FYI
GBS/CIDP Foundation International
For Your Information

2010 2009 2008 2007 2006 2005 2004 2003 2002 2001 2000 1999 Beyond GBS/CIDP

Search our Newsletters
Search
Spring 1999
Different types of GBS
Regional variants of CIDP may be distinguished from other neuropathies

Printer Friendly Version

Chronic Acquired Demyelinating Polyneuropathy Variants

Richard J. Barohn, M.D., Professor of Neurology
Lois C.A. and Darwin E. Smith, Distinguished Chair in Neurological Mobility Research, Acting Chairman, Department of Neurology
University of Texas Southwestern Medical Center at Dallas

One of the primary clinical hallmarks of chronic inflammatory demyelinating polyneuropathy (CIDP) consists of progressive or relapsing symmetrical weakness in both proximal and distal muscles over at least eight weeks.

This is usually accompanied by various degrees of sensory and reflex loss. Eight weeks is generally considered to be the dividing line between acute inflammatory demyelinating polyneuropathy (Guillain-Barré Syndrome) and CIDP. However, more than 90% of GBS cases have reached their maximum degree of weakness by four weeks.
Therefore, one of the first "temporal" variants of acquired inflammatory demyelinating polyneuropathies are the patients who have progression of weakness between four and eight weeks (Table 1). This group of patients has been labeled "subacute inflammatory demyelinating polyneuropathy" or SIDP. Some physicians treat patients with SIDP as if they have GBS and some approach therapy as if the disease was CIDP. The usual issue is whether or not prednisone should be used for therapy since prednisone is one of the first line therapies for CIDP but not for GBS. Intravenous immunoglobulin (IVIG), which is an acceptable treatment for both GBS and CIDP may be a reasonable first line therapeutic option for SIDP patients. It is known that some SIDP patients improve spontaneously without any therapy.

Another group of variants are instances in which the patient has otherwise typical CIDP but the neuropathy occurs in the setting of another ongoing medical disease. We have called this situation "CIDP with concurrent disease". Some examples of concurrent diseases which have been associated with CIDP include HIV infection, lymphoproliferative disorders such as lymphoma and osteosclerotic myeloma, chronic active hepatitis, inflammatory bowel disease, and multiple sclerosis (Table 1).

Table 1
Chronic Acquired Demyelinating
Polyneuropathy Variants
Temporal Variants:
Subacute Inflammatory Demyelinating Polyneuropathy (SIDP)
Concurrent Illness Variants:

Concurrent Illness Variants:
HIV Infection
Lymphoma
Osteosclerotic myeloma
Monoclonal gammopathy
Chronic active hepatitis
Inflammatory bowel disease
Connective tissue disease
Bone marrow & organ transplants
CNS demyelination
Nephrotic syndrome
Diabetes mellitus
Hereditary neuropathy
Thyrotoxicosis

Distribution Variants:
Multifocal Motor Neuropathy (MMN)
Multifocal Acquired Demyelinating Sensory and Motor Neuropathy (MADSAM)
Distal Acquried Demyelinating Symmetric Neuropathy (DADS)
?? Pure Sensory Variants

?? Axonal Variants

Patients who have a serum monoclonal gammopathy of uncertain significance are often placed in this group if they have otherwise typical CIDP. In general, patients with CIDP and with concurrent illness receive standard therapy for midi but often additional therapy is directed toward the associated disease process.

As mentioned above, patients with typical CIDP have symmetrical proximal and distal weakness in the arms and legs. Other proximal muscles that are often weak are muscles of facial expression and neck flexors and extensors. There are some variants of CIDP in which the weakness is very asymmetric with one arm or leg being involved exclusively or predominantly. In addition, the weakness in these cases tends to be mostly in the distal hand and foot muscles, supplied by individual and peripheral nerves (such as the median, ulnar, radial, or peroneal). These chronic acquired demyelinating peripheral neuropathies with this multifocal asymmetric distal distribution have two forms. One form has no sensory involvement, i.e. no numbness tingling in the hands or feet. This pure motor chronic acquired demyelinating neuropathy variant is called multifocal motor neuropathy (MMN). Like patients with CIDP, the nerve conduction studies show electrical changes that reflect a demyelinating neuropathy. MMN patients will frequently demonstrate the phenomena of conduction block in peripheral nerves. The sensory nerve conduction studies are normal in MMN. Another laboratory features that distinguishes MMN from CIDP is the presence in the serum of GM1 ganglioside antibodies, which occur in approximately 50% of MMN patients (Table 2).

Table 2

Table 2 Chronic Acquired Demyelinating Peripheral Neuropathies				
	CIDP	DADS	MMN	MADSAM
Clinical				
Weakness	Symm P > D	Symm D	Asymm D>P	Asymm D>P
Sensory Loss	+	++	-	+
LAB				

NCS Demyel	+	+	+	+
Prolonged DL	+	+	+	+
CSF Protein	+	+++	+	+
Monoclonal Protein	Occas	IgM	-	-
GM1 Ab	Rare	-	++	Rare
Bx Demyel	+	+	-	+
TREATMENT RESPONSE				
Prednisone	+	Poor	-	+
Plasma Exchange	+	Poor	-	?
IVIG	+	Poor	+	+
Cyclophosphamide	+	Poor	+	+

P = proximal; D = distal; Symm = symmetric; Asymm = asymmetric; NCS = nerve conduction study; Demyel = demyelination; DL = distal lantency; CSF = cerebrospinal fluid; Ab = antibody; Bx = biopsy; IVIG = intravenous immunoglobulin

MMN patients usually do not respond well to prednisone but improvements can be obtained with IVIG therapy plasmapheresis, and chemotherapy.

The other multifocal variant of chronic acquired demyelinating neuropathy has features similar to MMN except there is definite sensory involvement with numbness and tingling in the distribution of individual peripheral nerves. This neuropathy was first described by Richard Lewis, Austin Sumner and colleagues in 1982. We believe this neuropathy should be termed either the Lewis-Sumner Syndrome or Multifocal Acquired Demyelinating Sensory and Motor (MADSAM) neuropathy. MADSAM neuropathy patients usually have elevated spinal fluid protein, which is similar to city while in MMN the spinal fluid protein is normal. Another distinguishing feature is the absence of antibodies to GM1 ganglioside in MADSAM neuropathy (Table 2.). In addition, many MADSAM neuropathy patients respond well to prednisone therapy, similar to CIDP, whereas MMN patients do not respond to prednisone. Like CIDP and MMN, MADSAM neuropathy patients may improve with IVIG treatment. We believe that while MADSAM neuropathy patients have some features that are similar to CIDP and MMN, the disorder is probably more closely related to CIDP.

Another chronic acquired demyelinating neuropathy variant are patients who have symmetric exclusively distal sensory and motor deficits in the hands and feet. These patients complain of numbness or tingling in the hands and feet, and sometimes they notice weakness in these regions. On examination, the physician finds distal sensory loss with either no evidence of weakness or the weakness is exclusively distal. In other words, there is no weakness in the facial, neck, or proximal arm or leg muscles. Some patients in this group also have significant gait unsteadiness and tremor. Motor nerve conduction studies in this group of patients reveals demyelination and they often have markedly prolonged distal motor latencies. The most striking laboratory finding in this group of patients is that they usually have an IgM kappa monoclonal protein in the serum and 50% of the time one can also detect antibodies directed against myelin-associated glycoprotein (MAG). This group of patients has been referred to as a subgroup of CIDP with IgM kappa/MAG antibodies. Some other typical CIDP patients can have monoclonal proteins and these patients are often included in the group of patients with concurrent illness, as noted above. However, we and others have been impressed that the patients with an IgM kappa/MAG neuropathy appear to be distinctly different. In an attempt to define or name these syndromes by their clinical phenotype, in our clinic we refer to these patients as Distal Acquired Demyelinating Symmetric (DADS) neuropathy. It is important to identify this DADS neuropathy subset of patients because they have a different response to therapy

compared to typical CIDP and the other chronic acquired demyelinating variants. DADS neuropathy patients are very resistant to therapy with prednisone, IVIG, plasmapheresis, or chemotherapy. Some patients may show mild improvement over many years of therapy but it is often difficult to detect. This is in contrast to most midi MMN, and MADSAM patients in which a beneficial response to therapy can usually be seen within a month or two after initiating treatment. Therefore, while we usually attempt a course of immunosuppressive therapy in patients with DADS neuropathy we counsel the patients at the onset that they may not improve, or improvement may take many months, and the benefit may be modest.

Other forms of chronic acquired demyelinating neuropathy may exist. Perhaps there are pure sensory forms of CIDP without any evidence of motor involvement either on the clinical exam or electrophyslologic studies. While a few centers have identified such patients, we are still not convinced of the existence of a pure sensory CIDP variant. Another controversial issue is whether or not there are pure "axonal" forms of midi MMN, or MADSAM. We believe that more patients with these possible axonal variants need to be reported before their existence can be generally accepted. Certainly, many patients with all of the above mentioned variants of acquired chronic demyelinating polyneuropathy can have some nerves with significant axonal damage.

In 1958, declares Austin described two patients with a recurrent steroid-responsive polyneuropathy. Over the next 17 years. additional similar cases were gathered at numerous neuromuscular clinics leading up to Dr. Peter Dyck's important paper in 1972 defining CIDP as a distinct treatable entity. Over the last two-and-a-half decades, it has become apparent that other forms of chronic acquired demyelinating polyneuropathy occur and that their clinical, laboratory and response to therapy are somewhat different from typical CIDP. While we still do not know the underlying radiobiology of the chronic acquired demyelinating polyneuropathies and in many ways our therapies remain only partially effective, it is important for neurologists to be aware of the variants of chronic inflammatory demyelinating polyneuropathies and not group them all as typical CIDP. We believe the categorization of the chronic acquired demyelinating polyneuropathies in the scheme outlined above allows the practitioner to more easily place patients into broad groups for both diagnostic and therapeutic purposes. Hopefully this process contributes to our ultimate goal of improving our understanding of these unusual neuropathies and leads to optimal management of our patients.