Hypertrophic mononeuropathy

PETER GRUEN M.D.¹ AND DAVID G. KLINE M.D.²

¹University of Southern California Keck School of Medicine, Department of Neurological Surgery, Los Angeles, California; and ²Louisiana State University, Department of Neurosurgery, New Orleans, Louisiana

✓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 mononeuropathies⁸: “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.³ 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.¹⁰ 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.⁸ 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-

Abbreviation used in this paper: LHM = localized hypertrophic neuropathy.

tive for S100 protein consistent with their perineurial origin.^{1,7} Many authors^{4,5,7,8} refer to perineuriomas and LHNs interchangeably. In addition to perineurioma there are a number of other onion bulb-shaped neuropathies, some of 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.²

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.”¹⁰ 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.”¹³ Others proposed that the mechanism “may be a localized reaction to nerve trauma or entrapment.”¹⁴

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

1. Bilbao JM, Khoury NJ, Hudson AR, Briggs SJ: Perineurioma (localized hypertrophic neuropathy). *Arch Pathol Lab Med* **108**:557–560, 1984
2. Chang Y, Horoupian DS, Jordan J, Steinberg G: Localized hypertrophic mononeuropathy of the trigeminal nerve. *Arch Pathol Lab Med* **117**:170–176, 1993
3. Gruen JP, Mitchell W, Kline DG: Resection and graft repair for localized hypertrophic neuropathy. *Neurosurgery* **43**:78–83, 1998
4. Heilbrun ME, Tsuruda JS, Townsend JJ, Heilbrun MP: Intraneural perineurioma of the common peroneal nerve. Case report and review of the literature. *J Neurosurg* **94**:811–815, 2001
5. Isaac S, Athanasou NA, Pike M, Burge PD: Radial nerve palsy owing to localized hypertrophic neuropathy (intraneural perineurioma) in early childhood. *J Child Neurol* **19**:71–75, 2004
6. Iyer VG, Garretson HD, Byrd RP, Reiss SJ: Localized hypertrophic mononeuropathy involving the tibial nerve. *Neurosurgery* **23**:218–221, 1988
7. Johnson PC, Kline DG: Localized hypertrophic neuropathy: possible focal perineurial barrier defect. *Acta Neuropathol* **77**:514–518, 1989
8. Mitsumoto H, Wilbourn AJ, Goren H: Perineurioma as the cause of localized hypertrophic neuropathy. *Muscle Nerve* **3**:403–412, 1980
9. Peckham NH, O’Boynick PL, Meneses A, Kepes JJ: Hypertrophic mononeuropathy. A report of two cases and review of the literature. *Arch Pathol Lab Med* **106**:534–537, 1982
10. Phillips LH II, Persing JA, Vandenberg SR: Electrophysiological findings in localized hypertrophic mononeuropathy. *Muscle Nerve* **14**:335–341, 1991
11. Stanton C, Perentes E, Phillips L, Vandenberg SR: The immunohistochemical demonstration of early perineurial change in the development of localized hypertrophic neuropathy. *Hum Pathol* **19**:1455–1457, 1988
12. Takao M, Fukuuchi Y, Koto A, Tanaka K, Momoshima S, Kuramochi S, et al: Localized hypertrophic mononeuropathy involving the femoral nerve. *Neurology* **52**:389–392, 1999
13. Tsang WY, Chan JK, Chow LT, Tse CC: Perineurioma: an uncommon soft tissue neoplasm distinct from localized hypertrophic neuropathy and neurofibroma. *Am J Surg Pathol* **16**:756–763, 1992
14. Yassini PR, Sauter K, Schochet SS, Kaufman HH, Bloomfield SM: Localized hypertrophic mononeuropathy involving spinal roots and associated with sacral meningocele. Case report. *J Neurosurg* **79**:774–778, 1993

Manuscript submitted March 19, 2007.

Accepted in final form May 11, 2007.

Address reprint requests to: Peter Gruen, M.D., 1200 North State Street, Suite 5046, Los Angeles, California 90033. email: jpgruen@usc.edu.