Hypertrophic mononeuropathy

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Hypertrophic localized mononeuropathy is a condition that comes to clinical attention as a painless focal swelling of a peripheral nerve in an arm or leg and is associated with a slow but progressive loss of motor and sensory function. Whether the proliferation of perineurial cells is neoplastic or degenerative—an ongoing controversy among nerve pathologists—for some patients resection of the involved portion of a nerve with autologous interposition grafting results in better functional outcome than allowing disease to follow its natural course. Patients with a painless focal enlargement of a nerve associated with progressive weakness and/or sensory loss may benefit from surgery for resection and grafting.

KEY WORDS • localized hypertrophic neuropathy • mononeuropathy • nerve graft • perineurioma

Hypertrophic Mononeuropathy is a slowly progressing disease of a single large peripheral nerve (such as the peroneal, ulnar, or radial) that begins insidiously and progresses inexorably to profound functional (predominantly motor) loss with disability.

Pathological Characteristics and Surgical Decision-Making

Arrest and sometimes improvement in deficits are seen after resection and grafting. This treatment strategy is appropriate for a disease process that is localized to a relatively short portion of a nerve, but will not work for patients with mononeuropathy because this condition affects an entire nerve or long length of nerve. Although the presentation and electrophysiological workup are identical for patients with mononeuropathy of any origin, determining an accurate and specific diagnosis, natural history, and prognosis are essential for rational surgical decision-making.

Patient Presentation

The presentation of LHN is similar to that of other mononeuropathies: “a slowly progressive painless focal lesion of a peripheral nerve with a frequently palpable enlargement along the nerve’s course in the extremity.” In 1998 we reported on 15 patients with LHNs who underwent surgery at Louisiana State University. In our case series we found lesions in peripheral nerves of major limbs, with no greater incidence in the upper or lower limbs. None of our patients had a history of trauma to the involved extremity. The symptoms came on slowly and had been present for a mean of more than 6 years, in most cases also associated with atrophy, severe weakness, and, less frequently, sensory loss. Since the 1998 report we have treated five additional cases of LHN, and two of these have undergone resection and graft repair.

Diagnostic Tests

Electrophysiological (electromyography and nerve conduction velocity test) findings in patients with LHN are consistent with progressive thinning of myelin sheath followed by axonal degeneration. By the time a patient with this condition presents to the surgeon, results on muscle sampling usually show denervational changes.

Pathophysiological Aspects of LHN

Histological Characteristics. Histologically, LHN is characterized by a proliferation of perineurial cells. Even before the advent of immunohistostaining technology in 1980, a proliferation of morphologically identified perineurial cells was proposed as the cause of localized hypertrophic neuropathy. Perineurial cells normally surround nerve fascicles and are distinguished from Schwann cells by their immunoreactivity for epithelial membrane antigen and lack of reactivity for S100 protein.11–13

On microscopy, LHN is characterized by concentric whorls (“onion bulbs”) of epithelial membrane antigen-reactive, S100 protein-negative perineurial cells surrounding nerve fibers. The cells that make up the hypertrophic localized mononeuropathy onion bulb do not stain posi-
ative for S100 protein consistent with their perineurial origin.17 Many authors4,5,7 refer to perineuriomas and LHNs interchangeably. In addition to perineurioma there are a number of other onion bulb-shaped neuroepithelial diseases in which are mononeuropathies.6 Differences in architectural arrangement and degree of cellularity between the perineurial and Schwannian forms of localized hypertrophic mononeuropathy suggest important fundamental differences in the pathogenesis of various forms of onion-bulb mononeuropathies.3

Pathogenesis of LHN. The pathogenesis of LHN is unclear. Proliferation of perineurial cells is thought by some pathologists to be neoplastic,1 but others believe that trauma or “an undefined stimulus” incites perineurial multiplication and whorl formation “probably representing a hyperplastic reaction to nerve damage.”15 Based on their analysis, some authors have suggested that the term perineurioma “should be reserved for the neoplasm composed only of perineurial cells and presenting as a soft tissue tumor.”11 Others proposed that the mechanism “may be a localized reaction to nerve trauma or entrapment.”10

Surgical Decision-Making

The patient’s prognosis is an important consideration in deciding whether or not to operate, and what surgery to perform. The natural history of LHN is progression to severe, primarily motor, loss of function with disability. Peckham and colleagues9 recommended surgery for LHN because its long-term prognosis is better than that of other onion bulb neuropathies.

Resection of the lesion with autologous interposition of nerve graft material is the operation of choice. Localized hypertrophic neuropathy causes well-circumscribed areas of focal enlargement that are easily excised. Removal of a segment of nerve involved with the presumed LHN is no more difficult than the resection of any well-circumscribed benign nerve tumor. Autologous graft is usually sural, sutured or glued into place. In our series patients had better outcomes with shorter grafts.3 Although outcome after nerve graft repair is not great, without surgery, progression over a period of years usually leads to complete functional loss.

Despite the relatively late diagnosis and severe neurological deficits, our patients’ function after resection and grafting was better than it would have been had the disease been allowed to progress to complete loss of motor function.3 The surgeon must differentiate between a focal pathological process and a systemic problem that could affect other parts of the same nerve, involve long segments of a nerve, and/or affect more than a single major peripheral nerve.

Unfortunately without resection of the involved segment, the prognosis for nerve function is bleak: most patients who do not undergo surgery experience progressive, severe, and usually primarily motor deficits.

Conclusions

The clinical presentation (history, examination, and electrophysiological test results) of mononeuropathies of whatever origin are similar, but their pathophysiology and natural history (degenerative, neoplastic, ischemic, etc.) are very different. Therefore a precise diagnosis that identifies neuropathies with a progressive natural history and which are limited in involvement to a portion of a single nerve gives the patient and the surgeon the option of acting preemptively with resection and interposition autologous nerve grafting. This may provide a better functional outcome than allowing the neuropathy to run its natural course.

References


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