Demyelinating Neuropathy of the 1a Afferent Nerve Fibers

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Abstract

We describe a female patient with a selective demyelinating disease of the 1a afferent sensory nerve fibers. After suffering from fever for 3 days the patient developed disorder of balance, dizziness, muscle cramps and altered sense of position and muscle tension of the trunk and extremities. Neurological examination revealed positive Romberg’s sign with no improvement during follow-up of 8 years. Laboratory and imaging studies showed no remarkable findings. However, ENMG demonstrated a permanent slow conduction affecting selectively the 1a afferent nerve fibers. We conclude that the patient suffered from an acute and probably immune-mediated demyelinating disease restricted to 1a-afferent nerve fibers, with a prompt remission but persistent sequelae.

Keywords: Dysimmune neuropathy; Guillain-Barré syndrome; Nerve conduction velocity; 1a afferents; Muscle spindle; Muscle cramps

Introduction

Polyneuropathy means dysfunction of the peripheral nerves. There are several types of polyneuropathies: axonal, demyelinating [1] and those associated with metabolic changes [2]. Polyneuropathy may selectively affect either heavily myelinated Aα and Aβ nerve fibers or thin Aδ and C nerve fibers [3], or be restricted to either motor or sensory nerve fibers [4]. It is thus essential to investigate the possible alteration in every nerve fiber group (Figure 1). We describe a patient who suffered from a selective demyelination of 1a-afferent Aα nerve fibers.

Case Presentation

A 55-year old female patient had a three-day fever in July 2008. Fever was associated with difficulty breathing but without any cough or rhinitis. In about a month persistent neurological symptoms developed, consisting of difficulty with balance, dizziness and muscle spasms, as well as strange dysesthesias: feeling of hard muscle tension and feeling that the trunk or the extremities get into distorted positions. An essential finding was also pathological Romberg’s sign, with eyes shut the patient fell backwards but with eyes open she could stand on one leg. The first ENMG study [5] was performed 2.5 years after the appearance of neurological symptoms and a demyelinating...
which persisted in the follow-up (Table 1).

neuropathy of the 1a (Aα) nerve fibers [6] was discovered (Figure 2, 3).

Table 2: Neurological symptoms and signs and investigations of the patient.

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<tr>
<td>Disorders of the balance, dizziness, cramps, dysesthesias, muscular fatiguability</td>
<td>Disorders of the brain and spinal cord normal. Neuro-ophthalmological study normal.</td>
<td>ENMG: 1a afferent slowing, all other neurography normal, needle EMG of the extremities and trunk normal. Blood sedimentation rate, complement C3 and C4, immunoglobulins, serum protein electrophoresis, studies for rheumatic disease normal. 2-h value in glucose tolerance test low (1.9-2.5 mmol/l), fasting glucose normal, S-insuline normal, FS-C-Pept, P-Pi, S-Korsol, and carnitinematab. normal.</td>
<td>Muscle cramps spreading during water running, from the foot muscles to the more proximal lower extremity muscles. ENMG (Table 2).</td>
<td>Muscle cramps during water running, from the foot muscles to the more proximal lower extremity muscles. ENMG, SEP.</td>
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Table 2: Follow up of the neurography.

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<td>Medianus mot</td>
<td>52.7</td>
<td>≥34&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Medianus F</td>
<td>28.0</td>
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<tr>
<td>Peron prof mot</td>
<td>45.2</td>
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<td>43.9</td>
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<tr>
<td>Peron F</td>
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<td>Med sekahermo dx</td>
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<td>≥63&lt;sup&gt;e&lt;/sup&gt;</td>
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<td>Med sens 3. sormi</td>
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<td>Radialis sens dx</td>
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<td>Peron superf sens</td>
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<td>Z=4.4&lt;sup&gt;¢&lt;/sup&gt;</td>
<td>33.3</td>
<td>32.8</td>
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<td>H-refl n. medianus</td>
<td>18.0</td>
<td>Z=3.2&lt;sup&gt;¢&lt;/sup&gt;</td>
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The last neurological study was performed 8 years after the onset of symptoms in August, 2016. The patient told that the symptoms were still going on: Disorders of balance, fatiguability of the hands and neck, as well as muscle twitches and cramps. However, there was no progression of symptoms. In the clinical neurological study Romber’s sign was still pathological and tandem walking backwards was impossible. Muscle strength was in general slightly, but symmetrically decreased (4/5). In October 2016, ENMG study showed a similar 1a afferent slowing as the previous studies (Table 2). Somatosensory evoked potential study of the median nerve showed increased latency of the responses at Erb’s point (11.5 ms; p=1.52 %) and at the contralateral somatosensory cortex (N20 response 21.6 ms, p=0.95 %; p value is the percentage of normal people which could reach the value measured according to the height-corrected normal values of the laboratory; the limit of normality is 2.0 %).

**Discussion**

The patient was a dental technician, previously healthy, and working full-time. Medical history revealed that 3 months before symptom onset she had received an Imovax vaccination for poliomyelitis. The neurological symptoms began after a 3 day fever in July 2008. The disease became chronic and caused permanent disability and decreased the patient’s working hours. During the following years regular exercise allowed some relief.

From the beginning the main symptoms were dizziness and disorders of balance. Moreover, after physical exercise and during night-time she experienced muscle cramps that tended to spread to neighboring muscles: for example during water running the cramps started at first in the toe muscles and then spread into more proximal...
The measured values were practically as 2.5 years after the symptom onset the nerve conduction values at the Erb’s point and cortically. These responses reflect primarily the 1a afferents (Table 1) (Figure 2 and 3) [6,7]. The median nerve somatosensory evoked potential (SEP) latencies were also increased at the Erb’s point and cortically. These responses reflect primarily the function of 1a afferent nerve fibers; because they have a faster conduction velocity than the A beta or motor nerve fibers do [6]. All other nerve conduction values and also needle EMG were normal. The latency (arrow) is slowed, 32.8 ms, compared to the length-corrected normal value (thin cursor).

The findings in the neurological examination were slight: The Romberg’s sign was pathological, impaired balance with swaying and falling to the right or back when the eyes were closed. But with eyes open the patient was able to stay, even for a longer period, on either leg.

A distinct finding was detected in all four ENMG studies performed, but only in variables reflecting the function of the 1a afferents (Table 1) (Figure 2 and 3) [6,7]. The median nerve somatosensory evoked potential (SEP) latencies were also increased at the Erb’s point and cortically. These responses reflect primarily the function of 1a afferent nerve fibers; because they have a faster conduction velocity than the A beta or motor nerve fibers do [6]. All other nerve conduction values and also needle EMG were normal. It is possible, that also the responses of beta nerve fibers may have played a role in SEP latencies because the alpha fibers were slowed down in this patient. As the first ENMG study was performed as late as 2.5 years after the symptom onset the nerve conduction values at the acute phase were lacking. The measured values were practically similar in all the four ENMG studies during the follow-up time.

The delayed proprioceptive messages of the foot muscles may explain the impairment of balance and altered Romberg’s sign, and slowing of the afferent nerve impulses of the neck and back muscles may explain the dizziness. The upper cervical muscles and their proprioceptive afferent activity are important in the appreciation of the position of the head in the gravity field, and in overall balance control.

We may ask how the findings in ENMG correlate with the neurological symptoms of the patient. In all four ENMG studies there was a permanent slowing of the 1a afferent nerve fibers (Table 2), but no sign of axonal damage was evident. When there is an axonal damage on the 1a afferent nerve fibers, the amplitude of the median mixed nerve response diminishes and the H-reflex responses disappear because of the afferent nerve fiber paucity. However, in the patient both H-reflexes and myotatic reflexes were brisk, even though the H-reflex latency was increased. The neurological symptoms in the lower extremity may be explained by a poor timing: there was an essential delay in the delivery of the proprioceptive information from muscles to the central nervous system compared to normal situation. The delayed proprioceptive messages of the foot muscles may explain the impairment of balance and altered Romberg’s sign, and slowing of the afferent nerve impulses of the neck and back muscles may explain the dizziness. The upper cervical muscles and their proprioceptive afferent activity are important in the appreciation of the position of the head in the gravity field, and in overall balance control.

On the other hand the patient also expressed symptoms which may be connected to the hypersensitivity and increased spontaneous activity of 1a sensory receptors in muscle spindles. The patient described peculiar dysesthesias such as feelings of powerful muscle tension and sensations that the limbs and trunk are spontaneously distorted to peculiar positions, which they were not. These dysesthesias may be explained by spontaneous activation of the proprioceptive sensory afferents. The tendency for the extensive muscle cramps spreading into different muscle compartments may be explained by the hypersensitivity of the proprioceptive afferents that can strengthen the persistent inward current (PIC) of the respective motor neurons of the spinal cord. PIC mechanism normally increases the strength of the active muscles and this happens in part by the increased peripheral proprioceptive activation [7]. The central activation of PIC takes place via the noradrenaline and serotonin pathways [7]. Consequently, hyperactivity of PIC may lead to strong cramps, and a typical phenomenon in these cramps is the tendency to spread to the neighboring muscles, as the patient described during the water running exercise.

The primary reason for the demyelination of the 1a afferent nerve fibers was not found, but the involvement of the central nervous system was excluded by MRI imaging and by extensive serum and cerebrospinal fluid examinations. There was evidence of a rapid recovery, but the persistence of neurological symptoms was in line with the repeated ENMG findings demonstrating slow conduction in 1a afferents. In our patient we could follow only the sequelae of the primary disease, which took place for more than 2.5 years before the first ENMG study. It can be assumed that the values of the 1a afferent nerve fibers had been more pathological at the earlier stages of the disease.

Dysimmune neuropathy may selectively affect a certain structure of the axon or nerve sheath [8], such as the myelin sheaths or nodes of Ranvier of the 1a afferent nerve fibers. There are very narrowly targeted autimmune neuropathies, for example acute motor or sensory axonal neuropathy (AMAN, ASAN), as well as multifocal motor neuropathy and motor conduction block neuropathy [9,10]. However, previous literature does not report any dysimmune
neuropathy targeting only to the myelin sheath of the 1a afferent Aα sensory fibers. In order to recognize this entity, we would like to suggest that mixed nerve conduction velocity of the median nerve as well as the H-reflex measurements should be a part of ENMG studies for the accurate diagnostics of specific polyneuropathies.

References