**CLINICAL VIGNETTE**

# Guillain-Barré Syndrome Variant

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A 50-year-old female presented with bilateral occipital headache and intermittent paresthesias of bilateral upper and lower extremities for one week. She also noted facial weakness and numbness as well as urinary incontinence for two days. She was initially evaluated in the emergency room and discharged home on prednisone and acyclovir for a presumptive diagnosis of Bell's palsy. Her facial weakness worsened and she returned to the emergency room the following day and was admitted. She reported generalized malaise and chills for the past week but denied fever, diplopia, dysphagia, and dysarthria. There was no abdominal pain, diarrhea, cough, or sick contacts and no history of similar symptoms in the past. Her review of systems was otherwise unremarkable. The patient's past medical history was significant for cervical degenerative disease, obstructive sleep apnea, and central obesity. She denied significant family history and was not on any chronic medications prior to admission.

Her physical exam revealed a temperature of 36.8°C, blood pressure 164/106 mmHg, pulse 112 beats per minute with significant orthostatic changes, Respiratory rate was 19/bpm, and oxygen saturation of 97% on room air. Cardiac examination revealed regular tachycardia. Neurological examination was significant for prominent facial diplegia with right side slightly weaker than the left, areflexia throughout, decreased sensation to touch in a patchy distribution throughout, and ataxic gait. The remainder of the exam was unremarkable.

Initial, laboratory evaluation was notable for a white blood cell 17.9 x $10^9$/L, hemoglobin 13.8g/dL, sodium 135mmol/L. Thyroid stimulating hormone, hemoglobin A1c, erythrocyte sedimentation rate, c-reactive protein, vitamin B12, and folate levels were within normal range. Extensive rheumatologic work-up was negative. Serum anti-GQ1b IgG, anti-GM1 IgM, and anti-GM1 IgG were negative. Cerebrospinal fluid (CSF) studies were significant for zero white blood cells and an elevated albumin of 90mg/dL. CSF viral and bacterial PCR panels were negative as well as CSF bacterial and fungal cultures. Magnetic resonance imaging of the brain with and without contrast was unremarkable. Magnetic resonance imaging survey of the spine was unremarkable.

Based on clinical and CSF findings, the patient was diagnosed with Guillain-Barré syndrome variant. She was admitted and treated with intravenous immunoglobulin 400mg/kg/day for five days with improvement in her symptoms. Her blood pressure and tachycardia improved with nebivolol and amlodipine. She also received intensive physical therapy.

***Discussion***

Guillain-Barré syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy with varying presentations and outcomes.[1] The condition was initially described by Landry in 1859.[1,2] Sixty years later, Georges Guillain, Jean-Alexandre Barré, and Andre Strohl discovered albuminocytologic dissociation in the CSF of two soldiers who developed acute paralysis and areflexia that resolved spontaneously.[1,2] Albuminocytologic dissociation refers to CSF with an increase in protein concentration and normal cell count.[2] The condition is now referred to as Guillain-Barré syndrome or Guillain-Barré-Strohl syndrome.[1]

There are approximately 100,000 new cases diagnosed annually world-wide.[3] Multiple variants exist and are characterized by the type of nerve fibers involved (motor, sensory, sensory and motor, cranial, or autonomic) and primary mode of fiber injury (demyelinating vs axonal).[1] GBS may be subdivided into acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and Miller-Fisher syndrome (MFS).[1,2] AIDP is the most prominent variant in the Western world. Overlap syndromes also exist, including GBS-MFS overlap.[2] GBS is presumed to be autoimmune in etiology, typically precipitated by an infection that generates antibodies that cross react with gangliosides at nerve membranes resulting in nerve damage and impaired nerve conduction.[4]

Miller Fisher Syndrome (MFS) is characterized by the triad of ophthalmoplegia, ataxia, and areflexia without weakness. Most patients present with at least two features and often have an elevated CSF protein and characteristic autoantibody, anti-GQ1b.[1]

In two-thirds of cases, GBS is preceded by an infection two to four weeks prior to symptom onset.[1] Common pathogens associated with the condition include *Campylobacter jejuni*, Zika virus, and the severe acute respiratory syndrome coronavirus 2.[5] Influenza A virus, Cytomegalovirus, Epstein-Barr virus, and *Mycoplasma pneumoniae* have also been implicated.[3] Some vaccinations, including influenza A and the previous brain-derived Semple rabies vaccines, have also been implicated as they instigate an immune response.[5]

In its typical presentation, patients often present with neuropathic or radicular pain, numbness, paresthesias, or limb weakness.[2] The limb weakness is often rapidly progressive, bilateral, relatively symmetric, and ascending in distribution.[1,2] Symptoms may progress rapidly or have a step-wise progression. Weakness ranges from mild to severe flaccid quadriplegia. Approximately 30% of patients progress to respiratory failure. Areflexia or hyporeflexia is also prominent. Facial nerves are affected in 70% of cases. Autonomic instability, including sinus tachycardia, bradycardia, labile blood pressure, or cardiac arrhythmias, is also common.[1]

Maximal weakness plateaus within the first four weeks of illness. Patients then enter a plateau phase of variable duration, days to weeks to months, followed by a recovery phase of variable duration.[2] If symptoms continue to progress after four weeks, a subacute inflammatory demyelinating polyradiculoneuropathy is suggested. If symptoms progress after eight weeks, a chronic inflammatory demyelinating polyradiculopathy should be considered.[1]

Diagnosis is straight forward when patients exhibit typical symptoms. Diagnosis is based on clinical features and may be supported by CSF studies, EMG studies, and the presence of auto-antibodies in the setting of particular variants.[2] Features required for diagnosis include progressive weakness in legs and arms (sometimes initially only in legs) and areflexia or hyporeflexia in weak limbs.[3] Albuminocytologic dissociation in CSF is a classic finding in GBS. However, during the first week of symptoms, 50% of patients may have a normal CSF protein level. Hence a normal CSF protein level does not rule out the diagnosis.[2] EMG studies may be useful when they show signs of polyneuropathy in areas that have not been clinically involved. They can also aid in differentiating between axonal and demyelinating variants.[2] However, EMG studies may be normal in early stages of the disease.[5] Auto-antibodies may be present in certain variants of GBS. However, they may solely be detectable in serum for several days or weeks, which limits their use. Anti-GM1 and anti-GD1a IgG antibodies are often seen in patients with AMAN.[4] Anti-GQ1b antibodies are present in approximately 90% of patients with MFS.[4] Given the existence of multiple variants, some not well described, diagnosis may be challenging in atypical presentations.[3]

The treatment for GBS includes intravenous immunoglobulin (IVIg 0.4g/kg for five days) or plasma exchange (usually 200-250 mL/kg in five sessions) along with supportive care. Intravenous immunoglobulin (IVIg) is more commonly used given its ease of administration and milder side effects.[6] No randomized controlled studies have been performed to assess the effect of plasma exchange or IVIg in patients with milder forms of GBS.[2] Experts recommend treating all patients who require assistance with ambulation, are bed-bound, or are on a ventilator. In milder cases where patients are able to walk without assistance, but exhibit rapid progression of symptoms, or develop autonomic dysfunction, bulbar or facial weakness, treatment with IVIg or plasma exchange is recommended to prevent further nerve damage and progression of symptoms.[6]

Approximately 40-50% of patients treated with IVIg or plasma exchange show no improvement in symptoms at four weeks or have progression in symptoms.[6] At that time, another round of IVIg or plasma exchange may be considered. A phenomenon termed treatment-related fluctuation occurs in about 10% of patients. These patients experience a secondary deterioration of symptoms after initial improvement and typically improve with retreatment with either IVIg or plasma exchange.[4]

Despite current treatment, GBS remains a challenging disease. Approximately 30% of patients progress to respiratory failure, 20% are unable to walk independently at 6 months, and the mortality rate is 3-10%. Residual fatigue and pain are common months to years after initial symptoms onset.[2] Relapse occurs in approximately 5% of patients, often within the first two months.[6]

Scoring symptoms, such as the Erasmus GBS outcome score, have been developed to assist in predicting a patient's probability of independent ambulation at six months. The Erasmus scoring system includes age, preceding diarrhea, and the modified GBS disability score at two weeks to aid in prognostication.[1]

Our patient presented with intermittent paresthesias of her bilateral upper and lower extremities, facial numbness, facial weakness, areflexia, ataxia, and dysautonomia. She reported malaise and chills, but there was no clear inciting infectious etiology. CSF studies revealed albuminocytologic dissociation. Anti-GQ1b antibodies were negative. She was diagnosed with GBS variant. Given the presence of facial weakness and dysautonomia, she received treatment with IVIg for five days. She had no progression in her neurological symptoms and showed significant improvement. Her tachycardia and hypertension improved with nebivolol and amlodipine. By day of discharge, patient's ataxia was much improved and she was ambulating independently. During the following weeks, she continued to show resolution of symptoms.

**REFERENCES**


1. **Dimachkie MM, Barohn RJ**. Guillain-Barré syndrome and variants. *Neurol Clin*. 2013 May;31(2):491-510. doi: 10.1016/j.ncl.2013.01.005. Epub 2013 Feb 19. PMID: 23642721; PMCID: PMC3939842.
2. **van Doorn PA**. Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). *Presse Med*. 2013 Jun;42(6 Pt 2):e193-201. doi: 10.1016/j.lpm.2013.02.328. Epub 2013 Apr 28. PMID: 23628447.
3. **Willison HJ, Jacobs BC, van Doorn PA**. Guillain-Barré syndrome. *Lancet*. 2016 Aug 13;388(10045):717-27. doi: 10.1016/S0140-6736(16)00339-1. Epub 2016 Mar 2. PMID: 26948435.
4. **van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA**. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat Rev Neurol*. 2014 Aug;10(8):469-82. doi: 10.1038/nrneurol. 2014.121. Epub 2014 Jul 15. PMID: 25023340.

5. **Shahrizaila N, Lehmann HC, Kuwabara S**. Guillain-Barré syndrome. *Lancet*. 2021 Mar 27;397(10280):1214-1228. doi: 10.1016/S0140-6736(21)00517-1. Epub 2021 Feb 26. PMID: 33647239.
6. **Verboon C, van Doorn PA, Jacobs BC**. Treatment dilemmas in Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry*. 2017 Apr;88(4):346-352. doi: 10.1136/jnnp-2016-314862. Epub 2016 Nov 11. PMID: 27837102.