Diagnostic value of combined magnetic resonance imaging examination of brachial plexus and electrophysiological studies in multifocal motor neuropathy

Značaj kombinovane primene elektrofizioloških ispitivanja i ispitivanja magnetne rezonance brahijalnog pleksusa za potvrdu dijagnoze multifokalne motorne neuropatije

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Abstract

Background/Aim. Multifocal motor neuropathy (MMN) is an immune-mediated disorder characterised by slowly progressive asymmetrical weakness of limbs without sensory loss. The objective of this study was to investigate the involvement of brachial plexus using combined cervical magnetic stimulation and magnetic resonance imaging (MRI) of plexus brachialis in patients with MMN. We paid special attention to the nerve roots forming nerves inervating weak muscles, but without detectable conduction block (CB) using conventional nerve conduction studies.

Methods. Nine patients with proven MMN were included in the study. In all of them MRI of the cervical spine and brachial plexus was performed using a Siemens Avanto 1.5 T unit, applying T1 and turbo spin-echo T1 sequence, axial turbo spin-echo T2 sequence and a coronal fat-saturated turbo spin-echo T2 sequence.

Results. In all the patients severe asymmetric distal weakness of muscles inervated by radial, ulnar, median and peroneal nerves was observed and the most striking presentation was bilateral wrist and finger drop. Three of them had additional proximal weakness of muscles inervated by axillar and femoral nerves. The majority of the patients had slightly increased cerebrospinal fluid (CSF) protein content. Six of the patients had positive serum polyclonal IgM anti-GM1 antibodies. Electromyoneurography (EMG) showed neurogenic changes, the most severe in distal muscles inervated by radial nerves. All the patients had persistent partial CBs outside the usual sites of nerve compression in radial, ulnar, median and peroneal nerves. In three of the patients cervical magnetic stimulation suggested proximal CBs between cervical root emergence and Erb’s point (prolonged motor root conduction time). In all the patients T2-weighted MRI revealed increased signal intensity in at least one cervical root, truncus or fasciculus of brachial plexus.

Conclusion. We found clinical correlation between muscle weakness, prolonged motor root conduction time and MRI abnormalities of the brachial plexus, which was of the greatest importance in the nerves without CB inervating weak muscles.

Key words: peripheral nervous system diseases; diagnostic techniques and procedures; brachial plexus; magnetic resonance imaging; electrophysiology.

Apstrakt

Uvod/Cilj. Multifokalna motorna neuropatija (MMN) je imunska posredovano obolelosti perifernih nerva koje karakteriše sporo napredovanje asimetričnih slabosti mišića ekstremiteta, bez poremećaja senzibiliteta. Cilj rada bio je da se ispita značaj kombinovane primene magnetne stimulacije u cervicalnom nivou i magnetne rezonance (MR) brahijalnog pleksusa u potvrdu proksimalnih blokova provođenja kod obolelih od MMN. Takođe, željeli smo da utvrdimo da li postoje znaci oštećenja nervnih korenova koji grade nerve koji inervišu klinički slabe mišiće, kod kojih konvencionalnim ispitivanjim provođivosti perifernih nerva nije registrovano postojanje blokova provođenja (BP). Metode. U studiju je bilo uključeno devet bolesnika sa klinički i elektrofiziološki potvrđenom dijagnozom MMN. Svim bolesnicima urađen je...
Multifocal motor neuropathy (MMN) is a chronic, slowly progressive immune-mediated neuropathy, characterized by progressive, predominantly distal, asymmetric limb weakness, mostly affecting upper limbs, minimal or no sensory impairment, and the presence of multifocal persistent partial conduction blocks (CB) on motor, but not sensory nerves. It is a rare disorder with an estimated prevalence of 1–2/100,000 individuals, more frequently present in men. MMN predominantly affects young people and almost 80% of patients develop first symptoms between 20 and 50 years of age. Evidence of CBs is the electrophysiological hallmark of MMN and must be found at sites distinct from common entrapment or compression syndromes. CBs may occur in any motor nerve, but have been more frequently reported in the distal segment of upper limb nerves. Very proximal CBs located in the sites above Erb’s point cannot be detected by routine nerve conduction studies (NCS). Transcranial magnetic stimulation (TMS) technique combined with peripheral conduction time can detect CB between root emergence and Erb’s point (motor root conduction time). Proximal CB may be also confirmed by increased signal in cervical roots, truncus or fasciculus of the brachial plexus by magnetic resonance imaging (MRI). Supportive diagnostic criteria include elevated serum anti-GM1 antibodies.

The purpose of this study was to investigate the involvement of cervical roots, truncus or fasciculus of brachial plexus by MRI examination in patients with the proven diagnosis of MMN, especially in the cases without conventional electrophysiological proof of the CB. Our hypothesis was that MRI of the brachial plexus combined with magnetic stimulation at cervical level could give valuable contribution to confirmation of proximal CB. These are not accessible to evaluation by conventional nerve conduction studies.

Methods

The clinical diagnosis of MMN was based on the presence of a chronic or stepwise progressive asymmetric limb weakness with a multilineuropathic distribution affecting the muscles of at least two distinct motor nerves lasting at least two months, and minimal or no sensory loss or symptoms and absence of clinical upper motor neuron signs.

Electrophysiology

The standard methods of motor and sensory NCS and concentric needle EMG were performed. Motor NCS included distal motor latencies, compound muscle action potential (CMAP) amplitudes, conduction velocities and F wave latencies. Motor NCS were performed up to Erb’s point in the median (recording: m. abductor pollicis brevis), ulnar (recording: m. abductor digitii minimi), radial (recording: m. extensor indicis) nerves, and up to the popliteal fossa in the deep peroneal (recording: m. extensor digitorum brevis) and tibial (recording: m. hallucis brevis) nerves. EMG was defined according to Europen Federation of Neurological Society/Peripheral Nerve Societies guidelines. It was defined as definite motor CB: negative CMAP area reduction on proximal versus distal stimulation of at least 50% whatever the nerve segment length (median, ulnar and peroneal). Negative CMAP amplitude on stimulation of the distal part of the segment with motor CB must be > 20% of the lower limit of normal and > 1 mV (baseline negative peak) and an increase of proximal negative peak CMAP duration must be ≤ 30%; probable motor CB was defined as a negative CMAP area reduction of at least 30% over a long segment of an upper limb nerve with an increase proximal negative peak CMAP duration ≤ 30%, or negative CMAP area reduction of at least 50% (the same as definite) with an increase in proximal negative peak CMAP duration > 30%, and normal sensory nerve conduction in upper limb segments with CB and normal sensory nerve action potential amplitudes, evidence for conduction block must be found at sites distinct from common entrapment or compression syndromes. Antidromic sensory NCS were investigated in the median, ulnar, radial and sural nerves. Concentric needle EMG was performed in proximal and distal upper and lower limb muscles.

In addition to conventional NCS, paravertebral magnetic stimulation at cervical level via a round coil (outer dia-
meter 90 mm) centered over the spinous process of C7 was applied in order to detect the most proximal conduction blocks. Motor root conduction time (MRCT) was calculated by subtracting latency of motor evoked potentials evoked by cervical magnetic stimulation and total peripheral motor conduction time (PMCT) obtained by electrical stimulation of corresponding nerve. PMCT was estimated from the latencies of the CMAPs and F-waves as follows (latency of CMAPs + latency of F-waves − 1)/2. MRCT was accepted as prolonged only for the peripheral nerves along which conductive block in more distal segments has not been previously found. MRCT was considered normal if the latency was shorter than 1.46 msec. We have decided to accept as possible proximal conductive blocks only cases with clear MRCT prolongation, since a possible inability to achieve supramaximal stimulation by magnetic stimulation leaves the least impact on latencies, contrary to significantly lower amplitudes and areas in such cases 5,11.

Serum and cerebrospinal fluid analyses

Serum IgG and IgM antibodies to ganglioside GM1 were measured by enzyme linked immunosorbent assay (ELISA) before immunoglobulin treatment 12,13. The presence of monoclonal gammopathy was investigated by serum immunoelectrophoresis and immunofixation. CSF was examined for total protein concentration and cell count by standard procedures and by isoelectric focusing agarose gel electrophoresis for oligoclonal bands 8.

MRI of cervical spine and brachial plexus was performed in all patients using a Siemens Avanto 1.5 T unit. The following sequences were applied: an axial turbo spin-echo T1 sequence (FoV 280 mm, slice thickness 3.0 mm, TR 561 ms, TE 11 ms, flip angle 150 degree, acquisition number 1, base resolution 320), an axial turbo spin-echo T2 sequence (FoV 280 mm, slice thickness 3.0 mm, TR 3600 ms, TE 127 ms, flip angle 170 degree, acquisition number 1, base resolution 512), a coronal fat-saturated (FS) turbo spin-echo T1 sequence (FoV 350 mm, slice thickness 2.5 mm, TR 7500 ms, TE 157 ms, flip angle 170 degree, acquisition number 1, base resolution 384). The T1 sequences were also made after application of paramagnetic contrast 14.

Results

Nine patients (5 male, 4 female), the mean age of 38 (range 22–53) years had the history of MMN (Table 1). The mean duration of the disease was 6.3 (range 3–12 years). In 7 of 9 (78%) patients the first symptom was asymmetric weakness of the finger extensors without wasting of the arm muscles (Figure 1). The course of the disease in all the patients was stepwise progressive, resulting in severe, asymmetric, distal weakness of muscles inervated by radial, ulnar, median and peroneal nerves and the most striking presentation was bilateral wrist and finger drop. Three of them (No 5, 7, and 8) had additional proximal weakness of muscles inervated by axillar and femoral nerves. In one patient (No 5) there was the facial nerve involvement with mental muscle myokimia and in one patient also the occurrence of seropositive myasthenia gravis 6.

In six patients (No 1, 2, 5, 6, 7, 8) polyclonal IgM anti-GM1 antibodies were detected. Eight patients had a slightly elevated CSF protein content, ranging from 0.46 to 0.84 g/L (mean 0.58 g/L). In the patient No 5 with the very severe clinical presentation, oligoclonal IgG bands were detected in CSF.

Neurogenic EMG pattern was found in all affected muscles. Demyelination of the motor nerves and CBs were detected in all the patients at sites distinct from common entrapment syndromes, most frequently in the radial nerve (7/9), suggesting the diagnosis of MMN. In all of the analyzed patients MRI of the brachial plexus revealed asymmetric increased signal intensity on T2-weighted ima-
### Clinical, electrophysiological and magnetic resonance imaging (MRI) features of patients with multifocal motor neuropathy (MMN)

<table>
<thead>
<tr>
<th>Patient's number</th>
<th>Sex / age (years) at onset</th>
<th>Muscle weakness related to the distribution of individual nerve</th>
<th>Motor nerves with CMAP (% of CMAP amplitude reduction)</th>
<th>MRI changes of brachial plexus</th>
<th>TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male / 49</td>
<td>Male / 49</td>
<td>Bilateral radial, right median, bilateral peroneal, right tibial</td>
<td>Right peroneal (66%), left peroneal (50%)</td>
<td>Increased signal intensity in both C7 roots</td>
<td>Prolonged MRCT*</td>
</tr>
<tr>
<td>Male / 25</td>
<td>Male / 25</td>
<td>Bilateral radial, right median, bilateral peroneal, right tibial</td>
<td>Right radial (70%), left median (50%)</td>
<td>Increased signal intensity in upper trunk left and C6 root left</td>
<td>Extremely prolonged MRCT*</td>
</tr>
<tr>
<td>Male / 30</td>
<td>Male / 45</td>
<td>Left median, bilateral radial</td>
<td>Left ulnar (80%), left median (50%)</td>
<td>Increased signal intensity in C6 root left and C8 root left</td>
<td>Prolonged MRCT*</td>
</tr>
<tr>
<td>Male / 53</td>
<td>Female / 37</td>
<td>Bilateral radial, bilateral median, left ulnar, bilateral radial, left axillary</td>
<td>Right radial (75%), right radial, (40%), left ulnar (45%)</td>
<td>Increased signal intensity in C6 and C7 roots on the right side</td>
<td>Prolonged MRCT*</td>
</tr>
<tr>
<td>Female / 52</td>
<td>Female / 26</td>
<td>Bilateral radial, bilateral median, left ulnar, bilateral radial, left femoral</td>
<td>Left radial (60%), left ulnar (56%)</td>
<td>Increased signal intensity in inferior fasciculus right and C7 root left</td>
<td>Increased signal intensity in inferior fasciculus right and C7 root left</td>
</tr>
<tr>
<td>Female / 22</td>
<td>Female / 22</td>
<td>Bilateral radial, bilateral median, left ulnar, right median</td>
<td>Left radial (45%), left ulnar (45%)</td>
<td>Increased signal intensity in inferior fasciculus right and C7 root left</td>
<td>Increased signal intensity in inferior fasciculus right and C7 root left</td>
</tr>
</tbody>
</table>

*MRCT – Motor root conduction time; CB – conduction block; CMAP – compound muscle action potential.
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ges as well as increased signal intensity on T1-weighted images after gadolinium enhancement. However, three patients (No 1, 2 and 7) with severe muscle weakness related to distribution of right median nerve, but without CB on conventional electroneurography on this nerve, were subjected to cervical magnetic stimulation. In all of them substantial MRCT prolongation (2–5 times longer) was obtained when motor evoked potentials was registered in corresponding thenar muscles, indicating the presence of proximal CB (Table 2). In those patients MRI of the brachial plexus also revealed high signal intensity in roots from which arises median nerve, corresponding to proximal CBs detected by paravertebral cervical magnetic stimulation (Figures 2 and 3).

### Discussion

The clinical presentation and electrophysiological studies fulfilled criteria for the diagnosis of definite MMN in all the presented patients, also supported by serum and CSF findings. Similarly to many other reports, the upper limb onset with finger extension weakness as the first clinical manifestation of the disease was present in two-thirds of our patients. Three patients of our cohort had additional proximal weakness of muscles innervated by axillary and femoral nerves. On the contrary, some authors show that lower limb onset is present in 27% of patients with MMN.

In the majority of the analyzed patients in our study, CSF analyses show a slightly elevated protein content (0.58 g/L), which is in line with the data from the literature. In six out of nine (66.7%) patients of our cohort polyclonal IgM anti-GM1 antibodies were detected. This result is in agreement with previous ones in which these antibodies were found in 22–85% of patients with MMN, but its relationship to the pathogenesis of the disease still remains unclear. Although there was no relationship between the antibody finding and the disease severity and there was no decline in anti-GM1 titer with immunomodulatory treatment, a consensus statement of the American Academy of Electrodiagnostic Medicine included anti-GM1 antibody in the possibly supportive laboratory criteria for MMN diagnosis. It is especially important in situations where a definite diagnosis of MMN cannot be made on clinical and neurophysiological grounds.

### Table 2

<table>
<thead>
<tr>
<th>Patient’s number</th>
<th>Registration site</th>
<th>MEP latency</th>
<th>CMCT&lt;sup&gt;1&lt;/sup&gt;</th>
<th>CMCT&lt;sup&gt;2&lt;/sup&gt;</th>
<th>MRCT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cortical</td>
<td>spinal</td>
<td>CMCT&lt;sup&gt;1&lt;/sup&gt;</td>
<td>CMCT&lt;sup&gt;2&lt;/sup&gt;</td>
<td>MRCT</td>
</tr>
<tr>
<td>1</td>
<td>median right</td>
<td>30.75</td>
<td>19.03</td>
<td>9.64</td>
<td>4.74</td>
</tr>
<tr>
<td></td>
<td>ulnar right</td>
<td>27.63</td>
<td>20.64</td>
<td>6.99</td>
<td>5.57</td>
</tr>
<tr>
<td>2</td>
<td>median right</td>
<td>32.3</td>
<td>17.02</td>
<td>15.28</td>
<td>7.54</td>
</tr>
<tr>
<td></td>
<td>ulnar right</td>
<td>31.02</td>
<td>21.51</td>
<td>9.51</td>
<td>7.82</td>
</tr>
<tr>
<td></td>
<td>median left</td>
<td>25.05</td>
<td>17.39</td>
<td>7.66</td>
<td>5.82</td>
</tr>
<tr>
<td></td>
<td>ulnar left</td>
<td>28.07</td>
<td>20.16</td>
<td>7.91</td>
<td>5.87</td>
</tr>
<tr>
<td>7</td>
<td>median right</td>
<td>23.41</td>
<td>15.08</td>
<td>8.33</td>
<td>5.29</td>
</tr>
</tbody>
</table>

All the values represent the absolute/relative latencies of evoked responses expressed in msec.

MEP – motor evoked potential; PMCT – peripheral motor conduction time;
CMCT<sup>1</sup> (central motor conduction time) = Cortical MEP latency – spinal MEP latency;
CMCT<sup>2</sup> (Cortical MEP latency – PMCT; MRCT (motor root conduction time) = PMCT – spinal MEP latency

Prolonged MRCT indicates by asterixes.

Fig. 2 – T2 FS sequence magnetic resonance imaging (MRI) shows increased signal intensity in both C7 roots in patient with multifocal motor neuropathy (the patient No 2).

Fig. 3 – T2 FS sequence of magnetic resonance imaging (MRI) shows increased signal intensity in C6 and C7 roots on the right side in a patient with multifocal motor neuropathy (the patient No 7): a) without contrast; b) with contrast.
It is well known that the neurophysiologic hallmark of the MMN is the presence of CBs in motor nerves, which is supposed to be the underlying cause of muscle weakness.\(^3,^4,^10\) Accordingly, CBs are most commonly found in long arm nerves that innervate weak muscles. One of the possible explanations for this is that motor axons in the arm nerves have slower potassium conductance than motor axons in leg nerves.\(^21\) These differences could contribute to the greater susceptibility of arm motor axons for developing CB.\(^15,^21,^22\) In line with this results we found CBs in all patients included in the study at sites distinct from common entrapment trunks, most frequently in radial nerve. In the majority of patients with MMN the distribution of muscle weakness correlated with the CBs detected by NCS.\(^2,^16,^23\) However, CB may be localized in proximal nerve segments and may be difficult to be detected by conventional NCS,\(^5,^24\) as was the case in three patients\(^1,^2,^7\) of our cohort. The significance of MRI in these cases is valuable, because the pattern of signal alteration in brachial plexus closely correlates with the distribution of muscle weakness and together with magnetic stimulation at cervical level could be helpful in detection of proximal CB in the affected nerve.\(^6,^14,^24,^26\)

In addition, MRI may give some contribution to differential diagnosis of inflammatory neuropathies – MMN and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and lower motor neuron disease (LMND). In MMN MRI shows asymmetrically increased signal intensity on T2-weighted images sequences with evidence of nerve swelling in 40–50% of patients, while in CIDP MRI usually depicts diffuse and homogenous signal enhancement. However, in patients with LMND there are no such findings.\(^6\)

Our results suggest that in all the examined patients MRI showed asymmetric focal lesions in the cervical roots and structures of brachial plexus. This finding was particularly significant in our three patients in whom MRI showed high signal intensity in the C6 and C7 roots corresponding with the affection of right median nerve and proximal CBs detected by magnetic paravertebral stimulation. A similar finding was reported by Arunachalam et al.\(^1\). Using triple stimulation technique, they found the presence of proximal CBs in 7 out of 10 analyzed MMN patients indicating proximal demyelination.

**Conclusion**

The involvement of cervical roots, truncus or fasciculus of brachial plexus detected by MRI examination, along with the prolonged motor root conduction time detected by cervical magnetic stimulation could be valuable in detection of proximally localized CB in patients with clinically highly suspected MMN. In that way both methods are noninvasive tools providing assessment of proximal nerve segments integrity in patients with MMN without CB on routine NCS.

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