

The Treatment of Painful Neuropathies in Patients with Waldenstrom's Macroglobulinemia

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The successful treatment of neuropathic pain in patients with Waldenstrom's macroglobulinemia, as in all forms of neuropathic pain, begins with an accurate localization of the pain generator. There are many mimics of peripheral neuropathy which can be distinguished based on clinical and electrophysiologic criteria. It is also important to be able to characterize the type of nerves involved before a clear understanding of the etiology of the pain can be determined. Isolated small fiber involvement often produces a very painful neuropathy with a relatively normal exam and nerve conduction studies. Even in the absence of autoantibodies directed against neural antigens, WM can produce a painful small fiber neuropathy which can be very responsive to immunomodulatory therapy. In these patients, direct involvement of the small fibers can be visualized on skin biopsies and improvement has been demonstrated following immunosuppression.

If no specific therapy for the painful neuropathy can be achieved then symptomatic therapy becomes the focus for patient management. There are essentially three distinct sites where pain can be modulated via pharmacologic means. One can attempt to block sodium channels preventing the generation of the initial action potential at the site of the peripheral nerve. The second place to intervene in the perception of neuropathic pain is at the connection between the first and second order neurons in the dorsal horn of the spinal cord. This occurs via the blockade of calcium channels, which prevents the release of neurotransmitters involved in pain such as substance P and glutamate. One can also improve the degree of descending pain inhibition by increasing the amount of serotonin and norepinephrine passing through the periaqueductal gray synapsing onto the dorsal horn second order neurons. Finally there is significant value to chronic opiate therapy for those patients severely affected. An understanding of the mechanisms available will dictate the use of rational polypharmacy.

Finally, one should also consider the use of non-pharmacologic therapies. There is significant evidence for many nutritional supplements, such as alpha lipoic acid and N-acetyl carnitine. There is also a growing interest in pain interventions such as infrared light therapy and neuromodulation.