Posterior Reversible Encephalopathy Syndrome After The Treatment Of Guillain-Barré Syndrome With IVIG: A Case Report

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Abstract — Guillain-Barré syndrome (GBS) is an autoimmune-mediated peripheral demyelinating disorder. Posterior reversible encephalopathy syndrome (PRES) is frequently seen in hypertensive crisis due to altered capillary membrane permeability. Concurrence of GBS with PRES is rare. We reported a 35-year old Caucasian woman who presented with seven days of ascending paresthesia, weakness, and severe back pain; examination disclosed absent deep tendon reflexes and weakness. Findings of increased level of CSF protein by lumbar puncture and demyelinating features by electrophysiologic studies supported the clinical diagnosis of GBS. Intravenous immunoglobulin (IVIG) was started on day 2 of admission. Five hours after receiving her first dose of IVIG, she had an episode of visual loss followed by a generalized tonic-clonic seizure. MRI revealed hyperintensity in the bilateral parieto-occipital regions consistent with PRES. Treatment with IVIG was switched to plasmapheresis. Her neurological symptoms stabilized and she had no further seizures. By three months she fully recovered without any neurological deficits; her initial PRES lesions also completely resolved on MRI. IVIG treatment in a newly diagnosed GBS patient produced clinical and imaging manifestations of PRES.

II. CASE REPORT

We report a 35 year old previously healthy Caucasian woman who was initially admitted to an outside hospital for pneumonia and subsequently developed ascending weakness, distal paresthesias and severe back pain over a seven day period. Upon transfer to our institution, her examination showed bilateral arm and leg weakness; proximal upper extremities (Medical Research Council [MRC] 3/5), distal upper extremities (MRC 2/5), lower extremities (MRC 4/5). Deep tendon reflexes were absent in both upper and lower extremities; sensory examination was normal. Lumbar puncture was performed on day 2 of admission and showed an increased level of protein (126 mg/dL), mildly increased white blood cells (13 cells/mm$^3$) due to a contamination of red blood cells (2093 cells/mm$^3$) and a normal level of glucose (66 mg/dL). Neurophysiologic studies at 10 days after onset of symptoms showed electrodiagnostic evidence consistent with a sensorimotor polyneuropathy, with demyelinating features, supporting the clinical diagnosis of GBS (Table 1), including absent sensory nerve action potentials in right median and ulnar, but normal in sural, nerves; absent or prolonged F-waves latencies and significantly prolonged distal latencies of all motor nerves tested. The patient did not have symptoms of dysautonomia.

IVIG was initiated on day 2 of admission (eight days after onset of the symptoms). About five hours after receiving the first dose of IVIG, she had an episode of acute vision loss followed by generalized convulsions for 2 minutes and altered mental status. She developed respiratory distress due to her compromised forced vital capacity (FVC, down to 600 mL/min) and required intubation. No prominent hypertension was appreciated. EEG showed no epileptiform discharges except for general slowing. Brain MRI with contrast showed bilateral parietal-occipital hyperintensities on T2/FLAIR (Figure 1A and 1B) with unremarkable findings on...
TABLE 1: EMG findings of the patient on day 10 after the symptoms onset, and status post first session of plasmapheresis.

<table>
<thead>
<tr>
<th>Nerve stimulated</th>
<th>Distal Latency (msec)</th>
<th>Amplitude (motor= mV, sensory =µV)</th>
<th>Conduction velocity (m/sec)</th>
<th>F-wave (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right NL</td>
<td>Right NL</td>
<td>Right NL</td>
<td>Right NL</td>
</tr>
<tr>
<td>Median (m)</td>
<td>9.5 ≤3.8</td>
<td>3.3 ≥6</td>
<td>49.4 ≥52</td>
<td>39 34.8</td>
</tr>
<tr>
<td>Ulnar(m)</td>
<td>5.6 ≤3</td>
<td>3 ≥8</td>
<td>46.4 ≥50</td>
<td>35 32.6</td>
</tr>
<tr>
<td>Median (s)</td>
<td>NR ≤3.4</td>
<td>NR ≥15</td>
<td>NR ≥50</td>
<td>NR ≥50</td>
</tr>
<tr>
<td>Ulnar(s)</td>
<td>NR ≤3.0</td>
<td>NR ≥14</td>
<td>NR ≥50</td>
<td>NR ≥50</td>
</tr>
<tr>
<td>Peroneal nerve(m)</td>
<td>7.1 ≤6</td>
<td>0.5 5</td>
<td>43.2 ≥50</td>
<td>59 44.7</td>
</tr>
<tr>
<td>Peroneal nerve(s)</td>
<td>7.1 ≤6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial Nerve(m)</td>
<td>6.4 ≤5.6</td>
<td>3.7 ≥8</td>
<td>50.4 ≥50</td>
<td></td>
</tr>
<tr>
<td>Sural nerve (s)</td>
<td>3.4 ≤4.4</td>
<td>17 6</td>
<td>37.9 ≥40</td>
<td></td>
</tr>
<tr>
<td>Superficial peroneal(s)</td>
<td>2.6 ≤4.4</td>
<td>18 6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Brain MRI with FLAIR sequence showing bilateral parietal-occipital hyperintensity (A and B). A repeated MRI in 3 months showing that previous lesions have been resolved (C and D).

ADC/DWI/SWAN/contrast sequences (data not shown). IVIG regimen was aborted and, instead, she was given a course of five sessions of plasmapheresis, with each session administered every other day. Her FVC improved to normal (2 L/min) after finishing her second session of plasmapheresis. Upon discharge, she had only mild weakness of the right upper and lower extremities (MRC 4+/5). A brain MRI 3 months later revealed that the previously noticed abnormal lesions had completely resolved (Figure 1C and 1D). She made a full recovery without any residual neurological symptoms in vision, motor and sensory realms.

III. DISCUSSION

The association between GBS and PRES was first reported in 1996. However, the concurrence of PRES in GBS may have been underestimated. Recently, anecdotal case reports showed clinically silent PRES might occur in GBS patients and patients might manifest only minimal CNS symptoms such as hypersomnia."

PRES could appear as an initial manifestation of GBS but more commonly occur 3-14 days after the onset of GBS symptoms, such as sensory-motor dysfunction and back pain. Prognosis varied. More than half of previously documented cases recovered to functional independence, while some experienced devastating neurological complications such as stroke or cardiac dysfunction, for example, takotsubo cardiomyopathy.

Several hypotheses have been raised about potential mechanisms associating GBS and PRES. One hypothesis was based on the observation that dysautonomia occurs in some GBS patients, a finding that may be due to the imbalance between myelination and demyelination of autonomic innervations to cardiovascular regulation, thereby causing mixed parasympathetic/sympathetic hyperactivity and catecholamine surge. The autonomic dysregulation could cause hyperperfusion and cerebral vasogenic edema, which may in turn cause PRES. Another hypothesis was based on the systemic cytotoxic effects of molecules produced in the setting of GBS. Those toxic molecules, such as elevated levels of CSF chemokines and cytokines, may disturb the dynamic changes of blood-nerve barrier in functional and morphological status, and could also directly cause endothelial injury leading to PRES.
Regarding the relationship between PRES and GBS, however, it remains uncertain whether PRES occurred as a complication of GBS, provoked by IVIG, or by the combination of the two. Our patient quickly developed PRES five hours after receiving IVIG, suggesting that her PRES might have been associated with IVIG therapy via as yet to be determined mechanisms. Previous clinical reports supported our observation that PRES might occur as a complication of IVIG therapy.\textsuperscript{12} Notably, no hypertension or any dysautonomic symptoms were identified prior to initiating IVIG treatment, findings typically observed in PRES linked with GBS. The onset of IVIG-induced-PRES may occur in hours (such as our case) or delayed usually 1 to 5 days after IVIG administration based on previous case reports. Possible pathophysiological mechanisms of IVIG induced-PRES include vasogenic edema, cerebrovascular endothelial dysfunction, serum hyperviscosity or the roles of cytokines.\textsuperscript{1}

The onset of age in patients with PRES associated with GBS varied broadly, ranging from 17 to 82 years.\textsuperscript{6,13} Interestingly, most of these patients tended to be older (92% aged over 55) and were predominantly seen in females.\textsuperscript{7} Our case was a previously healthy 35 years old adult female. After the IVIG treatment was switched to plasmapheresis, she did not have worsening vision symptoms but a full recovery from both GBS and PRES in three months. Thus, PRES in GBS may, at least at the early stage, have a better, or benign, and reversible, course.

In addition to IVIG, plasmapheresis has been recommended in the guideline as one of the first line treatments for GBS.\textsuperscript{15} The mechanisms of plasmapheresis include removal of pathologic antibodies, cytokines, and immune complexes. Additionally, plasmapheresis has an immune-modulatory role with Th1/Th2 shift, which might have effects beyond a simple removal of antibodies.\textsuperscript{14} Although administration of plasmapheresis in practice has some limitations when compared to IVIG, such as requiring a central line and a facility with specific equipment, the efficacy in treating GBS between these two modalities is essentially equivalent.\textsuperscript{15}

IV. Conclusion

The concurrence of PRES in GBS can be encountered in clinical practice and may be underestimated if CNS symptoms are not apparent or are not recognized. Knowledge of PRES as a potential, although less common, significant complication of GBS is important, particularly when administering IVIG because IVIG treatment is recommended by the guideline of American Academy of Neurology.\textsuperscript{16} PRES could be caused with IVIG treatment.\textsuperscript{12,14} Early recognition and appropriate management of PRES in GBS by switching regimen from IVIG to plasmapheresis is recommended to ensure a promising prognosis of GBS and prevent the occurrence of possible severe CNS neurological deficits.

REFERENCES

Questions (please choose one single answer):

1. What is not the common symptom of GBS?
   - A) Facial weakness
   - B) Dysautonomia
   - C) Back pain
   - D) Papilledema

2. When does PRES usually appear after the occurrence of GBS?
   - A) Simultaneously
   - B) 1-2 days
   - C) 3-14 days
   - D) 3-4 weeks

3. What is the most common precipitating factor of PRES syndrome?
   - A) Dialysis
   - B) Hypertension
   - C) IVIG
   - D) Preeclampsia

4. What is the most common side effect of IVIG?
   - A) Headache
   - B) Fatigue
   - C) PRES syndrome
   - D) Aseptic meningitis

Correct answers:

1. D. Patients with GBS usually endorse symptoms of weakness of bilateral lower extremities in an ascending pattern. Facial weakness can occur up to 50% of the cases. Meanwhile, back pain is also one of the common presenting features during the acute phase. Dysautonomia has been reported up to occur up to 70% of GBS patients, most commonly tachycardia, and orthostatic hypotension. Papilledema is not a common feature of GBS.

2. C. PRES could appear as an initiating manifestation, but more commonly 3-14 days after the occurrence of GBS symptoms based on published case series review.

3. B. PRES could occur under the situation such as hypertensive crisis, kidney disease, malignancy, dialysis dependency, transplantation, IVIG etc. The most common precipitating factor is hypertension which observed in up to 53% of the cases.

4. A. IVIG has been reported to cause various central nervous system side effects, such as headache (up to 75%), fatigue (up to 29%), chills (up to 19%), and less often PRES syndrome, or aseptic meningitis.