+	Decreased
Rt. FDI	++	++	RFR	High	Broad	+	Decreased
Rt. Biceps	Nil	Nil	None	Normal	Normal	No	Normal

*APB: abductor pollicis brevis; TA: tibialis anterior; VM: vastus medialis; FDI: First dorsal interossei; EDC: extensor digitorum indicis; RFR: rapid firing rate; PSW: positive sharp waves; Fibs: Fibrillation potential.

with MMNCB. More than three-quarters of patients respond to IVIG, while 20% receive prolonged remission. Our patient responded well on IVIG and on follow up, improving day by day.13 IVIG is administered at a dose of 0.4 g/kg/day for five days. Some clinicians administer IVIG in 2 days by administering at 1 g/kg per day. The follow-up maintenance IVIG infusion dose ranges from 0.4 g/kg once weekly to 2 g/kg every 8 weeks depending upon the patient's condition. We only administered 5 daily doses to our patient. In refractory cases, the treatment options are immunomodulatory agents such as cyclophosphamide, mycophenolate mofetil, azathioprine, and rituximab. Oral cyclophosphamide has been reported effective in sustaining disease remission but caution is with its side effects.[14] Multiple comparative randomized controlled trials (RCTs) are needed to establish the efficacy of immunomodulatory drugs in MMNCB. The prognosis for this condition is generally favorable, with approximately 70-80% of patients showing a positive response to treatment. Even in cases where therapy is not effective, weakness tends to progress slowly, and a significant majority of patients, up to 94%, are able to maintain their employment.

In conclusion, our case underscores the importance of considering MMNCB as a potential diagnosis in children with progressive asymmetric limb weakness. Early recognition and prompt initiation of appropriate treatment, such as IVIG, can lead to favorable outcomes in these patients. Further studies and more reported cases are needed to better understand the unique aspects of MMNCB in the pediatric population and optimize its management.

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Table IV: Comparison between the prior reported cases of multifocal motor neuropathy with the conduction block

Patient	1	2	3	4	5	Our
Age/Gender	6/M*	12/M	10/M	8/M	9/M	14/M
Prodrome	-	Chest Infection	-	-	-	-
Affected muscles	Bilateral upper limbs	Bilateral foot and hand	Left upper limb	Left upper limb	Bilateral upper limb	Bilateral foot and hand
Cranial nerve involvement	-	-	-	-	-	-
Sensory disturbance	-	-	-	-	-	-
EMG/NCS	CB	CB	CB	CB	CB	CB
Antibodies to gangliosides	-	Anti GQ1 b	NS6S-IgM	GM1,GM2	GM2,GD1a	GM3,GD1b
Interval (onset to treatment)	4 years	5 days	2 years	6 months	4 years	1 years
Treatment	IVIG	IVIG	IVIG	IVIG	IVIG	IVIG
Authors	Moroni I,et al[1]	Ramdas S,et al[2]	Edelman F,et al[7]	Ishigaki H,et al[8]	Maeda H,et al[9]	-

*M: male; CB: conduction block; EMG: Electromyography; NCS: Nerve conduction studies

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AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

SZ & M: Identification, diagnosis and management of the case, drafting the manuscript, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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