Multifocal Motor Neuropathy

1. INTRODUCTION

Multifocal motor neuropathy (MMN) is a relatively recently recognized clinical entity that was formally described by Parry and Clark in the mid-1980s (1,2). The clinical presentation in each of the patients in this original series had suggested a diagnosis of motor neuron disease, but nerve conduction studies showed multifocal conduction block in motor nerves. The recognition that this syndrome represented a form of a chronic demyelinating neuropathy has spawned much debate regarding its relationship to other chronic demyelinating neuropathies such as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and the Lewis-Sumner syndrome, and has also raised the possibility that patients with the disorder might respond to immunosuppressive therapy. What are the clinical and electrophysiological features of MMN, and how does it differ from other chronic demyelinating neuropathies? What is the diagnostic accuracy of anti-GM1 antibodies? Do patients with MMN respond to immunosuppressive therapy, and what is the long term prognosis for patients with this disorder? These and other questions are the focus of this chapter.

2. DIAGNOSIS

2.1. What Are the Typical Clinical Manifestations of MMN?

MMN is a syndrome first described in detail by Parry and Clark in the mid 1980s (1,2) and since recognized and reported by a number of other investigators (3–9). The literature on MMN largely comprises case series in which patients were included based on the presence of particular clinical symptoms and findings on examination, with or without the presence of specific electrophysiological features—typically, conduction block in motor nerves with normal sensory nerve conduction studies.

Because the clinical features have been used to define the syndrome (i.e., have served as the gold standard for the diagnosis), there is no objective way of determining the range of clinical manifestations that may be seen in this disorder. Many case series have described the clinical features of a group of patients, but estimation of the spectrum of clinical manifestations that may be encountered is constrained by the clinical criteria that were used to select patients for inclusion in the study. For example, because most case series only included patients with no or minimal sensory symptoms, it is not surprising that sensory symptoms and signs have been reported to occur very infrequently in patients with MMN. A few studies have included patients on the basis of electrophysiological criteria alone (6), and these provide more meaningful characterization of the clinical manifestations of the disorder.
In their original report, Parry and Clark described five patients who were initially erroneously diagnosed with motor neuron disease (2). The descriptions since then (3,5–9) have, for the most part, reiterated the clinical features described in the original case series (Table 13.1). One subtle refinement of the clinical syndrome was recognized by Krarup and colleagues in their description of three patients with this syndrome who had relatively little atrophy in muscles with marked weakness (4). The larger case series have consistently shown that men are more commonly affected than women, and that disease onset is typically in the fifth decade of life. Weakness is most commonly distal, with the hands affected more frequently than the feet. Atrophy is common, although less marked than might be expected on the basis of the severity of weakness. Cramps and fasciculations are variable. Minor sensory symptoms may be present, but sensory findings on examination are minimal or absent (Table 13.1).

2.2. How Frequently Does Conduction Block Occur in MMN, and Is There a Predilection for Involvement of Proximal or Distal Nerve Segments?

Whether conduction block is always found in MMN depends in part on how the disorder is defined. If the diagnostic criteria require the presence of conduction block, then it will, by definition, be present in all patients. The question is more meaningful, however, if the syndrome is defined clinically. Before considering the evidence, it is helpful to clarify a few concepts. Conduction block is typically defined as a reduction in response amplitude following proximal stimulation relative to the response amplitude following distal stimulation. Although there is general agreement that an amplitude reduction of 50% or more is sufficient to define conduction block, controversy persists as to whether 20–49% reductions should also be taken to imply the presence of conduction block. One approach has been to define amplitude reduction of 50% as definite conduction block and amplitude reduction of 20–49% as partial conduction block. In defining the presence of conduction block it is also necessary to consider the degree of temporal dispersion—that is, the extent to which the duration of the proximal response is increased relative to that of the distal response. Because the amplitude of a response will decline as a function of increasing temporal dispersion (because of phase cancellation), amplitude reduction should only be used to define conduction block when there is little temporal dispersion (typically less than 15%). In the presence of more marked temporal dispersion, conduction block should rather be defined in terms of a reduction in the area of the response between distal and proximal sites of stimulation.

It should also be recalled that routine nerve conduction studies only examine relatively distal segments of nerves. Median and ulnar nerve studies do not evaluate nerve segments more proximal to just above the elbow, and peroneal and tibial conduction studies do not examine nerve segments more proximal than the knee. In order to evaluate more proximal nerve segments in the upper limbs, for example, it is necessary to stimulate nerves in the axilla, at Erb’s point, and/or at the level of the spinal roots. If conduction blocks occur exclusively in proximal nerve segments, they will not be detected by routine nerve conduction studies. In considering studies that have incorporated such proximal stimulation, it is important to be aware of the technical difficulties inherent to proximal nerve segment stimulation. Because it is difficult to administer supramaximal stimuli to proximal nerve segments, reductions in response amplitude may reflect submaximal stimulation rather than true conduction block. One approach to ensuring that a stimulus of