Peroneal Nerve Tumor


Abstract

Intranuclear perineurinoma, or localized hypertrophic mononeuropathy (LHM), is a focal lesion that produces a slowly progressive mononeuropathy in a peripheral nerve. The authors describe the clinical presentation, magnetic resonance (MR) neurography characteristics, and pathological characteristics of a perineurinoma involving the peroneal nerve. Although there has been much debate surrounding the cause of this lesion, a literature review supports the argument that this is a neoplastic lesion, best referred to as intranuclear perineurinoma. Surgical management includes excision to prevent progression of palsy and placement of a nerve graft if clinically indicated.

A 28-year-old woman presented with a 2-year history of progressive right peroneal nerve palsy. Magnetic resonance neurography revealed a right common peroneal nerve mass. At surgery, the mass was easily excised, leaving significant nerve fascicles intact. Intraoperative biopsy was not performed nor was a nerve graft placed. Pathological investigation demonstrated onion bulb–shaped whorls consistent with the appearance of intranuclear perineurinoma; immunochemical analysis confirmed the diagnosis.

A review of the literature supports the argument that perineurinoma, or LHM, is a neoplastic process, making “intranuclear perineurinoma” the most appropriate name. The authors also demonstrate the utility of MR neurography in the identification of isolated nerve tumors and review the surgical management of this lesion.

The authors describe a 28-year-old woman with progressive right peroneal palsy in whom they operated 2 years after onset of symptoms and who had no remaining function in the peroneal nerve. Special sequencing of magnetic resonance imaging studies revealed an abnormal enhancing segment of peroneal nerve, 6 cm in length. At exploration, the authors identified “an abnormal mass extending approximately 4 cm within the thigh just proximal to the bifurcation of the common peroneal nerve. . . .” Stimulation through the normal portion of the nerve demonstrated good contraction of the muscles in the patient’s foot. . . . “This is not surprising because, from the authors’ description of the extent of the tumor, proximal stimulation might also stimulate the entire sciatic nerve in a retrograde fashion; conduction could occur through the intact and uninvolved tibial half of the sciatic nerve to the plantar flexors and foot muscles.

The authors stimulated the peroneal portion at the tumor location and produced no foot function consistent with data from preoperative clinical and electrical studies. Thus, they concluded from their observations that because the patient’s paresis had been complete for longer than 2 years and because there was “conduction of impulses,” graft repair was not indicated. They concluded that conduction was demonstrated through preserved fascicles. No nerve action potential studies were attempted. Had such studies been done, we suspect there would have been no conduction across the lesion. Under that circumstance the outcome would have been persistent severe or complete deficit. A choice to resect the entire cross-section of the nerve and replace it with autologous grafts may or may not have worked in this particular nerve, especially given its length. Often what appear to be uninvolved fascicles in this disease are actually fascicles with some degree of change, but less severe than the more involved portion of the nerve. Over time those changes usually progress and become more severe. It is often impossible to “shell out such lesions as might be done with a schwannoma or neurofibroma and maintain function or recovery of function.” The proof of such in this case is that the follow up at 2 and 5 years after onset of deficit showed no recovery of peroneal function and the patient’s foot drop remained as complete as it had been preoperatively.

Following frozen section diagnosis of onion-bulb neuropathy in a young person without a family history or other stigmata of diseases such as Dejerine-Sottas, Refsum, or Charcot-Marie-Tooth, resection of the nonfunctioning or poorly functioning segment (determined by the absence of or a greatly diminished intraoperative nerve action potential) may be appropriate if there is a chance for improvement of function by repair. One can then proceed to a graft repair and sometimes achieve some degree of recovery. Since the 1998 publication by Gruen, et al,1 we have managed six more cases of what we term “localized hypertrophic neuropathy.” In one instance, the physical length of involvement precluded success by grafts; in another, the process involved C-8 and T-1 spinal nerves and the lower trunk of the plexus, and resection and repair of such elements are not successful. It is too early to say whether the other four graft repair procedures will be successful. It was also too early to speak of this for at least two of the three graft repair cases reported in 1999 by Simmons and referred to by Heilbrun, et al., that is, the femoral repair occurred only 10 months and the brachial plexus repair only 2 months postsurgery.

Presently, the origin, pathogenesis, and terminology to be used for these hypertrophic lesions remains controversial.8 They usually affect only one peripheral nerve in a given individual, but can affect multiple plexus elements, which are usually adjacent. The hypertrophic process damages a focal or localized area of nerve, but tends to progress and gradually to remove function of the nerve or plexus element(s) involved. The 30 lesions we have seen and operated on have had a typical histological appearance, with partially or fully demyelinated axons that are reduced in caliber, but surrounded by connective tissue in an onion bulb–shaped whorl pattern. These changes are best seen on examination of the cross-section of the nerve. When tested using special stains, the tissues are for the most part negative for S-100 protein, except where there is still some myelin left; the pericytes in the sworls of connective tissue are positive for epithelial membrane antigen (EMA). These patients have not had a hereditary hypertrophic neuropathy. We have used the diagnostic term “localized hypertrophic neuropathy,” whereas others might have termed the lesions “perineurinomas.”
Results from studies in which early changes in lesions were compared with the state of more mature and definitive hypertrophic ones have suggested as a pathogenesis, a migration of EMA-positive cells from damaged or abnormal perineurium to the endoneurial cell layer.1,2 What force or process damages the perineurium is, however, unclear. These pericytes subsequently proliferate and form collagen, which damages myelin and the axons. Fletcher3 asserts that many of these lesions are perineuriomas (a term coined earlier by others) and benign neoplasms. Indeed, the lesions studied by Emory and colleagues1 had partial or complete deletions of chromosome 22, providing further support for the concept that they are neoplastic rather than reactive. Most of the time, from a surgeon’s perspective, the hypertrophic lesions appear more reactive than tumors. We hope that further genetic studies will resolve these issues.

Further confusion is provided by the terminology used in the literature. The term “localized hypertrophic neuropathy” has sometimes been used interchangeably with “perineurioma.”6 Other authors believe that localized hypertrophic neuropathy “has sometimes been used interchangeably with ‘perineurioma.’”6 Our respondents cite the reasoning of Scheithauer and colleagues5 that the two lesions can be differentiated by their distinct immunohistochemical staining patterns. They further state that the lesions they have studied share the particular staining pattern assigned by Scheithauer and others to perineuriomas.1,5 It seems to us that this distinction alone is enough to warrant the consistent use of “localized hypertrophic neuropathy” and “intraneural perineurioma” interchangeably. We think that the newer data supporting a genetic alteration in this lesion is enough to tip the scales in favor of calling it an “intraneural perineurioma.” The argument as to whether the mass represents a reactive process or a neoplastic one continues to resonate between the two lesions. As a result, we continue to contribute to the controversy over terminology by designating them “localized hypertrophic neuropathy.”

Thanks to the authors for presenting a case that raises so many fascinating questions.

References


Response: Thank you for the opportunity to reply to Drs. Kline, Gruen, and Cummings. Their insightful response to our article raises several interesting points.

Regarding the surgical management of this lesion, we defer to the extensive experience of Drs. Gruen and Kline and agree that intraoperative nerve action studies may have optimized our intraoperative planning.7 To clarify our actions, we noted that the intraoperative stimulation through what appeared to be normal nerve fascicles located proximal, adjacent, and distal to the lesion produced “contraction of the muscles in the patient’s foot,” and not merely stimulation through the proximal portion of the nerve. Had we performed nerve action potentials, we suspect that we would have measured only a low or no amplitude potential. Whether it would have been technically feasible or beneficial to perform a nerve graft continues to be a question in our minds.

Nonetheless, we disagree with our respondents’ assertion that it is appropriate to use the terms “localized hypertrophic neuropathy” and “intraneural perineurioma” interchangeably. Our respondents cite the reasoning of Scheithauer and colleagues5 that the two lesions can be differentiated by their distinct immunohistochemical staining patterns. They further state that the lesions they have studied share the particular staining pattern assigned by Scheithauer and others to perineuriomas.1,5 It seems to us that this distinction alone is enough to warrant the consistent use of different names to describe the two lesions.

Nevertheless, Kline, et al., continue to use the term “localized hypertrophic neuropathy” because the lesions “appear more reactive than tumors.”8 Drs. Johnson and Kline4 make the observation that on a photomicrograph a localized hypertrophic neuropathy appears similar to a nerve after transection. For that reason, they postulate that this lesion represents a reactive process. We think that the newer data supporting a genetic alteration in this lesion is enough to tip the scales in favor of calling it an “intraneural perineurioma.” The argument as to whether the mass represents a reactive lesion or a neoplastic one continues to resonate because intraneural perineurioma and localized hypertrophic neuropathy are rare, and as such, it is difficult to say with certainty that there is no overlap between the lesions. Thus, we recommend that chromosomal studies be added to the immunohistochemical analyses undertaken to clarify further the nature of this lesion.

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