Multifocal Motor Neuropathy With Anti-GM1 Antibody: A Filipino Case Report

Gabriel Alejandro B. Baroque, MD, Mary Lou Anne Y. Cabacang, MD, Alejandro C. Baroque, MD

ABSTRACT

As far as we are aware of, we report the first documented case of a 51-year-old Filipino female with multifocal motor neuropathy who presented with asymmetric weakness, unusually in the lower extremity, and confirmed with anti-GM1 antibody.

The treatment of intravenous immunoglobulin with a total dose of 2 g/kg was initiated and repeated every two months with noticeable improvement based on electromyography and nerve conduction studies.

Apart from the unreported Filipino case of multifocal motor neuropathy substantiated by features in clinical, electrophysiologic, antibody testing and response to immunotherapy, the unique occurrence in a female and involving the lower extremity in this rare disorder deserve this present documentation. Multifocal motor neuropathy is seen more in males with a ratio of 2.7:1. It is described as a pure motor disease without sensory deficits and predominantly affects the upper extremities. The diagnosis for the disorder is supported by determination of ganglioside GM1 antibodies.

Keywords: multifocal motor neuropathy, case report

INTRODUCTION

The aim of the report is to document, for the first time, a case of multiple motor neuropathy (MMN) in a Filipino who presented with asymmetric weakness and confirmed as having high anti-GM1 antibody titers coupled with abnormalities in electromyography (EMG) and nerve conduction studies (NCS).

MMN is a rare disorder which was reported in 1986 by Chad, et al.[1] It is described as asymmetric motor weakness which is seen more on the upper extremities without sensory deficits.[2-8] This can be associated with fasciculations and cramping.[2] MMN has a prevalence of 0.6 per 100,000 individuals where males are predominantly involved with a ratio of 2.7:1.[6,9]

Pestronk, et al.,[10,11] described MMN to be associated with elevated ganglioside GM1 antibodies. [10] GM1 is localized in both the myelin and axolemma of peripheral nerves. The greatest population is found in the nodes of Ranvier.[6] This is the basis for the immunologic pathology associated with MMN.

The clinical criteria based on the European Federation of Neurological Societies/Peripheral Nerve Society are divided into three separate criteria. A) The core criteria; wherein the patient must manifest with: one, 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 one month (if symptoms and signs are present only in the distribution of one
nerve, only a possible diagnosis can be made). Two, no objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs. B) Supportive clinical criteria are: 1. Predominant upper limb involvement, 2. Decreased or absent tendon reflexes in the affected limb, 3. Absence of cranial nerve involvement, 4. Cramps and fasciculations in the affected limb, 5. Response in terms of disability or muscle strength to immunomodulatory treatment. C) The exclusion criteria are: 1. Upper motor neuron signs, 2. Marked bulbar involvement, 3. Sensory impairment more marked than minor vibration loss in the lower limbs, 4. Diffuse symmetric weakness during the initial weeks.[4,6]

Electrophysiologic criteria for MMN are as well divided into three categories: Definite motor conduction block, probable motor conduction block and normal sensory nerve conduction in the upper limb segments with conduction block.[4,6]

The other supportive criteria in the diagnosis of MMN are elevated immunoglobulin M (IgM) anti-GM1 antibodies, an increased cerebrospinal fluid (CSF) protein (<1 g/l), magnetic resonance imaging associated with a diffuse nerve swelling of the brachial plexus and clinical improvement following intravenous immunoglobulin (IVIg) treatment.[4,6]

**Patient Information:**

The patient is a 51-year-old female from the Philippines who presented with chronic left foot weakness. In 2009, the patient experienced left foot drop with no other accompanying symptoms such as numbness, back pain, paraesthesias and bowel/bladder incontinence. There was no history of any previous surgeries or trauma. During this time, EMG and NCS of the lower extremities were done which showed a left peroneal neuropathy and conduction block on the right ulnar nerve. She was advised to undergo exploration of the nerve; however, the patient declined and opted for medical management. She underwent a series of rehabilitations and was given Vitamin B complex tabs which afforded vague subjective improvement. In June 2018, a subsequent follow-up required a repeat EMG and NCS that now showed involvement of the left upper extremity.

**Clinical Findings:**

Upon a consult with us, there were no cognitive deficits and cranial nerve examination was not yielding. In particular, the eye movements were full and there was no tongue atrophy or fasciculations. Cerebellar examination was considered to be good. The patient’s right wrist flexors, bilateral hip flexors and right dorsiflexion/plantar flexion had a manual motor testing of 4/5. Her left knee flexion and left dorsiflexion/plantar flexion were noted to be weaker, compared to her other weak joint movers, having a manual motor testing of 2/5. The patient also could not move her toes on her left foot. There was noted atrophy on her left tibialis anterior muscle and abductor hallucis longus (Figure 1). There were no sensory deficits and deep tendon reflexes were normoactive over both upper extremities and hyperactive over both lower extremities. Hoffman’s and Babinski signs were not present and the jaw jerk was normal.

**Diagnostic Assessment:**

EMG and NCS done in November 2018 revealed that the right median and right ulnar nerves had conduction block at the level of the elbow up to the supraclavicular fossa and at the level of the axilla.
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up to the supraclavicular fossa, respectively. There was reduced to absent, compound muscle action potential (CMAP) amplitudes on the bilateral peroneal and bilateral tibial nerves. There were normal F wave responses on the right median, right ulnar and right tibial nerves. Sensory nerve conduction studies showed normal results. On needle examination, there was active denervation with chronic neurogenic changes on the muscles tested. These findings are consistent with MMN. (Figures 2-3).

Anti-GM1 antibody test was done in December 2018 which revealed a high titer of 1:12800 (Normal: <1:800).

Intervention:
Intravenous immunoglobulin (IVIg 2 g/kg spread over five days) was administered in December 2018, and marked improvement of left knee flexion and plantar flexion were observed, yet plantar

Figure 2. Serial nerve conduction studies (NCS) of the right ulnar nerve. Comparing the NCS done in November 2018 (A) and June 2019 (B), there is noted improvement of the CMAPs gleaned from proximal partial conduction blocks.

Figure 3. Serial nerve conduction studies (NCS) of the left peroneal motor nerve, showing absent evoked responses, comparing the NCS done in November 2018 (A) and June 2019 (B).
dorsiflexion remained weak. The patient now was also able to move her toes on her left foot.

**Followup and Outcomes:**
Follow-up IVIg same dose infusions were made in February and April 2019 and gradual motor strength improvements of the affected extremities continued.

A repeat electromyography-nerve conduction velocity (EMG-NCV) in June 2019 showed significant improvement in the ulnar motor NCS which previously showed conduction block on stimulation at the Erb’s point, although with decreased CMAP amplitude. Left peroneal motor nerve conduction studies show increased CMAP amplitude. There was presence of F-wave response on the right ulnar nerve. On needle examination, there was absence of the previously noted spontaneous discharges in the right medial head of the gastrocnemius, left tibialis anterior, right first dorsal interosseous and right biceps brachii. In conclusion, there was improvement in the NCS and needle EMG (Figures 2-3).

However, after the hospital admission in April 2019, she was lost to followup until August 2019 wherein she complained of being unable to move her toes on the left foot with difficulty on plantar flexion. She still could not do dorsiflexion. Now, she was complaining of right hand weakness as well. Motor examination showed a finger abduction of 1/5 on both hands, left knee extension of 2/5, dorsiflexion and plantar flexion of the left foot 2/5.

On admission in August 2019, she underwent infusion of IVIg for five days and on discharge she showed marked improvements in her motor examination with the finger abduction improving to 5/5, left knee extension 5/5, plantar flexion 5/5 and dorsiflexion 2/5. The patient was able to ambulate; however, the left foot drop remained.

**DISCUSSION**

We document for the first time, a rare case of MMN occurring in a female from the Philippines. Uniquely, besides being a female, she clinically presented with asymmetric weakness of the lower extremity. The diagnosis of MMN was based on electrophysiologic motor conduction blocks, sparing sensory nerves, presence of anti-GM1 serum antibody and favorable response to IVIg. There have been few cases of patients with MMN that have been reported. Future local prevalence studies are highly recommended.

MMN is a rare disorder that can be easily misdiagnosed. Its prevalence is 0.6 per 100,000 individuals.[5] The onset of this disorder is generally before 50 years of age in 80% of the cases and it is predominantly seen in males with a ratio of 2.7:1. [5,6,9] It presents as a progressive or stepwise asymmetric weakness without any sensory involvements. [5,6] The upper extremities are usually affected in this disorder. Differential diagnoses for this disorder are chronic inflammatory demyelinating polyneuropathy (CIDP), particularly the pure motor form and Lewy-Is-Sumner syndrome which has a sensory component. MMN can be differentiated from CIDP by the apparent diffuse presentation of the latter, associated sensory abnormalities and hyporeflexia.[5] The diagnosis of MMN can be done by careful history and physical examination of the patient. Clinical criteria supported by electrophysiologic studies and ganglioside GM1 antibodies should be considered in making such diagnoses. As for the treatment, IVIg infusion is the first line treatment for MMN [4,5], and early treatment initiation may improve long-term impairment.[12]

**CONCLUSION**

We report for the first time a Filipino diagnosed with MMN showing compatible features of asymmetric weakness with atrophy, electrophysiologic motor conduction blocks, sparing sensory nerves and positive anti-GM1 antibody test. The unique occurrence in a Filipino female, mainly involving the lower extremity encouraged us to document this present case of MMN, rare at that.

**ETHICAL CONSIDERATIONS**

The investigators obtained approval of the University of Santo Tomas Hospital (USTH) Research Ethics Committee (REC) for the case report. CARE guidelines were carefully adhered to in the preparation of this manuscript.

**Declaration of Conflict of Interest**

The principal investigator was given authority by the team to present this case to avoid any potential competing interest in review or publication.

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