The authors report a case of a 65-year-old woman with small cell lung cancer who had profound, progressive lower extremity weakness, intermittent blurred vision, a dry mouth, and orthostatic hypotension. Results of laboratory and electrodiagnostic studies were consistent with the diagnosis of Lambert-Eaton myasthenic syndrome. The patient was treated with one course of intravenous immunoglobulin and had significant improvement.

(Key words: Lambert-Eaton myasthenic syndrome, small cell lung cancer, intravenous immunoglobulin, autoimmune disorder, voltage-gated calcium channels, case report)

Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disorder of neuromuscular transmission. It is characterized clinically by muscle weakness, hyporeflexia or areflexia, and autonomic dysfunction. Characteristic electrodiagnostic studies reveal low-amplitude muscle action potential and an incrementing response with strong voluntary contraction. Lambert-Eaton myasthenic syndrome develops as a result of antibodies directed at the presynaptic voltage-gated calcium channels (VGCC) and is often associated with small cell lung cancer. It has been treated with multiple medications such as guanidine, pyridostigmine bromide, diaminopyridine, and prednisone, all of which have limited or delayed responses or have significant adverse reactions. Plasma exchange has also been used with significant symptomatic improvement, which peaks at 2 weeks and subsides by 6 weeks. More recently, intravenous immunoglobulin (IVIG) has been used—but with limited clinical data. We report a case of Lambert-Eaton myasthenic syndrome associated with small cell lung cancer that was in remission and treated with IVIG.

Report of case

A 65-year-old woman followed up by oncologists at the Milton S. Hershey Medical Center for small cell lung cancer believed to be in complete remission was referred for neurologic evaluation after developing progressive lower extremity weakness of 1 month's duration. The patient reported difficulty walking and rising from her chair, as well as a heavy sensation in her legs. She reported no difficulty combing her hair or brushing her teeth and denied any specific numbness. She had occasional blurred vision, but denied having double vision. She also complained of a dry mouth during the past month and reported recently being diagnosed with postural hypotension. She denied speech or swallowing difficulties. Her medical history was notable for small cell lung cancer diagnosed in October 1998, for which she was in remission after chemotherapy and radiation treatment. She also had a history of hypothyroidism and was an ex-smoker. Her family history was negative for any significant neurologic disease, but her mother had had breast cancer.

On initial neurologic examination, the patient spoke fluently and had unimpaired mental status. Cranial nerves were intact. Her neck was supple, and her neck flexors and extensors were normal. She had normal strength in her upper extremities, but had a viselike grip in both hands. In her lower extremities, she had significant weakness of her proximal muscles, but distally was strong. Deep tendon reflexes were absent with the exception of a trace triceps jerk in her left upper extremity. She was then treated with IVIG at a dose of 2 g/kg over 2 days. Three weeks after IVIG, the patient had marked improvement in

From the Pennsylvania State University College of Medicine, Hershey, Pennsylvania, where Dr Peterlin is a resident and Dr Kothari is associate professor of neurology as well as director of the neurology residency program in the division of neurology, and where Dr Flood is assistant professor of medicine in the division of oncology.

Address correspondence to Milind J. Kothari, DO, Division of Neurology, Pennsylvania State College of Medicine, PO Box 850, MC H037, Hershey, PA 17033.

E-mail: mkothari@psu.edu

Peterlin et al • Case report

Use of intravenous immunoglobulin in Lambert-Eaton myasthenic syndrome

B. Lee Peterlin, DO
William Flood, MD
Milind J. Kothari, DO

From the Pennsylvania State University College of Medicine, Hershey, Pennsylvania, where Dr Peterlin is a resident and Dr Kothari is associate professor of neurology as well as director of the neurology residency program in the division of neurology, and where Dr Flood is assistant professor of medicine in the division of oncology.

Address correspondence to Milind J. Kothari, DO, Division of Neurology, Pennsylvania State College of Medicine, PO Box 850, MC H037, Hershey, PA 17033.

E-mail: mkothari@psu.edu

Report of case

A 65-year-old woman followed up by oncologists at the Milton S. Hershey Medical Center for small cell lung cancer believed to be in complete remission was referred for neurologic evaluation after developing progressive lower extremity weakness of 1 month's duration. The patient reported difficulty walking and rising from her chair, as well as a heavy sensation in her legs. She reported no difficulty combing her hair or brushing her teeth and denied any specific numbness. She had occasional blurred vision, but denied having double vision. She also complained of a dry mouth during the past month and reported recently being diagnosed with postural hypotension. She denied speech or swallowing difficulties. Her medical history was notable for small cell lung cancer diagnosed in October 1998, for which she was in remission after chemotherapy and radiation treatment. She also had a history of hypothyroidism and was an ex-smoker. Her family history was negative for any significant neurologic disease, but her mother had had breast cancer.

On initial neurologic examination, the patient spoke fluently and had unimpaired mental status. Cranial nerves were intact. Her neck was supple, and her neck flexors and extensors were normal. She had normal strength in her upper extremities, but had a viselike grip in both hands. In her lower extremities, she had significant weakness of her proximal muscles, but distally was strong. Deep tendon reflexes were absent with the exception of a trace triceps jerk in her left upper extremity. She had difficulty ambulating and used a wheelchair. Her initial laboratory data are summarized in the Table.

The patient underwent an electrodiagnostic study whose results were consistent with a presynaptic disorder of neuromuscular transmission. Results of right median, ulnar, and sural sensory studies were normal for her age. Results of a right ulnar motor study were normal, as were the F responses. Right peroneal and tibial motor studies showed borderline reduced amplitude, while the right median motor study showed significantly reduced amplitude. Repetitive stimulation at 3 Hz showed a 14% decrement (Figure 1). With 10 seconds of isometric exercise, there was a greater than 400% increase in the motor amplitude (Figure 2). She was then treated with IVIG at a dose of 2 g/kg over 2 days. Three weeks after IVIG, the patient had marked improvement in
strength. She was ambulating better and able to do a semi-deep knee bend and rise without assistance. She could walk without assistance, but used a cane for security. On examination 3 months later, she continued to show improvement in strength.

Discussion

There are two types of LEMS—LEMS associated with carcinoma and LEMS without carcinoma. Patients with either type have disease on an autoimmune basis. Sixty percent of LEMS patients have the type associated with small cell lung cancer, as did our patient. Our patient was 65 years old, slightly higher than the mean age (57.9) of patients with LEMS associated with carcinoma. However, 80% of patients with LEMS are older than 40 years.4 The symptoms of LEMS appear to result from a decrease in the release of the neurotransmitter, acetylcholine. The release of acetylcholine at presynaptic motor nerve terminals of the neuromuscular junction and at autonomic neurons depends on calcium influx through VGCC. Voltage-gated calcium channels are L, N, and P/Q types. In the nervous system, VGCC are found at the neuromuscular junction, autonomic neurons, and central nervous system.4 Voltage-gated calcium channels are blocked in patients with LEMS.5 Antibodies against the P/Q VGCC type inhibit acetylcholine release from the motor nerve terminals, resulting in muscular weakness. Antibodies against N, P, and Q types of VGCC inhibit autonomic neurons, resulting in such symptoms as dry mouth, dry eyes, orthostatic hypotension, constipation, and, in males, erectile impotence.3,4 Ninety percent of patients with LEMS have antibodies against P/Q type VGCC,1 as did our patient.

As with our patient, onset is usually subacute. She presented with proximal leg weakness of 1 month’s duration, which is characteristic of patients with LEMS. She had intermittent blurred vision. While 70% of patients with LEMS have mild and transient cranial nerve symptoms (eg, diplopia, ptosis, dysphagia),6 opthalmoplegia is unusual. She also complained of a dry mouth and had orthostatic hypotension. Such autonomic symptoms are seen in 80% of patients with LEMS.6 Results of electrodiagnostic studies in our patient were characteristic of LEMS, with a low-amplitude muscle action potential on single stimulus of a nerve, and with marked increase in the amplitude of the action potential of 100% or greater with strong voluntary contraction.2,7

Table.
Laboratory Data for 65-Year-Old Patient With Lambert-Eaton Myasthenic Syndrome

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>B12</td>
<td>323 pg/mL</td>
</tr>
<tr>
<td>folate</td>
<td>12.3 ng/mL</td>
</tr>
<tr>
<td>anti-Hu</td>
<td>negative</td>
</tr>
<tr>
<td>anti-Ri</td>
<td>negative</td>
</tr>
<tr>
<td>anti-Yo</td>
<td>negative</td>
</tr>
<tr>
<td>creatine kinase</td>
<td>37 U/L</td>
</tr>
<tr>
<td>aldolase</td>
<td>4.4 U/L</td>
</tr>
<tr>
<td>calcium</td>
<td>9.6 mg/dL</td>
</tr>
<tr>
<td>acetylcholine receptor antibody</td>
<td>0.28 nmol/L</td>
</tr>
<tr>
<td>VGCC* IgG auto-antibody</td>
<td>detected</td>
</tr>
</tbody>
</table>

*VGCC = voltage-gated calcium channels.
Despite treatment with chemotherapy and radiation, our patient still had LEMS. Routine treatment consists of various modalities, including pyridostigmine bromide, prednisone, azathioprine, and guanidine—all of which are associated with significant side effects and poor responses. Intravenous immunoglobulin infusion has been studied more recently in patients with LEMS. Bain et al reported an onset of effect of IVIG in their patients at 2 to 4 weeks. Furthermore, Rich et al reported improvement with IVIG to last 4 to 10 weeks, with no significant side effects, in three patients with LEMS associated with carcinoma. Thus, because of our patient’s severity of weakness and IVIG’s quicker onset of effect and lower side effect profile than the other available treatment modalities, we used IVIG. She had marked symptomatic improvement following one course of IVIG.

In summary, we report a case of a 65-year-old woman with LEMS associated with small cell lung cancer who was successfully treated with IVIG. Because of the relative safety and effectiveness of IVIG, its role in treating patients with LEMS with or without small cell lung cancer appears to be an increasingly strong option.

References


