ORIGINAL SCIENTIFIC ARTICLES

Multifocal Acquired Demyelinating Polyneuropathy In A Filipino Adult Male: A Case Report

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ABSTRACT

Multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) is a variant of chronic inflammatory demyelinating polyneuropathy (CIDP). It presents as a chronic, asymmetrical sensory-motor polyneuropathy with features of demyelination on nerve conduction studies. Management options include intravenous immunoglobulin and corticosteroid infusions. Prognosis is generally favorable but there have been reports of variable response to treatment. This condition is rare and local data on CIDP and its variants is limited, hence we report a case of a 64-year-old male presenting with 3 year history of progressive asymmetric numbness and weakness of all limbs. Sensory deficits began on the left hand and had progressed to involve the distal portions of all limbs, eventually developing weakness as well. The patient underwent multiple nerve-conduction studies, all of which showed findings congruent with MADSAM. He was given intravenous high dose methylprednisolone and was maintained on mycophenolate mofetil.

***Keywords**: Multifocal acquired demyelinating polyneuropathy (MADSAM); Chronic inflammatory demyelinating polyneuropathy (CIDP); multifocal CIDP; Methylprednisolone; Mycophenolate mofetil; case report*

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy is a rare chronic immune-mediated polyneuropathy with a prevalence of about 0.8-8.9 per 100,000.[3] Multifocal acquired demyelinating sensory and motor neuropathy or MADSAM is one of the 5 recognized variants of CIDP.[11] Diagnosis of this condition requires the fulfillment of clinical and electrodiagnostic criteria. The best treatment regimen has not yet been clearly established but first line modalities include corticosteroids, intravenous immunoglobulin (IVIg), and plasmapheresis. Response to treatment and prognosis is generally favorable but it still results in morbidity and treatment of the condition would last years. Treatment duration requires a maintenance period which poses risk for adverse events and significant economic burden for the patients, especially in the local setting where data on CIDP is limited. Here, we present a case of MADSAM, with progressive numbness and weakness of the extremities. He was given high dose methylprednisolone pulse therapy and was maintained on mycophenolate mofetil. This report aims to add on local data and raise awareness about CIDP.

CASE PRESENTATION

A 64-year-old man presented with a 3-year history of progressive numbness. The numbness had started on his left hand, described as feeling as if his skin was thicker on that part of his body. Consult was sought and nerve conduction studies were done. The test showed evidence of a chronic progressive sensorimotor demyelinating neuropathy

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Table 1. Neurologic Examination Findings

Motor Examination		
Normal tone Atrophy of the left thenar and hypothenar eminences, and interossei muscles No spasticity No rigidity No clonus		
Muscle Strength:	Right	Left
Neck Flexion	5/5	5/5
Neck Extension	5/5	5/5
Shoulder Abduction	5/5	5/5
Shoulder Adduction	5/5	5/5
Forearm Flexion	5/5	4/5
Forearm Extension	5/5	5/5
Wrist Extension	5/5	4/5
Wrist Flexion	5/5	4/5
Finger Abduction	5/5	3/5
Finger Adduction	4/5	3/5
Hand Grip	4/5	3/5
Hip Flexion	5/5	5/5
Hip Extension	5/5	5/5
Hip Abduction	5/5	5/5
Hip Adduction	5/5	5/5
Knee Flexion	5/5	5/5
Knee Extension	5/5	5/5
Foot Dorsiflexion	3/5	4/5
Foot Plantarflexion	5/5	5/5

Sensory Examination	Right	Left
Crude Touch, Pain, Temperature		
Upper Extremities	90% intact over the palmar aspect	70% intact over the palmar aspect
Lower Extremities	Intact	90% intact over the plantar aspect
Proprioception		
Upper Extremities	Intact	Intact
Lower Extremities	Intact	Intact
Vibration		
Upper Extremities	Impaired	Impaired
Lower Extremities	Impaired	Impaired
Romberg's Test: NEGATIVE		

Muscle Stretch Reflexes	Right	Left
Biceps	1(+)	0
Triceps	1(+)	0
Brachioradialis	0	0
Patella	1(+)	1(+)
Ankle	0	0

Pathologic Reflexes	No Babinski No Hoffman

Table 2. Nerve Conduction Studies done in 2024

Sensory Nerve Conduction

Nerve and Site	Onset Latency	Peak Latency	Amplitude	Latency Difference	Distance	Conduction Velocity
Sural L	No response					
Sural R	No response					
Superficial peroneal L	No response					
Superficial peroneal R	No response					
Median R						
Wrist	No response					
Palm	No response					
Ulnar R	No response					
Radial R	1.4 ms	2.3 ms	10 uV	2.3 ms	80 mm	57 m/s
Median L						
Wrist	No response					
Palm	No response					
Ulnar L	No response					
Radial L	1.6 ms	2.4 ms	17 uV	2.4 ms	90 mm	56 m/s

Motor Nerve Conduction

Nerve and Site	Latency	Amplitude	Latency Difference	Distance	Conduction Velocity
Tibial L					
Ankle	91 ms	2.5 mV	9.1 ms		
Popliteal fossa	23.3	1.8 mV	14.2 ms	430 mm	30 m/s
Tibial R					
Ankle	9.8 ms	2.0 mV	9.8 ms		
Popliteal fossa	23.6 ms	2.3 mV	13.8 ns	410 mm	30 m/s
Peroneal L					
Ankle	No response				
Fibula	No response				
Popliteal fossa	No response				
Peroneal R					
Ankle	No response				
Fibula	No response				
Popliteal fossa	No response				
Median R					
Wrist	10.5 ms	5.3 mV			
Elbow	16.7 ms	5.7 mV	6.2 ms	240 mm	39 m/s
Ulnar R					
Wrist	5.7 ms	8.4 mV	5.7 ms		
Below elbow	11.5 ms	7.2 mV	5.8 ms	250 mm	43 m/s
Above elbow	15.4 ms	1.7 mV	3.9 ms	50 mm	13 m/s
Median L					
Wrist	11.9 ms	9.8 mV			
Elbow	18.3 ms	9.2 mV	6.4 ms	240 mm	38 m/s
Ulnar L					
Wrist	No response				
Below elbow	No response				
Above elbow	No response				

F-Wave Studies

Nerve	F Latency
Tibial L	No response
Tibial R	No response
Median R	45.5
Ulnar R	39.1
Median L	45.5
Ulnar L	No response

H-Wave Studies

Nerve	H- Latency
Tibial L	No response
Tibial R	No response

congruent with the multifocal variant of chronic inflammatory demyelinating polyneuropathy (CIDP). The patient was then advised to observe his symptoms and repeat nerve conduction studies after a few months.

In the interim, numbness gradually progressed to involve his right hand and both feet. Numbness was worst on his left hand and was eventually associated with weakness of grip. The patient was worked up for systemic conditions such as diabetes, kidney disease, hypothyroidism, and vasculitis, and they were subsequently ruled out. A follow up nerve conduction study was done after a year which showed progression in the severity of nerve conduction abnormality. The patient was started on pregabalin and food supplements and was again advised to do a follow up nerve study.

The patient's symptoms persisted despite intake of medications. The persistence and progression of symptoms prompted the patient to seek further work up. About a year later, he did another nerve conduction study which showed further progression of the nerve injury. The patient was admitted and underwent a lumbar tap. He was then given methylprednisolone pulse therapy at 1 gram intravenously once daily for 3 days and was sent home on mycophenolate mofetil 500 mg/tab, 1 tab once daily.

Table 3. Cerebrospinal Fluid analysis results.

TEST	UNIT	RESULT
Opening Pressure: 13 cm H2O Closing Pressure: 8 cm H2O Clear, free flowing, colorless fluid		
Red Blood Cells	$x10^6/L$	5
White Blood Cells	$x10^6/L$	0
Total Cell Count	$x10^6/L$	5
CSF Protein	15-45 mg/dL	1489
CSF Glucose	40-70 mg/dL	55.14

DISCUSSION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic immune-mediated polyneuropathy. Prevalence varies per location but is reported to be anywhere from 0.8 to 8.9 per 100,000 people, with a 1:2 male predominance.[3] CIDP is characterized by a progressive or relapsing disease course evolving over a period of more than 8 weeks, with an electrophysiological or pathological evidence of peripheral nerve demyelination, and a positive response to immunosuppressive therapies.[11] The European Academy of Neurology and the Peripheral Nerve Society (EAN/PNS) Joint Task Force recognizes 6 clinical forms of CIDP, 1 typical and 5 variants, varying based on the presence of motor or sensory symptoms, their distribution, and the symmetry of the deficits.[11] Multifocal CIDP if one of the 5 recognized CIDP variants.

Multifocal CIDP, MADSAM, or Lewis Sumner Syndrome, was first reported in 1982 by Lewis and colleagues describing a chronic asymmetric sensorimotor neuropathy, mostly of the upper extremities with multifocal involvement of the peripheral nerves, with predominance of distal extremity involvement.[10] Here we present a patient with chronic progressive asymmetrical sensory and motor deficits which began the left hand and is mostly contained in the distal extremities, fitting the classic clinical feature of a multifocal CIDP.

The EAN/PNS Joint Task Force released a guideline on the diagnosis and treatment of chronic inflammatory demyelinating polyradiculopathy. The diagnosis requires the fulfillment of clinical and electrographic criteria.[11] On electrophysiologic testing, nerve conduction studies should show motor conduction abnormalities in at least 2 nerves in more than 1 limb and sensory conduction abnormalities in at least 2 nerves of the affected limbs. Our patient had undergone 3 nerve conduction studies in a span of 3 years, all showing evidence supportive of multifocal CIDP. His first NCV done in 2022 showed

distal motor nerve latency prolongation more than 50% above the upper limit on the both median nerves and both peroneal nerves, fulfilling the motor nerve conduction criteria. Sensory nerve conduction testing showed absence of response on the bilateral median and ulnar nerves, also fulfilling the sensory criteria. Subsequent testing only showed worsening of conduction abnormalities.

There are 3 first line treatment options recommended for the management of CIDP, namely corticosteroids, IVIg, and plasmapheresis.[4,5,7,11] It is notable that the best treatment regimen has not yet been clearly established but all three options have been shown by randomized clinical trials to be effective in the treatment of CIDP, showing significant improvement of symptoms over no treatment. Immunosuppressants such as cyclophosphamide, azathioprine, mycophenolate mofetil, and cyclosporin have been described in case series to show benefit in cases of CIDP refractory to the initial treatment or those with unsatisfactory response to initial treatment.[7] These agents may also be added as adjunct in patients on long term corticosteroid maintenance therapy to decrease the steroid doses being taken by the patient. Treatment duration, tapering, and long-term outcomes are an area of study that may be further explored. The general goal of treatment is to taper medications to discontinuation or at least to the lowest possible dose that will not result in relapse or progression of symptoms. Our patient underwent methylprednisolone pulse therapy and was sent home on mycophenolate mofetil. Mycophenolate mofetil (MMF) was chosen to avoid the long-term use of steroids and its adverse effects. Studies such as the 2010 report done by Bedi et al describe the efficacy and safety of MMF in the treatment of CIDP as an adjuvant therapy or as initial monotherapy.[2] Reports have shown typical CIDP to have better response to treatment compared to some of the the CIDP variants. Niu and colleagues recently published a report describing a Chinese cohort of CIDP patients followed up from March 2015 to March 2023.[8] They found that the MADSAM variant had a higher relapse rate than typical CIDP and the other variants reported, albeit not a statistically significant difference. This reflects the findings reported by Kuwabara and colleagues in a 2014 study including 100 patients with CIDP.[6] They reported that all 51 patients with typical CIDP included in the study were found to be responsive to at least 1 of the 3 first line treatments, whereas 23% of the 34 MADSAM patients reported were found to be refractory to any of the therapies. The reason behind this variability in treatment response remains unknown. One factor may be disease duration, with patients having longer disease durations being generally less responsive to treatment due to possible secondary axonal degeneration.[4,5] If this observation was to be applied to this case, this would make our patient difficult to treat. The patient was followed up about 3 months on MMF and reports persistence of numbness and feeling of paresthesia on his distal extremities, but no notable progression in the severity of deficits. He would have to be observed for a longer amount of time to assess response.

The duration of treatment and the available treatment options also pose significant financial burden for patients, especially in the local setting. The costs of hospitalization, the diagnostic tests, and the choices for management would be too hefty for the common Filipino citizen. The need for repeated infusions or maintenance therapy would further encumber the patient and their family. Further research is needed on this topic to ascertain the best regimen and the most cost-effective approach. Local data on CIDP, let alone MADSAM and the other variants, is lacking. This report aims to contribute to local data in the hopes of raising awareness locally about this condition.

CONCLUSION

We report a case of MADSAM seen in a 64-year-old male. There is limited data on the exact prevalence of the condition, even more so in the local setting, and the best

treatment regimen for CIDP has not yet been clearly established. MADSAM has been shown to have variable response to the different first line and adjunct treatments. This opens an area for research in the hopes of finding more effective and readily accessible treatment options for patients with MADSAM. Moreover, in a resource-deficient setting such as the Philippines, the cost of treatment of CIDP poses a significant financial burden on the patient which makes it more difficult to decide on the treatment modality to be given to a patient. Further research is needed to ascertain the best and mort cost-effective approach to the management of this condition.

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