Transcript Details

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Decoding CIDP: Pathogenesis, Diagnosis, and Clinical Clues

Announcer:
You're listening to *On the Frontlines of CIDP* on ReachMD. On this episode, we'll discuss the mechanisms and diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy, or CIDP, with Dr. Hans Katzberg, who is a Professor of Medicine at the University of Toronto. Let's hear from Dr. Katzberg now.

Dr. Katzberg:
CIDP is an immune condition, and similar to other neurological immune disorders, the immunological mechanisms are complex. The primary target is the myelin sheath—the insulation that covers the peripheral nerves—and essentially, there is an erroneous message where there are certain antigens on this myelin sheath that trigger autoreactive T-cells to infiltrate the peripheral nervous tissue, and then this begins, essentially, a targeted inflammatory response characterized by elevated cytokines. Some of these are TNF alpha, interferon and gamma, and interleukin-1, and this promotes inflammation and recruits additional immune cells. These include macrophages, which are then activated by the cytokines, and this phagocytes—or eats up—the myelin sheath component. So this strips away the myelin sheath and leads to the segmental demyelination that occurs.

In more recent years, there's been some antibodies that have been discovered that are actually targeted against nodal and paranodal proteins. These are not exactly on the myelin sheath but allow an attachment of the myelin to the nerve, and this can then destabilize this architecture and also lead to similar conduction slowing in blocks. But technically, according to the new classification, this new IgG4 antibody-mediated diseases are not considered CIDP.

So genetic and environmental risks have been looked at over the years to see if some of these might predispose to CIDP, and in spite of all this work, it appears to be primarily sporadic as a condition. There's been certain genetic predispositions that have been recognized. For example, HLA haplotypes, such as HLA-DRB1*13 and HLA-DQB1, and there's also been some genetic associations, including polymorphisms and certain genes that might regulate inflammatory cytokines and other cell-mediated immune responses. And environmental triggers—there's a number of them that have been linked to CIDP, and this includes similar triggers that have been linked, for example, to Guillain-Barre syndrome, so infections, viral or bacterial, surgeries, vaccinations and other stresses to the system that may activate the immune responses. However, despite these associations, direct causal pathways really have not been confirmed, so there's ongoing work in this field.

So the clinical features include raised suspicion for CIDP in contrast to Guillain-Barre syndrome, which is a very acute neuropathy and more of a chronic presentation. In fact, it's in the name. CIDP stands for chronic inflammatory demyelinating polyradiculoneuropathy. So greater than two-month of progression is usually what we use as a cutoff to distinguish it from Guillain-Barre. And then the hallmarks are progressive symmetric muscle weakness as well as distal weakness, and this can also be associated with hyporeflexia or areflexia, which indicates some of the characteristic features of demyelinating neuropathies, and also sensory symptoms: numbness and tingling paresthesias. Neuropathic pain, I think, is less common than in Guillain-Barre but can happen. The pattern is usually progressive or with a relapsing-remitting type pattern, and this can be mitigated by treatment, particularly early on.

So the EFNS/PSN guidelines have been critical and very helpful over the years in order to confirm a diagnosis of CIDP. So this integrates clinical, electrophysiological, and supportive criteria, which could include laboratory criteria or testing or as well as new imaging. You want to make sure that you're fitting the clinical criteria of more than two months of progression of motor and sensory deficits. And then the electrophysiology is key. That's where you want to be certain that you're having demyelination as part of the pathologic process, and there is certain criteria for those nerve conduction studies. For example, slowed nerve conduction velocities below 70 percent of the lower limit of normal, prolonged distal latencies greater than 130 percent of the upper limit of normal, and

conduction blocks, and to be certain that one is experiencing that more than 50 percent reduction usually is considered helpful. The other paraclinical tests that I mentioned—CSF can show elevated protein with white cell counts below 10, and then also, as I mentioned, imaging. So MRI showing inflammation when gadolinium is administered, or ultrasound, which can show increased cross-sectional area, can also be used as supportive criteria in addition to the more core clinical and nerve conduction criteria.

Announcer:
That was Dr. Hans Katzberg talking about the mechanisms and diagnosis of CIDP. To access this and other episodes in our series, visit *On the Frontlines of CIDP* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!