Guillain–Barré syndrome, transverse myelitis and infectious diseases

Yhojan Rodríguez, Manuel Rojas, Yovana Pacheco, Yeny Acosta-Ampudia, Carolina Ramírez-Santana, Diana M Monsalve, M Eric Gershwin, Juan-Manuel Anaya

Cell Mol Immunol. 2018 Jan 29;15(6):547–562. doi: 10.1038/cmi.2017.142

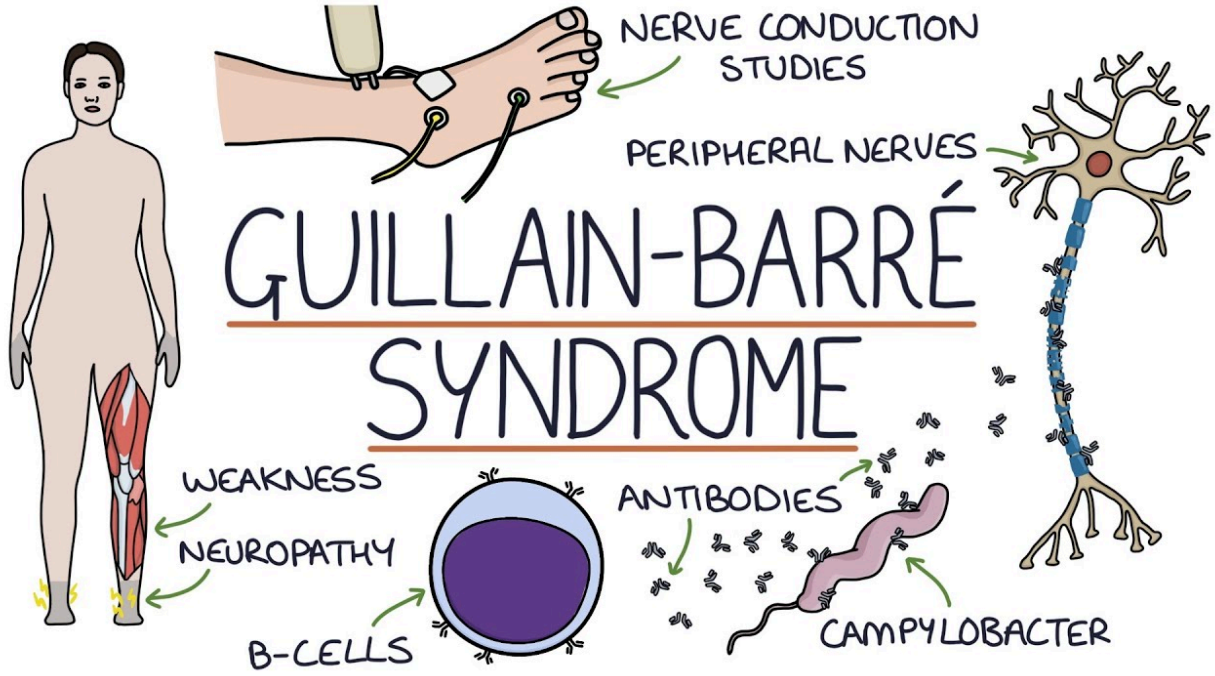
Abstract

Guillain–Barré syndrome (GBS) and transverse myelitis (TM) both represent immunologically mediated polyneuropathies of major clinical importance. Both are thought to have a genetic predisposition, but as of yet no specific genetic risk loci have been clearly defined. Both are considered autoimmune, but again the etiologies remain enigmatic. Both may be induced via molecular mimicry, particularly from infectious agents and vaccines, but clearly host factor and co-founding host responses will modulate disease susceptibility and natural history. GBS is an acute inflammatory immune-mediated polyradiculoneuropathy characterized by tingling, progressive weakness, autonomic dysfunction, and pain. Immune injury specifically takes place at the myelin sheath and related Schwann-cell components in acute inflammatory demyelinating polyneuropathy, whereas in acute motor axonal neuropathy membranes on the nerve axon (the axolemma) are the primary target for immune-related injury. Outbreaks of GBS have been reported, most frequently related to *Campylobacter jejuni* infection, however, other agents such as Zika Virus have been strongly associated. Patients with GBS related to infections frequently produce antibodies against human peripheral nerve gangliosides. In contrast, TM is an inflammatory disorder characterized by acute or subacute motor, sensory, and autonomic spinal cord dysfunction. There is interruption of ascending and descending neuroanatomical pathways on the transverse plane of the spinal cord similar to GBS. It has been suggested to be triggered by infectious agents and molecular mimicry. In this review, we will focus on the putative role of infectious agents as triggering factors of GBS and TM.

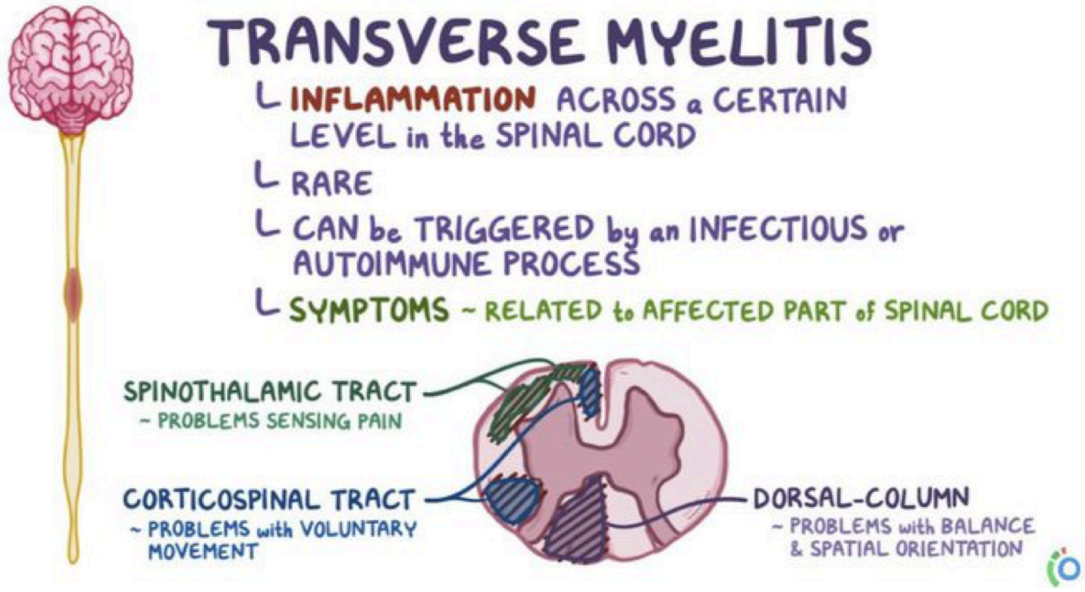
This article directly addresses the diagnostic challenge present in my patient's case. Acute fever, rapidly progressive b/l LE weakness, and urinary retention create uncertainty between GBS and transverse myelitis due to clinical overlap in presenting symptoms. This review highlights key differences in clinical presentation and pathophysiology, which are crucial for early recognition and management.

Neither GBS nor TM are due to infection itself, but rather neurologic disorders triggered by an immune overreaction to a primary infection; the body makes antibodies that attack the nervous system. In GBS, the immune system attacks the peripheral nervous system, primarily the myelin sheath. In TM, the immune system attacks the CNS, specifically the spinal cord; this overreaction causes inflammation of both the gray and white matter and the ascending and descending tracts. The overlap in presenting symptoms exists because both conditions interrupt motor, sensory, and autonomic pathways. This is clinically displayed as weakness, sensory changes, and bladder dysfunction (bladder dysfunction is less typical in GBS).

Around 75% of GBS cases occur w/in 6 weeks of an infection with the most common bacterial trigger being Campylobacter jejuni (associated w/ ~30-40% of cases). The specific antibodies created in GBS are coined "anti-ganglioside" antibodies. These antibodies cause nerve damage via triggering a complement cascade, macrophage activation, myelin destruction, and axonal injury.



TM interrupts the spinal tracts, so we should expect UMN signs. This is true, but complicated by the course of the disease. During the acute phase, 24 hours, the spine exhibits spinal shock. This initial spinal shock leads to physical exam findings of LMN disorders (flaccid paralysis, hyporeflexia, urinary retention). That is why urinary retention and bowel dysfunction are classic early signs of TM. As the initial spinal shock wears off, everything below the level of the lesion begins to “fire wildly” because impulses from the brain are no longer there to regulate them. This is when we start to see UMN signs (hyperreflexia, spasticity, + babinsky sign). The level of the spinal lesion will determine which parts of the body are affected. Knowing this information, careful physical examination and understanding of dermatomal distribution can be used to approximate the level of a lesion. Unlike GBS, the etiology of TM remains unknown in many cases.



The aforementioned phases of TM account for the early misdiagnosis between these two conditions. The initial spinal shock phase of TM presents very similarly to LMN disorders such as GBS, cauda equina, or conus medullaris compression. Because of the high level of clinical overlap, MRI of the spine w/ contrast is the most important diagnostic test. In TM, there will be a hyperintense lesion that typically extends ≥3 or more vertebrae. In GBS, the spine will appear completely normal. CSF fluid analysis will also have distinct and classic findings: GBS will show cytoalbuminogenic dissociation (high protein and normal WBC) vs. TM showing increased WBC w/ a lymphocytic predominance. The gold standard confirmatory test for GBS is a nerve conduction study, but this is not performed in the ED.

References

Rodríguez, Y., Rojas, M., Pacheco, Y., Acosta-Ampudia, Y., Ramírez-Santana, C., Monsalve, D. M., Gershwin, M. E., & Anaya, J.-M. (2018). Guillain–Barré syndrome, transverse myelitis and infectious diseases. *Cellular & Molecular Immunology*, *15*(6), 547–562. https://pmc.ncbi.nlm.nih.gov/articles/PMC6079071/