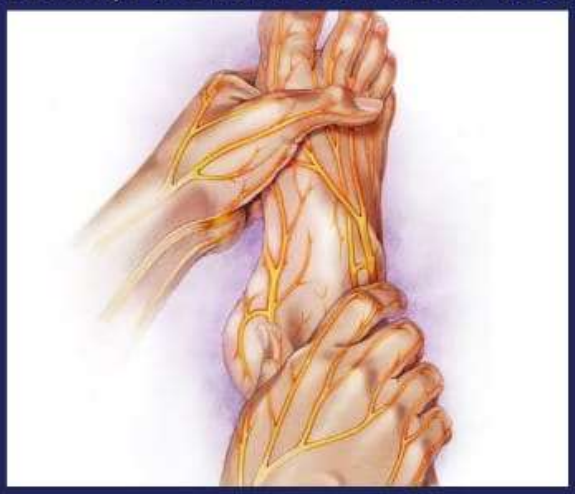
TEXTBOOK OF PERIPHERAL NEUROPATHY

Diagnosis,Evaluation and Treatment



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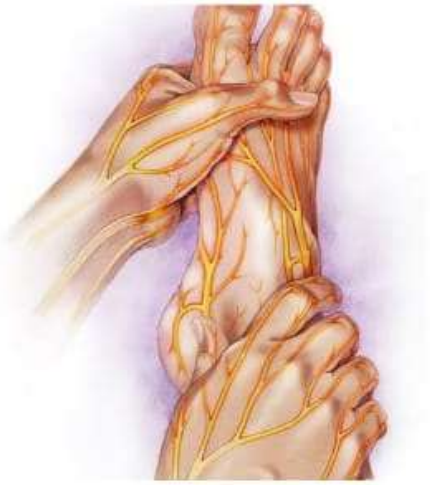

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L-Tryptophan

An unusual syndrome called eosinophilia-myalgia syndrome was recognized in 1989 in individuals taking preparations containing a contaminated L-tryptophan. A severe axonal sensorimotor poly- neuropathy, at times associated with inflammation and vasculopa- thy, was a prominent feature in some patients. The syndrome was to a large extent similar to Spanish “toxic oil syndrome.” Recovery from the neuropathy was slow and sometimes incomplete. Since the elimination of contaminated tryptophan, the syndrome is no longer seen.

Tumor Necrosis Factor-! Blockers

Adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade) are immunosuppressive medications used to treat rheu- matoid arthritis, inflammatory bowel disease, and other rheuma- tological conditions by blocking TNF-". They have been shown to trigger a demyelinating disease in the CNS similar to multiple scle- rosis. Additionally, demyelinating peripheral neuropathies, which can resemble MMN with conduction block or CIDP or its variants, may follow the use of antagonists to TNF-" (Alshekhlee et al., 2010; Stübgen, 2008). Clinically, the neuropathy is typically sensorimotor but may be purely sensory or purely motor. CSF protein may be nor- mal to moderately elevated. Nerve conduction studies show findings typical of a sensorimotor or purely motor demyelinating polyneurop- athy, with relative preservation of amplitudes distally accompanied by focal slowing and conduction blocks at non-entrapment sites. IVIG and plasma exchange typically are effective in treating the neuropathy, similar to other forms of demyelinating neuropathies. The decision of whether or not to stop the offending agent should be made on a case- by-case basis (Lozeron et al., 2009). Withdrawing the offending agent does not always reverse the immune process, and chronic immuno- modulating therapy (e.g., IVIG, steroids, immunosuppressive agents) may be necessary to control the inflammatory process and improve clinical outcome (Alshekhlee et al., 2010).

Vinca Alkaloids

Vincristine, the vinca alkaloid most used in chemotherapeutic regi- mens, causes a length-dependent sensorimotor polyneuropathy as its dose-limiting side effect. Vinblastine and two semisynthetic deriva- tives, vindesine and vinorelbine, are less neurotoxic. Vinca alkaloids function as mitotic spindle inhibitors. Like taxanes, their neurotoxicity is related to tubulin binding, which interferes with axonal microtubule assembly, thereby impairing axonal transport.

Vincristine produces a dose-dependent neuropathy with sensory symptoms beginning at 5 mg and motor symptoms at cumulative doses of 30–50 mg. There are several reports of vincristine-induced severe paralysis at conventional doses in patients with preexisting hereditary neuropathies. Paresthesias and pain, often starting in the fingers before the feet, and loss of ankle jerks are common initial findings. Distal muscle weakness and sensory impairment follow. Autonomic dysfunction—particularly gastroparesis, constipation, occasionally paralytic ileus, urinary retention, impotence, and orthostatic hypo- tension—may occur and is an early manifestation. Weakness, often accompanied by muscle pains, may evolve rapidly to severe motor impairment. Occasionally, isolated mononeuropathies have been reported. Cranial nerve involvement occurs infrequently and includes trigeminal sensory loss, ocular motility disorders, facial weakness, and recurrent laryngeal nerve palsies.

EDX studies reflect the degeneration of distal axons. SNAPs are reduced in amplitude, whereas NCVs are preserved. EMG shows denervation in distal muscles. The predominant pathological features are axonal degeneration and myopathic changes, with spheromembranous inclusions in the muscle fibers evident on electron microscopy. Reduction in dose or withdrawal from therapy at an early stage usually leads to eventual, though delayed, recovery. In up to 60% of patients, residual sensory symptoms and absent tendon reflexes may persist, and electrophysiological abnormalities continue. Co-administration of glutamic acid or ORG 2766, an adrenocorticotropic hormone-de- rived synthetic peptide, has shown promising results in reducing the severity of vincristine neuropathy in preclinical trials, but there was no benefit in a clinical trial. Neurotrophins have neuroprotective effects in experimental studies as well, although there is reticence to use these compounds in patients with established neoplasms because of the fear that growth factors may stimulate tumor growth.