CLINICAL VIGNETTE

Guillain-Barré Syndrome

Adam Solis-Cohen, MD[1] and Farid Abdelmalak, MD[1]

[1]UCLA David Geffen School of Medicine, Department of Medicine

Case Report

A 43-year-old woman with no significant past medical history presented with acute onset of upper and lower extremity weakness for one week. She also noted numbness and sensory loss of bilateral upper and lower extremities. She was on vacation at Lake Havasu when her symptoms began. She initially noted numbness in her hands, which progressed up her arms, also including her mouth. She then reported lower extremity weakness with increasing difficulty walking. She presented to an ER in Arizona and was transferred to UCLA for further evaluation and treatment.

Admission Vital signs were within normal limits. Physical exam was significant for mild, bilateral lower extremity weakness and diffuse lower extremity sensory loss. Labs included unremarkable CBC, BMP, and coagulation panel. MRI brain and cervical spine were unremarkable for any pathology. Thoracic and lumbar spine MRI was positive for smooth and mild enhancement along the surface of the conus medullaris and the cauda equina nerve roots. These findings, although nonspecific, were consistent with Guillain-Barré syndrome. The patient underwent lumbar puncture and CSF was significant for albuminocytologic dissociation. EMG and Nerve conduction study showed polyradiculopathy with predominant axonal involvement, particularly in bilateral lower extremities. She was treated with 4 days of IVIG and noted improvement in motor function during treatment. She was transferred to acute rehabilitation for further care. She received another IVIG treatment at the rehab facility and continued to make gradual improvements in functioning with physical therapy.

Discussion

Guillain-Barré syndrome (GBS) is the most common and most severe acute paralytic neuropathy with incidence of about 100,000 people per year.[1] The syndrome is also known as "acute inflammatory demyelinating polyneuropathy" and "acute motor axonal neuropathy" to describe different phenotypes.

Guillain-Barré syndrome is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots.[2] Molecular mimicry between microbial and nerve antigens is thought to be a driving force behind the development of GBS, as exemplified in the case of Campylobacter Jejuni infection. However, the interplay between microbial and host factors that dictates if and how the immune response is shifted towards unwanted autoreactivity is still not well understood.[3] Moreover, genetic and environmental factors that affect individual susceptibility to develop the disease are unknown.[4]

Pathophysiology

Existing evidence supports a mechanism of inflammatory neuropathy due to cross reactivity between neural antigens and antibodies that is induced by specific infections.[5] Glycans expressed on lipopolysaccharides of preceding infectious organisms are thought to be the common molecular mimic that triggers an immune response to these carbohydrate antigens located on microbial and axolemmal surface molecules.[3] The mechanism is believed to be antibody mediated complement fixing damage to myelin sheath (schwann cell components) in the case of demyelinating polyneuropathy and to axons (axolemma) in the case of axonal polyneuropathy. This is supported by the discovery of specific antibody biomarkers to neuronal membrane gangliosides (GM1 and GD1a). In Miller Fisher syndrome, anti GQ1B was shown to be disproportionately enriched in motor nerves that innervate extraocular muscles.[6] When compared to acute motor axonal neuropathy, the immunological cascade in acute inflammatory demyelinating polyneuropathy is less well understood due to a wider array of immune stimulants and to the lack of specific antibody biomarkers discovered.[1]

The **clinical characteristics** of GBS are a rapidly progressive bilateral weakness of the extremities, often with sensory and cranial nerve involvement 1-2 weeks after an infection (immune stimulation) with progression to peak clinical deficit in 2-4 weeks.[1,7] Weakness is classically ascending, usually starting distally but can be proximal.[1] Alternate presentations include Miller Fisher syndrome, which is characterized by the triad of ophthalmoplegia, ataxia, and areflexia. This is due to cranial nerve involvement resulting in facial, oculomotor, or bulbar weakness, which can extend to involve the limbs.[1] Patients with GBS can also have sensory loss, ataxia, and features of autonomic dysfunction.[1] Muscle pain or radicular pain is often present. Most patients have, or develop, reduced

tendon reflexes in the affected limbs.[1] Twenty to thirty percent of patients develop respiratory failure requiring mechanical ventilation.[1] Progressive weakness usually continues for 4 weeks and can last up to 6 weeks. Severity and duration is highly variable and can range from mild weakness with spontaneous recovery to quadriplegia and ventilator dependent without signs of recovery for several months or longer. Although severe cases are uncommon, GBS is remarkably clinically diverse, and includes several distinctive variants and atypical cases.[1]

The **diagnosis** of GBS is largely a clinical diagnosis but can be aided by cerebrospinal fluid (CSF) and electromyography (EMG). CSF studies show albuminocytologic dissociation – the combination of a normal cell count and increased protein level. Nerve conduction studies (NCS) abnormalities are most pronounced 2 weeks after the start of weakness.[8] NCS allow clinicians to divide GBS into acute inflammatory demyelinating polyneuropathy, acute motor axonal neuropathy, or acute motor and sensory axonal neuropathy.[9]

NCS in patients with acute inflammatory demyelinating polyneuropathy show features of demyelination, including prolonged distal motor latency and reduced nerve conduction velocity.[8] Features of axonal Guillain-Barré syndrome (acute motor axonal neuropathy or acute motor and sensory axonal neuropathy) are decreased motor, sensory amplitudes, or both.[10]

Treatment

Treatment of GBS requires supportive care, IVIG or plasmapheresis. Combination of plasma exchange followed by IVIG is not significantly better than plasma exchange or IVIG alone.[11] Supportive care includes monitoring of respiratory function with maximal inspiratory pressures and vital capacity to predict diaphragmatic strength and timely transfer to ICU if needed.[1] Negative inspiratory force (NIF) is a bedside test to measure respiratory muscle function. Normal is usually greater than 60cm water. If the NIF is dropping or nears 20cm water, respiratory support needs to be available. The Erasmus GBS Respiratory Insufficiency score (EGRIS) has been used as a prognostic tool to aid in determination of the need for artificial ventilation. Additional treatment includes monitoring of cardiac and hemodynamics, deep vein thrombosis prophylaxis, management of possible bowel and bladder dysfunction, early initiation of physical and occupational therapy, pain management, and psychosocial support.

Conclusion

This case illustrates a classic case of GBS. It exemplifies the presentation of acute inflammatory demyelinating polyradiculopathy after a nonspecific viral syndrome in an otherwise healthy adult. Treatment with IVIG and supportive care led to a gradual, modest improvement in her symptoms. Her lower extremity weakness persists, demonstrating the substantial morbidity associated with this neuropathy and the importance of continued aggressive physical therapy.

REFERENCES

1. **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. Review. PubMed PMID: 26948435.
2. **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. Review. PubMed PMID: 25023340.
3. **Willison HJ, Goodyear CS**. Glycolipid antigens and autoantibodies in autoimmune neuropathies. *Trends Immunol*. 2013 Sep;34(9):453-9. doi: 10.1016/j.it.2013. 05.001. Epub 2013 Jun 13. Review. PubMed PMID: 23770405.
4. **Blum S, McCombe PA**. Genetics of Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): current knowledge and future directions. *J Peripher Nerv Syst*. 2014 Jun;19(2):88-103. doi: 10.1111/jns5.12074. PubMed PMID: 25039604.
5. **Walling AD, Dickson G**. Guillain-Barré syndrome. *Am Fam Physician*. 2013 Feb 1;87(3):191-7. Review. PubMed PMID: 23418763.
6. **Liu JX, Willison HJ, Pedrosa-Domellöf F**. Immunolocalization of GQ1b and related gangliosides in human extraocular neuromuscular junctions and muscle spindles. *Invest Ophthalmol Vis Sci*. 2009 Jul;50(7):3226-32. doi: 10.1167/iovs.08-3333. Epub 2009 Feb 28. PubMed PMID: 19255160.
7. **Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC**. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. *Brain*. 2014 Jan;137(Pt 1):33-43. doi: 10.1093/brain/awt285. Epub 2013 Oct 26. PubMed PMID: 24163275.
8. **Hadden RD, Cornblath DR, Hughes RA, Zielasek J, Hartung HP, Toyka KV, Swan AV**. Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. Plasma Exchange/ Sandoglobulin Guillain-Barré Syndrome Trial Group. *Ann Neurol*. 1998 Nov;44(5):780-8. PubMed PMID: 9818934.
9. **Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR, Griffin JW, Asbury AK, Blaser MJ, McKhann GM**. Guillain-Barré syndrome in northern China. Relationship to Campylobacter jejuni infection and anti-glycolipid antibodies. *Brain*. 1995 Jun;118 (Pt 3):597-605. PubMed PMID: 7600081.
10. **Kokubun N, Nishibayashi M, Uncini A, Odaka M, Hirata K, Yuki N**. Conduction block in acute motor axonal neuropathy. *Brain*. 2010 Oct;133(10):2897-908. doi: 10.1093/brain/awq260. Epub 2010 Sep 20. PubMed PMID: 20855419.
11. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. *Lancet*. 1997 Jan 25;349(9047):225-30. PubMed PMID: 9014908.