GBS | CIDP Foundation International

Speaker Series Summary Episode 2: Variants of GBS and CIDP

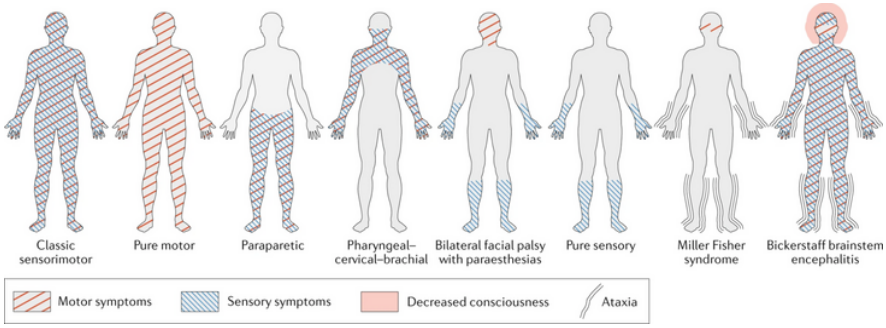
Overview

In this episode of our Speaker Series, we talked with Dr. Karissa Gable from Duke University about variants of GBS and CIDP, mimics, its symptoms, and how each are treated.

Summary

Understanding Variants	**Unfortunately, there isn't a single test that will determine whether someone has GBS, CIDP, or MMN. Therefore, finding out if a patient has a variant or mimic is even harder to determine. Doctors use the process of elimination to diagnose patients with our conditions by using the patient's symptoms, test results, and the progression of the patient's illness and condition. Therefore, Dr. Gable encourages patients to verbalize their experience and influences on their health such as family history by giving a chronological report to their physicians.** **Variants differ from the typical symptoms of conditions because:** 1. **Symptoms will affect some parts of the body more than others** 2. **Some exams will come back with regular results while simultaneously having exams with concerning data** 3. **Variants take more time and more tests to determine** a. **Some of these tests include an electrodiagnostic test or a repetitive nerve stimulation test** b. **Since there is not a diagnostic test present, doctors understand conditions through symptoms. Therefore, understanding the presence of variants takes 24 hours to weeks, especially when symptoms are progressive and changing rapidly.** c. **IGOS and INCBASE are long term studies supported by the Foundation to help widen the understanding of CIDP and GBS. IGOS stands for the International Guillain-Barre Outcomes Study and is the largest collaborative data-collection platform for GBS patients. INCBASE stands for Inflammatory Nerve Consortium Base and is a collaborative data-collection platform for CIDP patients** 4. **Doctors must evaluate how a patient moves and what a patient can feel separately in order to understand if there are variants present; some variants can solely affect motor nerves or sensory nerves**

CIDP	**CIDP is one of the most misdiagnosed condition in the peripheral nervous system, therefore typical CIDP looks like motor and sensory limitations for the span of 8 weeks, events of relapses and remission. Yet symptoms will include a lack of sensibility of arms and legs symmetrically (typically from imbalances proximal and distal distribution).** **CIDP atypical variants affect 10-20% of patients and include:** 1. **Distal Variant: 7-15% of patients who experience motor and sensory abnormalities affecting one's hands and feet symmetrically. This variant can look like a random foot drop, progression beyond 8 weeks, and loss of reflexes.** 2. **Multi-Focal or Lewis Sumner Syndrome: motor and sensory abnormalities can result in asymmetrical distribution of numbness and weakness, this variant typically affects the arms or one arm and one leg or via versa** 3. **Focal-Limb Onset: the rarest variant of CIDP, it affects one limb at the plexus level where nerves are coming out from the spinal cord** 4. **Pure Motor Variant: affecting only motor abilities** 5. **Pure Sensory Variant: affecting only sensory abilities resulting in no weakness or tingling and results in abnormal sensory nerve conduction data** 6. **Multifocal Motor Neuropathy (MMN): A Multifocal presentation resulting in possible hand, arm, leg, or foot weakness and paralysis, onset has an asymmetrical presentation but with progression it can become symmetrical**
GBS	1. **Pharyngeal-Cervical-Branchial Variant: affects both motor and sensory muscles in one's face and in some cases the arms as well** 2. **Bilateral Facial Palsy: cases include weakness in one's face and only sensory symptoms in the arms and legs but not weakness** 3. **Pure Sensory Variant: affects the coating of the nerve and myelin** 4. **Miller Fisher Syndrome: mild GBS that can overlap with other variants of GBS where it restricts eye movement or Internuclear ophthalmoplegia, causes difficulty walking or imbalance (ataxia), and loss of reflexes (typical with all variants). Miller Fisher syndrome can evolve into a classic lack of motor sensory in one's legs. The triad of Miller-Fisher syndromes are ataxia (imbalance), ophthalmoplegia (eye abnormalities), and loss of reflexes.** 5. **Bickerstaff Brainstem Encephalitis: affects the brain causing confusion, altered levels of consciousness, and causes changes in the brain that are visible with a MRI procedure because it had a gq1b antibody** 6. **Pure Motor: causing only motor symptoms of the entire body**

GBS (Continu.)	1. Classic Sensorimotor: resulting in motor and sensory symptoms affecting the entire body 2. Paraparetic: causes motor and sensory symptoms in one's legs 3. Acute Inflammatory Demyelinating Syndrome (AIDP): most common GBS variant with clinical symptoms of weakness or sensory changes that have symmetrical weakness in both feet and up or vice versa 4. Acute Motor Axonal Neuropathy (AMAN): rapidly progressive weakness and paralysis from its effect on primary motor nerves 5. Acute Motor Axonal and Sensory Neuropathy (AMSAN): acute onset of distal weakness, loss of deep tendon reflexes and sensory symptoms a. Differs from AMAN because it affects both motor and sensory nerves  *Photo credited by Dr. Bart C. Jacobs - Erasmus University MC Medical Center
Mimics	Mimics are found when treatments are not working and symptoms progress into other medical issues. Therefore, Dr. Gable recommends a SPEP immunofixation and/or S-light chain procedure to look for monoclonal antibodies and proteins. Mimics that look like CIDP: 1. Anti–myelin-Associated Glycoprotein (ANTI-MAG): Anti-mag can look like CIDP but does not respond well to IVIg or steroids. a. This condition can mimic distal CIDP where a patient's hands and feet are weak at first but progresses to other areas (predominantly numbness and weakness), mild cases with sensory changes use symptomatic treatment, more progressive leads to rituximab (b-cell depleting creating immunosuppression) b. 80-90% of patients with GBS or CIDP respond well to IVIg, so if there is a lack of response, doctors need to re-evaluate the diagnosis. Yet, slow progressive conditions like ANTI-MAG make it harder to detect with its pathology being different from other conditions c. If titers of ANTI-MAG antibodies, are less than 50%, it means that the treatment is working

Mimics (Continu.)	1. **Hereditary Amyloidosis:** **“a condition in which abnormal protein deposits (called amyloid) form in almost every tissue in the body.” (Mount Sinai.org) Symptoms can evolve to look like other conditions such as myeloma, vitamin deficiencies, or infectious sources that can be mimics of CIDP** 2. **Vasculitis Neuropathy:** **an underlying rheumatoid-neurological condition resulting in “systemic illness with inflammation in the blood vessels” that can restrict peripheral nervous system function (hopkinsmedicine.org).** 3. **ALS, Motor Neuron Disease, and Muscle diseases can look like motor CIDP or nerve and muscle junction** 4. **Chronic Immune Sensory Polyradiculopathy (CISP): has regular nerve conduction studies and imbalance with blocking and there is no other kind of contributing source of vitamin deficiency, hereditary, or toxin which can be a mimic of sensory CIDP** 5. **Paranodopathy: affects 10% of patients who are misdiagnosed with CIDP, where antibodies attack the paranode and the node at the site which affects nerve transition that could result in a block to that connection, looks like typical numbness and weakness affecting both arms and legs** a. **Neurofacin-155 (NF155) and Anti-Cortactin-Associated Protein (CASPR) are essential proteins for functioning of nerve impulses along myelinated axons and proper functioning of nerve conduction.** b. **The disruptions of NF155 proteins are common for younger patients and cause more tremors, imbalance (ataxia) sometimes nephrotic syndrome (kidney disease)** c. **The disruptions of CASPR proteins affects motor involvement causing weakness where the core of the nerve is affected** 6. **Pan-Neurofascin condition: people get very weak and sensory changes are almost immediately paralyzed and responds to b-cell depletion such as rituximab (which takes longer to treat especially since it does not respond to IVIg). Rituximab is one of the first treatments for conditions that IVIg cannot help with. Yet, it has a 40% efficacy rate, so some people opt out of taking it. Disclaimer: Significant nerve damage is harder to reverse!** 7. **Special case: CANOMAD syndrome can be a mimic of GBS or CIDP because it can affect eye movement, it changes the coding of the nerves resulting in abnormal nerve conductions and imbalanced neuropathy. It can mimic both because it deals with monoclonal protein, IG PA proteins, cold glutens, and other antibodies.**

Questions for the Speaker

Are there unknown variants that one can have, or could it be a combination of different variants?

- There are still a lot of unknowns, especially with the lack of testing for GBS and CIDP
- There is a spectrum of peripheral neuropathies which are often bucketed together by symptoms to be named a specific variant

Are variants of GBS and CIDP treated the same?

- Yes, they are treated the same as typical presentations of GBS or CIDP.
- IVIg is the typical first line of treatment and with time it will be refined with more understanding if someone has a specific variant.
- Symptomatic treatment focuses on making sure patient feels comfortable and uses pain management as well as neuropathic pain control drugs.

How is a nerve conduction procedure performed on one's eyes?

- Nerve conduction is not done on the eyes, but doctors perform a blink reflex test.

What blood work is done in the diagnostic process? Once IG is started, do you continue the blood work?

- Blood Work is performed to check for serum protein electrophoresis and immuno-fixation serum free light chains to rule out mimics and variants.
- Rechecks are not necessary unless there is a lack of response to treatments like IVIg

Is there a way to identify a mimic?

- Plasmapheresis or plasma exchange can indicate if a condition is a mimic because it works mostly for typical CIDP and GBS. It is not suitable for maintenance treatments because it involves puncturing veins that limit patient's access. In addition, plasmapheresis has its own risks with peripheral access without a central line.

Relevant Resources

Treatment guidelines - https://www.gbs-cidp.org/gbscidp-guidelines-for-treatment-and-diagnosis/

Treatments & Access page – https://www.gbs-cidp.org/treatments-access/

Centers of Excellence https://www.gbs-cidp.org/support/centers-of-excellence/

Doctor to Doctor consult - https://www.gbs-cidp.org/doctor-to-doctor/

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