CHRONIC INFLAMMATORY Demyelinating Polyradiculoneuropathy

The syndrome of acute inflammatory idiopathic polyneuropathy is well known, the predominantly motor type of which is recognised by the name of Guillain-Barre Syndrome (GBS), in which the maximum neurological deficit develops rapidly in days, plateaus for weeks and then subsides with the recovery occurring in weeks to months. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) has earned a comparatively recent recognition over the last 30 years or so. Its characteristics and diagnostic criteria have been described and are undergoing refinement with time. Its importance is underscored by the fact that it represents about 21% of all initially undiagnosed neuropathies. CIDP shares with acute inflammatory demyelinating polyradiculoneuropathy, the features of demyelination and mononuclear infiltration of peripheral nerves and its cytoalbuminologic dissociation in the cerebrospinal fluid. It differs in temporal evolution, course and prognosis and in its response to treatment. Although the earlier descriptions of cases of Guillain-Barre Syndrome (GBS) contain some patients who had a slower onset of disease and a protracted course, Austin is credited with first highlighting the disorder and indicating its responsiveness to corticosteroids. He described two cases of recurrent polyneuropathy and received thirty others with a similar case history going back to 1894. For a longtime, there were many different terminologies used by different authors to describe this disorder including chronic Guillain-Barre Syndrome, chronic relapsing neuropathy, recurrent and chronic relapsing Guillain-Barre Polyneuritis, relapsing motor polyneuropathy, and steroid responsive recurrent polyneuropathy. The term Chronic Inflammatory Polyradiculoneuropathy was first used by Dyck et al. who described natural history and pathological features of the disease in a large series of patients. Later on, the word demyelinating was added by him. Since then many other scientists have described their experience with the condition and a few large series have been published. Recently a consensus report on research criteria for diagnosis of CIDP has come out.

CLINICAL FEATURES

CIDP usually begins in a slowly progressive fashion in months but may, uncommonly, have a rapid initial onset of weakness indistinguishable from acute GBS. History of preceding infection is obtained much less commonly as compared to GBS, averaging in about 20-30% of patients. It affects all age groups and is commoner in males. The illness generally tends to be less severe than typical cases of acute GBS and most prominent symptom are of symmetric muscular weakness which is proxim as well as distal. Reflexes are usually lost within a few months of onset of disease. Weakness of musculature supplied by cranial nerves, most commonly facial or oropharyngeal weakness is seen in about 10-15% of cases. Sensory symptoms are present in most of the patients. A pure motor neuropathy or one with only sensory symptoms have been described but are uncommon. Rarely clinical features include ataxia, tremor and papilledema. Distinguishing feature of CIDP is a course prolonged over the years with fluctuations in the severity of symptoms.
LABORATORY FINDINGS

Cerebrospinal fluid
Albuminocytologic dissociation in cerebrospinal fluid (CSF) is typically seen. CSF albumin levels reported in two of the large series of patients averaged at 137.6±112.6 mg per decilitre\(^3\) and 134±112 mg per decilitre\(^4\). Uncommonly (0-20% of patients) it can be normal\(^2\). Pleoxytosis of CSF is quite rare and was seen in only 0-10% of patients\(^2\).

Nerve conduction studies
Slowing of motor nerve conduction velocities to less than 60%\(^4\) and prolonged distal latencies in several nerves are present weeks to months after the onset of disease\(^2\). Amplitude of muscle action potential is reduced and afferent nerves are similarly affected\(^7\). Multifocal conduction blocks have also been emphasised as a prominent feature\(^2\).

Pathology
Peripheral nerves as well as spinal nerve roots are affected by the pathological process. Segmental demyelination, remyelination, onion-bulb formation and mononuclear cell infiltration (neural and perivascular) have been found by various investigators\(^7\). In a small proportion of cases axonopathy has been detected. A few patients show absence of any pathological changes\(^4\). Mechanism of these changes is not very clear. Some of the researchers have found immunoglobulin deposits on the nerves of CIDP patients\(^18\).

Differential diagnosis
Relapses of acute GBS may look like CIDP but are distinguishable on the basis of their clinical course which does not get prolonged more than weeks with partial or complete recovery in between. CIDP, on the other hand, has a slower evolution and a protracted course going in months and years\(^2,16\). Other types of neuropathies that may sometimes present a clinical picture similar to that of CIDP need to be excluded. Common among these would be hereditary neuropathy, some of the neuropathies associated with systemic diseases and others associated with neoplastic and paraneoplastic disorders. Any family history of neuropathy or presence of bony abnormalities in the patient would need nerve conduction studies of immediate relatives. Dejerine-Sottas neuropathy (HMSN-III) may be specifically confusing as it can lead to thicker nerves as in CIDP. Some cases of hereditary neuropathy have been found responsive to prednisolone, a feature which remains unexplained\(^7,19\). Associations have been reported between an illness resembling CIDP and human immuno-deficiency virus infections, non-systemic vasculitis, systemic lupus erythematosis, sarcoidosis, ulcerative colitis and regional enteritis\(^2,7\). Polyradiculopathies also occur in association with lymphomas, myelomas and monoclonal gammopathies. Detailed evaluation and necessary investigations to exclude these disorders are part of the diagnostic process\(^7\).

TREATMENT

Cortico Steroids
Steroid responsiveness of CIDP was first described by Austin in 1958. Since then most of the researchers have confirmed his observation although the response to steroids is variable and often partial. Dyck et at\(^3\) found that, in their patients, steroids resulted in improvement in 39%, worsening in 14% and had no effect in 47%. Oh\(^20\) reported improvement in all the 10 cases but 5 of these relapsed when steroids were withdrawn. Dyck et al\(^15\) also showed, through a controlled trial, that steroid therapy resulted in a small but significant improvement. McCombe et al\(^16\) reported improvement in 65% of their patients treated with steroids. Some researchers have tried antimitotic drugs like azathioprine in
combination with steroids in patients poorly responding to steroids or relapsing after steroid treatment. They “appear to benefit” in some cases while in others no benefit was seen.

**Plasmapheresis**

Server and co-workers reported plasma exchange to be beneficial in treatment of CEDP. Dyck et al. confirmed its utility in a controlled trial. McCombe et al. found it useful in 61% patients.

**Gammaglobulin**

Infusions of intravenous gammaglobulin (IVIG) have also been used. In one large series, 17% reached complete remission, 40% improved but needed intermittent infusions to maintain improvement, 4% showed a short lasting improvement and 38% did not show any response. Cornblath mentions that pooling of data shows that clinically significant responses have been observed in 68% of patients treated with this modality. There seems to be no consensus on the treatment regime for CIDP. Many of the authorities utilise all the three modalities of treatment in accordance with patient response. Dyck and Arnason mention prednisolone as the drug of choice, but McCombe et al. think that plasma exchange can be used in preference to corticosteroids. Barohn et al. used steroids initially but also utilised plasmapheresis in addition for severely affected or poorly responding patients. Von Doom et al mention that WIG results in a much rapid improvement (days to weeks) as compared to months for steroid therapy. Ropper et al recommend WIG before beginning steroids in worsening patients and advise follow-up with plasma exchanges in unsuccessful cases.

**Course and prognosis**

The characteristic of CIDP is a chronic progressive or relapsing course spread over the years. About 67% of the patients have a relapsing course which can be further described into relapses during a monophasic course, a remitting and relapsing course and relapses during a progressive course. The progressive course without relapses will be seen in about 15% of patients, progressions being manifested in a continuous or a step wise fashion. The rest of the patients follow a slow monophasic course characterised by worsening of the condition followed by improvement. Course of the disease is usually modified by treatment although subsequent relapses are frequent. Patients with a relapsing course tend to have a more favourable prognosis as compared to those with a chronic progressive course. In a large series of patients 73% were recovered or only mildly disabled after an average 10 years of follow up while in another series only 40% of patients were in complete or partial remission without medication after a 34 month average follow-up.

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**REFERENCES**