Multifocal Motor Neuropathy With Conduction Block

Slow But Not Benign

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Objective: To describe a patient with multifocal motor neuropathy with conduction block who had annual clinical and physiological examinations for 18 years but declined treatment for personal reasons.

Design: Case report.

Setting: Collaboration between 2 academic tertiary care hospitals.

Patient: One patient with multifocal motor neuropathy with conduction block.

Results: At age 44 years, there was weakness and wasting of the left biceps with conduction block in the left musculocutaneous and right ulnar nerves. The left median nerve was inexcitable. The right median, ulnar, and left peroneal nerves developed axonal change (loss of distal compound muscle action potential amplitude) at years 5, 12, and 13. By 2005, new weakness had appeared in 20 muscles (16 in the arms); he could not use a keyboard, button buttons, or write his name. Nerves that initially showed conduction block became inexcitable over the course of the illness.

Conclusions: Multifocal motor neuropathy with conduction block is a disease that may be "only" slowly progressive but is not always benign. Nerves showing conduction block may develop axonal change. Better markers for this disease are needed.

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MULTIFOCAL MOTOR NEUROPATHY WITH CONDUCTION BLOCK (MMNCB) is characterized by slowly progressive weakness for years or decades.1 It is usually chronic but causes limited disability.2 Intravenous immunoglobulin (IVIG) therapy is effective in most patients,3 and natural history studies are therefore few.4 We studied a patient with MMNCB who refused IVIG therapy because he believed potential adverse effects were too dangerous, but he continued to appear for annual examinations.

REPORT OF A CASE

The patient was a showroom designer and an avid weight lifter. In 1987, at age 44 years, he noted loss of strength and twitching of the left biceps. He was first seen in December 1987. He reported stiffness and clumsiness of both hands, worse in cold weather. He could write, draw, button, and zip without difficulty. He had calf cramps but no other medical problems; he took no medication and there was no family history of neurological illness.

Examination showed normal cranial nerve functions. The left biceps was wasted; twitching was seen in both forearms and rarely in the right calf. The left brachioradialis, pronator teres, and supinator were weak against slight resistance. A cramp was induced during biceps testing. Tendon reflexes were absent in the left biceps, triceps, and ankle but normal elsewhere. Hoffmann and Babinski signs were absent. Sensation was normal for all modalities. All diagnostic studies gave normal results, including tests for GM1 antibodies, quantitative immunoglobulins, immunofixation electrophoresis, and cerebrospinal protein content (30 mg/dL). Nerve conduction studies showed evidence of MMNCB. Conduction block, defined as loss of compound

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muscle action potential (CMAP) amplitude exceeding 50% between 2 contiguous sites of stimulation,5 was identified in the left musculocutaneous and right ulnar nerves.

Annual clinical examinations occurred between 1987 and 2005. The Medical Research Council (MRC) grading system was used to assess muscle strength. Over 18 years, 20 muscles showed new weakness. Sixteen of 20 muscles were in the arms and 10 weakened by more than 2 MRC grades (Figure 1). Muscles showing the greatest change were the right finger extensors (3 MRC grades), right wrist flexors (3 MRC grades), and right first dorsal interosseous (4 MRC grades). In the legs, left toe flexion lost 4 MRC grades, and left ankle dorsiflexion and large toe extension decreased by 1 grade in 1993 with no further change. He lost the ability to type, use keys to open doors, turn the ignition key of his car, zip zippers, and turn on light switches.

As for serial electrophysiologic examinations, the left median nerve was inexcitable on the initial examination and remained so during all subsequent examinations. The left ulnar nerve showed no significant change over the 18 years of observation. In the right median nerve, conduction block was not identified on the initial examination but in 1991 focal, segmental conduction block appeared in 2 segments: elbow-wrist and axilla–Erb point (Figure 2A). In 1993, distal CMAP amplitude was markedly reduced (<1 mV) from all points of stimulation, eventually becoming inexcitable. We refer to the way axonal change (loss of distal CMAP amplitude) occurred as multifocal type I block. In the right ulnar nerve, the focal amplitude loss in the axilla–Erb point segment seen during the first examination persisted but the magnitude of amplitude loss declined because of a uniform loss of amplitude at all sites of stimulation, leading to a uniformly low-amplitude CMAP (Figure 2B). We termed the way axonal change occurred in this instance as diffuse, nonsegmental type II block.

The right peroneal and tibial nerves were normal throughout the observation period. The left peroneal nerve developed loss of CMAP amplitude from all points of stimulation between 1988 and 1992; the left tibial nerve showed low-amplitude CMAP responses throughout the study period. No conduction block was observed in the legs, though F responses were prolonged in the left tibial nerve.
All sensory conduction study results were normal throughout the study period. Needle electromyography showed minimal amounts of fibrillation potentials in the small hand muscles. Rare fasciculations were seen in needle electromyography of muscles in both arms and both legs throughout the study period.

COMMENT

This 18-year study of 1 patient with MMNCB gives an unprecedented view of the natural history of this disease. The clinical features are typical: male patient, middle age, asymmetric weakness that was first thought to be amyotrophic lateral sclerosis, and slow progression. The presence of conduction block and short duration of symptoms made him an ideal candidate for IVIG treatment but he demurred.

The progressively more severe weakness is attributed to the evolution of axonal loss (ie, loss of distal CMAP amplitudes). Motor nerves developed low distal CMAP amplitude in 1 of 2 ways: multifocal conduction block in different segments (type 1 conduction block) (Figure 2A), a process that can be caused by random foci of conduction block in the long nerves eventually causing loss of amplitude, and conduction block outside of standard stimulation sites with distal axonal loss (ie, distal to the most distal site of stimulation or proximal to the most proximal site of stimulation) (type II conduction block) (Figure 2B).

How areas of conduction block produce axonal loss is unresolved. Axonal loss may be the result of antganglioside antibodies directed against paranodal myelin, the internodal axonal membrane, or gangliosides. Alternatively, there may be areas of hyperpolarization in axons adjacent to the conduction block that cause axons to undergo axonal death and degeneration. Axonal degeneration may be a direct consequence of demyelination. The fact that weakness increases in the cold suggests a hyperpolarization effect because this type of block worsens in the cold.

Whatever the cause of axonal change, our studies show that inexcitability or low CMAP amplitude (ie, axonal features) may occur in nerves that previously showed conduction block. Inexcitable nerves in patients with multifocal motor neuropathy (MMN) make it more difficult to distinguish patients with MMN from those with progressive spinal muscular atrophy or with the lower motor neuron form of motor neuron disease. The clinical similarity of MMN and amyotrophic lateral sclerosis was emphasized in early reports. Our findings therefore confirm the observation of others that MMN may exist without identifiable conduction block. A more constant and meaningful marker of this disease is needed.

Explaining how to prevent axonal change in nerves showing conduction block will likely lead to understanding the basis for the rapid response to IVIG therapy experienced by most patients with MMN. Improvement from IVIG therapy is best predicted by the presence of conduction block and slowing of conduction velocity, implying that therapy should commence before axons are damaged. The effectiveness of IVIG therapy suggests that there is a reversible immunologic basis for the conduction abnormalities preceding axonal change.

The presence of axonal change is important because nerves so affected seem to be more resistant to IVIG therapy. Intravenous immunoglobulin treatment seems to slow the loss of CMAP amplitude and therefore the axonal degeneration associated with conduction block. If axonal change renders IVIG therapy ineffective, the evolution of such change seen in our patient suggests there may be a limited window to save a nerve from axonal damage, so that early treatment is needed.

Proximal leg muscles were entirely spared. This observation has been made by other investigators and has prompted a proposal that nerves supplying proximal muscles seem to be especially resistant to this disease. However, we observed nerves showing worsening conduction block in proximal segments with little change in strength or distal CMAP amplitude. Therefore, retained strength in a given muscle does not necessarily mean absence of disease in the nerve supplying the muscle. One third of nerves in patients with MMN show nerve conduction abnormalities without clinical weakness. Why axonal change evolves so rapidly in some nerves but slowly or not at all in others is unknown.

In conclusion, untreated MMNCB is indeed a slowly progressive disease but is not necessarily benign; early treatment is probably necessary to prevent evolution of axonal change in nerves affected by conduction block.

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REFERENCES


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