Case Records of the Massachusetts General Hospital

Weekly Clinicopathological Exercises
founded by richard c. cabot

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Case 13-1998

PRESENTATION OF CASE

A 23-year-old man was seen in the clinic because of progressive weakness and paresthesias.

He had been well until six months earlier, when he began to have difficulty climbing a flight of stairs quickly and noted intermittent tingling of the soles of his feet and toes. Two months later, he had increasing weakness in his legs, pain in the lower back, stiffness of the hands, and intermittent numbness of the toes and fingertips. Three months before this visit to the clinic, a tremor developed in the arms. The weakness worsened, and the feet and calves became numb, with tingling in the feet and fingertips. The patient’s balance was poor, particularly with his eyes closed.

There was no history of visual symptoms, dysphagia, slurred speech, dyspnea, sphincteric disturbances, muscle cramps, fasciculations or pain in the arms or legs, transient neurologic symptoms, weight loss, anorexia, skin changes, fever, chills, recent infection, risk factors for human immunodeficiency virus (HIV) infection, tick bite, allergies, recent immunization, exposure to neurotoxic chemicals, use of tobacco or illicit drugs, or excessive use of alcohol. The patient’s father had a mild tremor, but there was no family history of other neurologic disorders.

On examination, the pulse was 72, and the blood pressure was 110/65 mm Hg. The patient was unable to stand on his toes or heels, and a Romberg sign was present. Cranial-nerve functions were preserved, and the optic disks were normal. No muscle atrophy was seen; muscle tone was normal. Motor function was graded as follows (right/left): neck flexion and extension, 5/5; extensor hallucis longus, 4/4; extensor digitorum brevis, 4/4; ankle dorsiflexion and plantar flexion, 4+/4+; hip flexion and extension, 4+/4+; elbow flexion, 4+/4; abductor pollicis brevis, 4/5; first dorsal interosseus muscle, 5/4; and abductor digiti minimi, 5/4. The remaining muscles were normal. Vibratory sensation was decreased in the ankles and feet; sense of position was impaired in the toes; sensitivity to pinprick was reduced distally in the legs, with a proximal-to-distal gradient; and sensation of cold was normal. There was a postural tremor in the arms without dysdiadochokinesia or dysmetria. Tendon reflexes were absent at the ankles and hypoactive elsewhere. No hypertrophied nerves were palpated.

A lumbar puncture performed one month earlier showed a total protein concentration of 290 mg per deciliter, with a normal cell count. The results of serum protein electrophoresis with immunofixation and concentrations of IgG, IgM, and IgA were normal. Tests for antinuclear antibodies; antibodies to HIV, Borrelia burgdorferi, and hepatitis A, B, and C; and antibodies to myelin-associated glycoprotein (MAG), sulfatide, Hu, and ganglioside GM1 were negative. Conduction studies of the median and ulnar nerves performed six weeks before the current visit showed prolonged motor distal latencies, normal motor-nerve conduction velocities, the absence of sensory potentials, prolonged F responses, and normal electromyographic findings in the intrinsic hand muscles. The results of a magnetic resonance imaging (MRI) study of the brain, performed before and after the administration of contrast material, were normal. Routine and electron-microscopical examination of a specimen from a sural-nerve biopsy showed axonal degeneration and changes suggestive of remyelination.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Stasha C. Gominak*: This patient has chronic inflammatory demyelinating polyradiculopathy. The findings that suggest a neuropathy are the symmetric involvement of sensory and motor nerves, a sensory deficit with a graded distal-to-proximal distribution, and distal abnormalities of

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sensory and motor nerves on conduction testing. The patient could have had both a neuropathy and a myopathy, but most of the disorders presenting with this combination can be ruled out on the basis of other features of this case. The disorders that may present with both neuropathy and myopathy include inherited mitochondrial encephalomyeloneuropathies, acquired disorders such as hypothyroidism or hyperthyroidism, and disorders caused by exposure to toxic agents such as colchicine and chloroquine.1-4

Several clinical features suggest that this patient had a demyelinating neuropathy, including the preferential involvement of the large, myelinated fibers of the sensory system, the simultaneous onset of weakness in the arms and legs (rather than the typical distal symmetric presentation of axonal neuropathies), and the elevated concentration of protein in the cerebrospinal fluid, which is characteristic of both acute and chronic acquired demyelinating neuropathies and hereditary sensorimotor neuropathies. Finally, a tremor combined with a sensory gait ataxia is common in patients with neuropathy associated with anti-MAG antibody and is also seen in patients with chronic inflammatory demyelinating polyradiculopathy and hereditary sensorimotor neuropathies. Vasculitic neuropathy is not indicated by the findings in the nerve-biopsy specimen and is unlikely in the presence of a tremor and ataxia and in the absence of systemic findings and an elevated sedimentation rate.

The demyelinating neuropathies may be inherited or acquired, and the acquired forms may be acute or chronic. This patient clearly had a chronic disorder, but was it acquired or inherited? Demyelinating neuropathies have been associated with HIV infection, but this patient had no risk factors for HIV infection or evidence of the acquired immunodeficiency syndrome. Other infectious causes of demyelinating neuropathy, such as Lyme disease and hepatitis, were ruled out by laboratory testing.

We can rule out several of the inherited disorders that affect both central and peripheral myelin, such as adrenoleukodystrophy, adrenomyeloneuropathy, metachromatic leukodystrophy, and Krabbe's disease, because of the absence of characteristic findings on the MRI scan of the head and the absence of central nervous system signs or symptoms. Refsum's disease, which can present with a demyelinating neuropathy, an elevated protein concentration in the cerebrospinal fluid, and cerebellar ataxia, can be ruled out because of the absence of retinitis pigmentosa.

Inherited demyelinating neuropathies, known as Charcot–Marie–Tooth neuropathies, are also unlikely in this patient. Although his age is consistent with the diagnosis of Charcot–Marie–Tooth neuropathy type 1 or type 2, the absence of distal wasting and the normal results of proximal nerve conduction testing argue against this diagnosis. The characteristic electrophysiologic feature of type 1 is uniformly slow conduction along the entire nerve.6 In this patient, the distal latencies of the nerve were prolonged, but the more proximal motor-nerve conduction velocities were normal. The clinical presentation of type 2 resembles that of type 1 — slowly progressive distal wasting and weakness of the arms and legs — but type 2 is characterized by normal or nearly normal nerve conduction velocities and distal latencies. In addition, most of the Charcot–Marie–Tooth neuropathies are autosomal dominant, so the absence of a family history makes them unlikely in this case, although there are autosomal recessive as well as X-linked types.6 Five to seven separate types of Charcot–Marie–Tooth neuropathies have been identified. The classification schemes are based on the chromosomal abnormalities as well as the clinical presentations.

Over the years, chronic inflammatory demyelinating polyradiculopathy has been subdivided according to the clinical and electrophysiologic features. Patients with multifocal motor neuropathy have abnormalities of only the motor nerves, with or without conduction block. Other patients may have chronic inflammatory demyelinating polyradiculopathy that affects only the sensory nerves, but some authors believe that extensive electrophysiologic testing and a long follow-up period will reveal motor involvement as well.8 Chronic inflammatory demyelinating polyradiculopathy has also been subdivided on the basis of an associated monoclonal protein or an antibody to a specific myelin antigen.9 In this case, tests for anti-MAG and anti–ganglioside GM1 antibodies and immunofixation and immunoglobulin studies were performed in an attempt to assign the disorder to one of these subtypes.

Attempts to define clinical subtypes of chronic inflammatory demyelinating polyradiculopathy on the basis of associated monoclonal proteins or antibodies to specific myelin proteins have been only partly successful. There are many reported cases of chronic inflammatory demyelinating polyradiculopathy associated with either a monoclonal gammopathy of undetermined significance (MGUS) or antibodies to various components of peripheral-nerve myelin, with anti–ganglioside GM1 antibody the most common.9-13

In this case, the clinical presentation is typical of chronic inflammatory demyelinating polyradiculopathy associated with anti-MAG antibody, except for the patient's young age. (The disorder develops in the sixth or seventh decade, with a large predominance of cases in men.) The usual presentation i-
cludes slowly progressive distal and symmetric sensorimotor involvement of all four extremities. The perception of pain is usually affected to a lesser extent than sensation of joint position and vibration. A tremor and sensory ataxia are common. The electrophysiologic findings usually include prolonged distal latencies in the arms and legs. The anti-MAG antibody is usually an IgM monoclonal (M) protein, but sometimes, despite the absence of measurable M protein, anti-MAG antibody can still be detected.14-16 Immunohistochemical examination of the peripheral nerve reveals a separation of the Schwann-cell membranes, leaving wider spaces between the myelin lamellae. There is no cellular infiltrate, but IgM light chains have been reported to be bound to the abnormal myelin.5,14,15,17 MAG is one of several glycoproteins that have been implicated in the demyelinating neuropathies.11 There is sufficient evidence to suggest that the anti-MAG antibody is pathogenetic, but some authors believe that the IgM binding to this myelin protein is caused by the detachment of the lamellae from one another, which allows access to the antigen.17

Another clinical subtype of chronic inflammatory demyelinating polyradiculopathy is associated with osteosclerotic myeloma. This disorder does not present with manifestations of myeloma but instead presents with a slowly progressive distal sensorimotor neuropathy. Weakness is more prominent than sensory loss, and sensation of vibration and joint position are affected more than sensation of pain. Nerve conduction velocities can be very decreased, and the protein concentration in the cerebrospinal fluid is usually elevated. A monoclonal protein, usually a lambda light chain with IgG or IgA heavy chain, is almost always found on immunoelectrophoresis but can be missed on serum protein electrophoresis. Immunofixation was performed in this case, however, and the results presumably ruled out the presence of an M protein. Osteosclerotic myeloma and its associated features have been referred to as the POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin lesions) syndrome.18,19 The bone plasmacytoma may be isolated or multifocal.18 Since this patient did not undergo a bone survey, and since in some cases, an osteosclerotic lesion has been found in the absence of a monoclonal protein, I cannot rule out an osteosclerotic plasmacytoma.20

Although it has been difficult to establish clear pathophysiologic connections between specific antibodies and chronic inflammatory demyelinating polyradiculopathy, there is strong evidence that antibodies have a role in the pathogenesis of the acute form. Two anti-ganglioside antibodies, anti-GM1 and anti-GQ1b, are associated with the Guillain–Barré syndrome and its Miller–Fisher variant.21-24 Much of the recent literature supports the presence of a shared antigen on the capsule of Campylobacter jejuni and ganglioside GM1 of peripheral myelin. Campylobacter infection is thought to induce the formation of antibodies that react both with a protein on the bacterial coat and with ganglioside GM1 on peripheral myelin, resulting in autoimmune-mediated demyelination. A large percentage of patients with the Guillain–Barré syndrome have positive tests for recent campylobacter infection, as does an even larger percentage of patients with a similar illness called acute motor axonal neuropathy.25 The anti–ganglioside GQ1b antibody is found in 90 percent of the patients with the Miller–Fisher variant of Guillain–Barré syndrome.24 Also, anti–ganglioside GQ1b antibody can bind to the neuromuscular junction, causing conduction block through an autoimmune mechanism not associated with demyelination.25

This patient did not have any of the antibodies, monoclonal proteins, or specific clinical features associated with the subtypes of chronic inflammatory demyelinating polyradiculopathy. Moreover, little is known about the pathogenesis of this disorder, but what we know about other demyelinating neuropathies is relevant.

The Charcot–Marie–Tooth neuropathies, which have historically been considered demyelinating neuropathies, are now considered myelinopathies or dysmyelinating neuropathies.26,27 They are disorders of myelin development or maintenance usually caused by abnormalities of myelin-associated proteins. Excellent murine models have now been developed for several of these neuropathies.26,27 Charcot–Marie–Tooth neuropathy type 1A is caused by a duplication of the portion of chromosome 17 containing the gene for peripheral myelin protein 22.28,29 The PMP22 gene codes for a myelin-associated protein found in compact myelin, which is myelin wound in tight spirals with fixed periodicity where the intracytoplasmic and extracytoplasmic faces of the apposed Schwann-cell membranes are tightly bound to one another. By an unknown mechanism, PMP22 duplication causes the peripheral-nerve hypomyelination and so-called onion-bulb formation in the nerves that are characteristic of type 1A. A second phenotype, characterized by a hereditary tendency toward pressure palsies, is caused by a deletion in the same gene.27,28 A third phenotype, historically called Déjerine–Sottas disease but now known as Charcot–Marie–Tooth neuropathy type 3, is characterized by the very early onset of severe nerve involvement and results from another deletion in this gene.30 Thus, three different genetic abnormalities in the same gene can cause three very different phenotypes.

In contrast, two different genetic abnormalities
can give rise to the same phenotype. Although Charcot–Marie–Tooth neuropathy type 1B is phenotypically identical to type 1A, it results from deletions in the myelin protein zero (P0) gene, which is carried on chromosome 1,31,32 Mutations in this gene cause not only Charcot–Marie–Tooth neuropathy type 1B but also type 3,33 Formerly considered an autosomal recessive disorder, type 3 is now known to be caused by a sporadic mutation in the P0 or PMP22 gene, and its clinical presentation is the same in either case.30,33 Charcot–Marie–Tooth neuropathy type X is phenotypically identical to types 1A and 1B but is transmitted on the X chromosome.34 Abnormalities of connexin 32, a protein implicated in the formation of Schwann-cell membrane pores, is known to cause Charcot–Marie–Tooth neuropathy type X.34

Studies of mice with the same myelin-protein abnormalities as those described in patients with Charcot–Marie–Tooth neuropathies suggest that in some peripheral-nerve demyelinating disorders, myelin is abnormal from the onset of fetal development, whereas in other disorders, the myelin abnormalities appear later. Some deficiencies of myelin components lead to improper Schwann-cell maturation, some to the inability to fuse adjoining Schwann-cell membrane leaflets, and others to improper repair of myelin.26,27

The abnormal formation of myelin does not fully explain the slowly progressive, symmetric, distal muscle atrophy characteristic of Charcot–Marie–Tooth neuropathies. Myelin-associated proteins may also influence axonal growth or the signal to the Schwann-cell nucleus concerning the amount of myelin that has formed.26,27

In fact, the acquired demyelinating neuropathies may not always be demyelinating. Whether there is an axonal form of the Guillain–Barré syndrome or chronic inflammatory demyelinating polyradiculopathy is controversial.36,37 Indeed, the clinical presentation of the neuropathy may depend on the location of the targeted component of the myelin or axon. The clinical presentation of the neuropathy may depend on whether the nerve dysfunction occurs in compact myelin, the nodes of Ranvier, or the neuromuscular junction. Antibodies found in some patients with clinical signs of so-called demyelinating neuropathy have been shown to block ion channels at the nodes of Ranvier, causing conduction block without demyelination.38 This finding, along with the presence of antibodies that bind to the neuromuscular junction, may explain why some patients with the Guillain–Barré syndrome have severe, very rapid conduction block or inexcitable nerves, with very early fibrillation potentials. Thus, the acquired demyelinating neuropathies may ultimately include disorders that cause ion-channel blockade at the nodes of Ranvier and disorders that cause neuromuscular blockade with secondary demyelination or axonal atrophy.36,37

A recent article raised important questions about the electrophysiologic criteria for the diagnosis of a demyelinating neuropathy. In five cases, the recommended electrophysiologic criteria for demyelination were not met, yet the patients had good responses to corticosteroid treatment.39 The disease in this patient also does not meet the criteria, but making the diagnosis of a demyelinating neuropathy is crucial, because several therapies are available that are not used in cases of axonal neuropathy.40 I believe that this patient had chronic inflammatory demyelinating polyradiculopathy and that the diagnostic procedure was a nerve-conduction examination to document signs of demyelination, such as slowed nerve conduction or conduction block.

**Dr. E. Tessa Hedley-Whyte:** In the biopsy specimen, we found a normal number of thickly myelinated fibers, but the sheaths of some fibers were thin in relation to the axonal diameter, suggesting remyelination or regeneration. There were also a few clusters of small myelinating axons. In the teased-fiber preparation, we found some myelin ovoids but no evidence of segmental demyelination.

Electron-microscopical examination showed a few empty Schwann-cell lamellae that suggested the disappearance of unmyelinated axons. A macrophage filled with myelin figures indicated the presence of active axonal degeneration.

On the histogram, the slope of the ratio of myelinated fibers to axon was lower than normal, suggesting remyelination. The density of the myelinated and unmyelinated fibers was normal. No inflammatory cells were found.

**Clinical Diagnosis**

Chronic inflammatory demyelinating polyradiculopathy.

**Dr. Stasha C. Gominak’s Diagnosis**

Chronic inflammatory demyelinating polyradiculopathy.

**Pathological Discussion**

Dr. Didier P. Clos: The diagnostic procedure was a detailed neurophysiologic evaluation, including nerve conduction studies, electromyography, and somatosensory evoked potentials. The nerve conduction studies initially revealed markedly prolonged distal latencies throughout; normal compound responses in the hand muscles; low-amplitude, desynchronized compound responses in the foot muscles; normal velocities in the arms; and a moderate slowing of velocities in the legs (Table 1). No conduc-
tion blocks were noted. The marked prolongation of the F-response latencies is highly suggestive of primary demyelination of the motor-nerve fibers. Cervical-root electrical stimulation with a needle showed a marked delay in conduction to proximal and distal muscles in the arms symmetrically and partial proximal conduction block of fibers supplying the intrinsic hand muscles (Fig. 1 and Table 1).

The median, ulnar, and radial sensory-nerve action potentials were unobtainable bilaterally, but the right sural-nerve potential was normal. The median and ulnar somatosensory evoked potentials showed a delay of the N9 Erb’s point potential, indicating peripheral slowing, prolongation of the N9–P/N13 interpeak latency, probably because of slowed conduction at the spinal-root level, and normal central conduction time bilaterally.

Needle electromyographic examination showed spontaneous activity in the lower leg and intrinsic foot muscles, normal motor unit potentials, and a reduction in maximal recruitment patterns.

Blink reflexes were elicited in the orbicularis oculi muscles with stimulation of the supraorbital nerve on each side. The R1 response of the blink reflex was markedly delayed bilaterally.

Five months later, the neuropathy was still uncontrolled by therapy, and a follow-up neurophysiologic evaluation showed worsening of the conduction abnormalities (Table 2) and a more extensive distribution of spontaneous activity on electromyography.

The criteria for primary demyelination that are based on the degree of conduction slowing are met in this case.41 The demyelinating lesions predominantly affected the proximal and distal segments of nerves, as indicated by the conduction blocks documented on root stimulation and the markedly prolonged distal motor latencies; the intermediate segments exhibited nonspecific velocities. This pattern of demyelination included conduction block, absent or uneven slowing from nerve to nerve or between

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**Table 1. Initial Studies of Motor-Nerve Conduction and F Responses.**

<table>
<thead>
<tr>
<th>Nerve and Stimulation Site</th>
<th>Latency</th>
<th>Amplitude</th>
<th>Conduction Velocity</th>
<th>F Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Latency</td>
<td>Maximal</td>
<td>Minimal</td>
<td>Latency</td>
</tr>
<tr>
<td></td>
<td>msec</td>
<td>Latency</td>
<td>Latency</td>
<td>msec</td>
</tr>
<tr>
<td>Right median</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>7.4</td>
<td>8.5</td>
<td>51.8</td>
<td>57.5</td>
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<tr>
<td>Elbow</td>
<td>12.2</td>
<td>8.1</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Eighth cervical root</td>
<td>25.2</td>
<td>4.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right ulnar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>5.0</td>
<td>7.2</td>
<td>45.7</td>
<td>49.5</td>
</tr>
<tr>
<td>Below the elbow</td>
<td>9.4</td>
<td>6.8</td>
<td>48</td>
<td></td>
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<tr>
<td>Above the elbow</td>
<td>12.5</td>
<td>6.4</td>
<td>48</td>
<td></td>
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<tr>
<td>Eighth cervical root</td>
<td>17.8</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right peroneal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle</td>
<td>11.9</td>
<td>1.4*</td>
<td>No response</td>
<td></td>
</tr>
<tr>
<td>Below the fibular head</td>
<td>22.0</td>
<td>1.3</td>
<td>29</td>
<td></td>
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<tr>
<td>Popliteal fossa</td>
<td>26.6</td>
<td>1.4</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Right tibial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle</td>
<td>14.5</td>
<td>1.1*</td>
<td>135</td>
<td>142</td>
</tr>
<tr>
<td>Popliteal fossa</td>
<td>29.1</td>
<td>0.9</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

*The response was prolonged and desynchronized.

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![Figure 1. Recording of Right-Sided Cervical-Root Stimulation from Four Target Muscles.](image)
consecutive segments of the same nerve, and a patchy distribution of abnormalities exemplified by sparing of the sural-nerve action potential. These findings suggested the acquired, inflammatory nature of demyelination, as distinct from the uniform slowing of conduction noted in the inherited dysmyelinating neuropathies. However, the patterns of acquired demyelination do not differ among disorders with different courses such as the Guillain–Barré syndrome and chronic inflammatory demyelinating neuropathy, which are distinguished on clinical grounds. The progression of the disease over a period of months, as in this case, is characteristic of chronic inflammatory demyelinating polyradiculopathy. In contrast, the Guillain–Barré syndrome reaches its nadir within four weeks, although there are reports of variants with an acute onset and progression for more than four weeks. Documentation of concomitant laboratory abnormalities is the only feature that distinguishes idiopathic chronic inflammatory demyelinating polyradiculopathy from the demyelinating neuropathies associated with monoclonal gammopathy. A pattern of conduction abnormalities that is highly suggestive of the neuropathy associated with anti-MAG antibody is characterized by disproportionately prolonged distal latencies.

The lesions in chronic inflammatory demyelinating polyradiculopathy or the Guillain–Barré syndrome are not often purely demyelinating, and mild axonal degeneration is frequently documented by the electromyographic findings of fibrillations and positive sharp waves. Thought to result from the magnitude of the inflammatory process leading to demyelination, the degeneration of motor axons has been shown in animal models to vary with the degree of antigenic stimulation. The absence of sensory potentials in this patient's hand is of uncertain importance and was possibly due to axonal degeneration or desynchronization of nerve action potentials caused by demyelinating lesions.

In patients with chronic inflammatory demyelinating polyradiculopathy, sural-nerve biopsy may be misleading, since the characteristic features may be absent because of the patchy nature of the process. Axonal degeneration caused by a more proximal lesion may be the sole abnormality, as in this patient. Nerve conduction studies are preferable to biopsy because they are sensitive and noninvasive, provide better sampling, and can be easily repeated in difficult cases.

Chronic inflammatory demyelinating polyradiculopathy is thought to have an autoimmune pathogenesis, since the histologic patterns and response to immunosuppression resemble those seen in studies of chronic allergic neuritis in animals. However, circulating autoantibodies, including anti–ganglioside GM$_1$ antibodies, have rarely been found in patients with chronic inflammatory demyelinating polyradiculopathy. T-cell–mediated mechanisms may have an important role, as suggested by a study in which T lymphocytes from patients with chronic inflammatory demyelinating polyradiculopathy were stimulated by P$_2$ or P$_o$ bovine myelin protein or peptides. The variation in responses to therapeutic approaches, as exemplified in this case by a response to prednisone without a response to plasma exchange or intravenous immune globulin, may also help to define meaningful subtypes of this disorder.

The anatomical and physiologic correlations in demyelination have been established in animal models and in many series of patients in the past three decades. Focal demyelination frequently causes conduction failure or block, conduction slowing, and in some cases, a switch from saltatory to continuous conduction. The frequency and function of such a switch are unknown, since the fiber that is still conducting may be unable to sustain physiologic firing frequencies. Slowing of conduction occurs with remyelination because the nodes of Ranvier increase in number.

Finally, recent studies have focused on humoral mechanisms that may contribute to the disordered conduction and the generation of deficits in some of the acquired demyelinating neuropathies. In the Guillain–Barré syndrome and chronic inflammatory demyelinating polyradiculopathy, the cerebrospinal fluid may contain a chemical factor affecting the function of the sodium channels. In the rat, anti–ganglioside GM$_1$ antibody has been reported to affect potassium and sodium current in myelinated

<table>
<thead>
<tr>
<th>NERVE AND STIMULATION SITE</th>
<th>LATENCY</th>
<th>Amplitude</th>
<th>CONDUCTION VELOCITY</th>
<th>F RESPONSE</th>
</tr>
</thead>
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<tr>
<td>Right median</td>
<td>8.9</td>
<td>4.1</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Above the elbow</td>
<td>11.8</td>
<td>5.0</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Above the elbow</td>
<td>14.4</td>
<td>4.9</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Right ulnar</td>
<td>13.5</td>
<td>0.7*</td>
<td>No response</td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>17.6</td>
<td>2.9</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Ankle</td>
<td>18.0</td>
<td>0.7*</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

*The response was prolonged and desynchronized.
nerve fibers, although this finding has recently been challenged. Such mechanisms may be the reason why many patients report some improvement within hours or a few days after treatment with an intravenous infusion of immune globulin or plasma exchange. The relation of these mechanisms to the processes leading to demyelination is unknown, and they may sometimes occur without concomitant demyelination. There may be axonal disorders affecting the voltage-sensitive ion channels of the axolemma that cause conduction abnormalities in the so-called demyelinating range but without structural changes in myelin.

ANATOMICAL DIAGNOSIS

Chronic inflammatory demyelinating polyradiculopathy.

REFERENCES