CHAPTER **33**

SURAL NERVE BIOPSY

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A sural nerve biopsy involves the harvesting of a 3-5 cm section of the sural nerve, often at the level of the ankle, for microscopic evaluation. It is most often performed on select patients with severe, progressive idiopathic peripheral neuropathy in which clinical and non-invasive test results have remained inconclusive. The nerve biopsy may help confirm a diagnosis, distinguish between different types of nerve damage, and identify specific inflammatory or disease conditions of peripheral nerves.

The ability to properly perform a sural nerve biopsy is a service that the podiatric surgeon can offer to neurologists. It involves preoperative planning in conjunction with the pathology laboratories at both the hospital at which the surgery is to take place, and the specialized neurological histopathology laboratory where the specimen is to be sent. The actual surgical procedure is not demanding, but requires anatomic soft tissue dissection and minimal nerve handling for best results.

INDICATIONS

Several studies have demonstrated that the underlying etiology of patients presenting with peripheral neuropathy can be elicited by non-invasive measures in approximately 80% of the cases.[1] However, this leaves about 20% of those patients with idiopathic peripheral neuropathy. Other invasive studies besides nerve biopsy include muscle biopsy (which is often performed in combination with the sural nerve biopsy) and lumbar puncture/cerebral spinal fluid analysis. A nerve biopsy may help confirm a diagnosis, distinguish between types of nerve damage, or establish a condition evident on histologic or histochemical examination. The strategy of the interpretation is to seek out specific diagnoses with known appearances on histopathologic exam. The biopsy is most useful in confirming a diagnosis of peripheral neuropathy due to vasculitis, chronic inflammatory demyelinating polyneuropathy (CIDP), amyloidosis, sarcoidosis, leprosy, and tumor infiltration.[1] It may also be useful in distinguishing certain inherited myelinopathies and some axonopathies. Unfortunately, the biopsy may show nonspecific results in many cases such as when the peripheral neuropathy is secondary to a metabolic or nutritional disorder.[1]

PREOPERATIVE PREPARATION

A significant amount of preoperative preparation is required to ensure the nerve biopsy will be appropriately transferred for histologic and histochemical preparation and interpretation. The surgeon must first locate and notify the nerve histopathology laboratory of the date and time of the anticipated surgery. This lab will have paperwork that will be completed by the surgeon, give instructions on preparation of the specimen for the surgeon's hospital laboratory, and arrange transportation of the biopsy to their facility.[2] The surgeon's hospital laboratory may need to purchase glutaraldehyde solution and dry ice as part of the nerve preparation and should likewise be notified prior to the biopsy date. Therefore, it is best to negotiate these details at least a week prior to the anticipated surgical date.

Procedure

The most important criteria for nerve biopsy is that the nerve be purely sensory. Resecting a nerve with any degree of motor function could lead to loss of muscle strength and function. Traditionally, the sural nerve has been the nerve of choice for histologic examination, although other nerves such as the superficial peroneal and superficial radial nerves are options. The sural nerve is most accessible just posterior to the lateral malleolus at the level of the ankle joint. Alternatively, the sural nerve may be harvested at the level of the gastrocnemius muscle belly inferior to the knee, particularly when a muscle biopsy is also desired, because this allows both muscle and nerve to be harvested from the same incision.[3] We have experience primarily with biopsy of the sural nerve posterior to the lateral malleolus.

A firm understanding of the anatomic location of the sural nerve at the level of the ankle joint is helpful for the incision placement and soft tissue dissection. Eastwood et al detailed the distal course of the sural nerve in their dissection of 20 cadaveric lower limbs. They found the sural nerve to have a relatively constant course and is on average 1.4 ± 0.1 cm posterior to the distal tip of the fibula.[4] Additionally, the nerve can often be palpated at this level.

The procedure can be performed under intravenous sedation and local anesthesia. A bump under the ipsilateral hip will assist access to the lateral aspect of the ankle. An incision is placed overlying the sural nerve posterior to the fibular malleolus (Figure 1). The nerve is identified (Figure 2) and isolated with a vessel loop to minimize direct nerve handling. The nerve is than freed from its soft tissue attachments proximally and distally within the wound (Figure 3). A 3 cm section of nerve is typically requested by the neuropathology laboratory. Therefore, a 5 cm biopsy is usually taken to ensure adequate length. A sterile ruler can be used to confirm the proper length of your specimen. The nerve is transected distally and proximally then gently wrapped in a moist saline sponge that is then placed in a sterile container (Figures 4, 5). The wound is irrigated and closed in layers.

The sterile specimen container will immediately be taken to the hospital pathology laboratory where they will prepare the specimen for transfer to the nerve histopathology laboratory. If the delivery of the specimen to the neuropathology lab is completed in less than 6 hours then it may be refrigerated and delivered on wet ice. If transport is anticipated to be longer then 6 hours than the specimen must be fresh frozen in dry ice. A portion of the nerve specimen may be placed in a glutaraldehyde solution for semi-thin slices and evaluation under an electron microscope. Results are usually available within 2 weeks depending on the nerve histopathology laboratory used.

Postoperatively, the patient should expect to have permanent numbness on the lateral aspect of the foot along the course of the sural nerve. Occasionally the patient may experience shock-like or "phantom" pains as the healing of the remaining nerve begins; however, this is rarely permanent and can be treated with such medications as Neurontin or Elavil.[5]

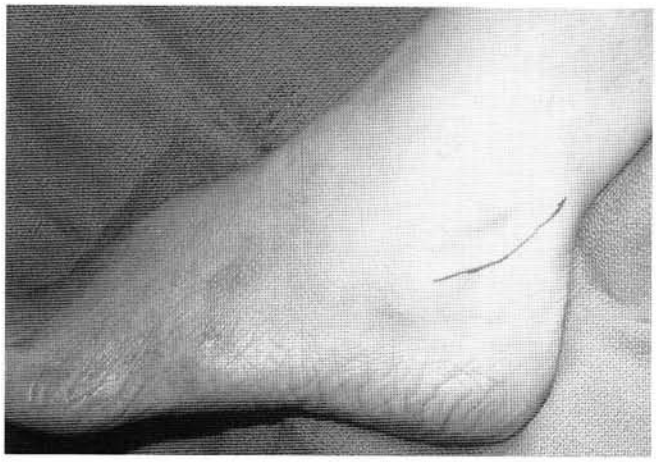

Figure 1. Skin incision for sural nerve biopsy, posterior to the lateral malleolus (~1.4 cm) overlying the sural nerve.

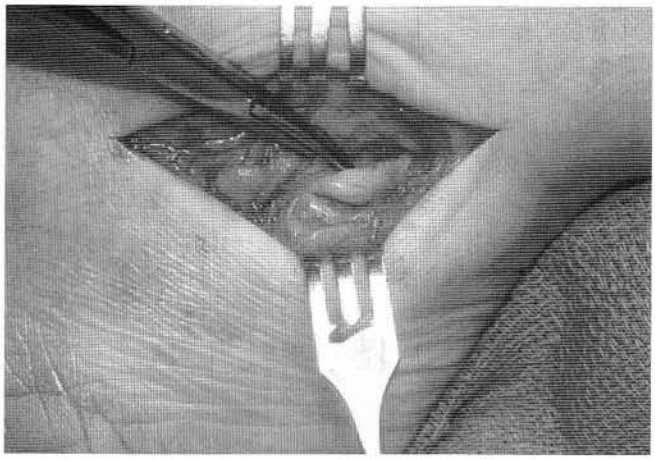

Figure 2. Identify the sural nerve within the subcutaneous tissue layer.

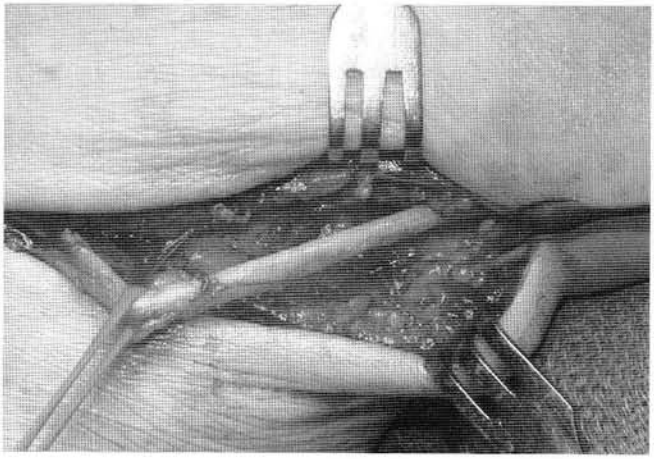

Figure 3. Use a vessel loop for minimal handling of the nerve and carefully free the nerve from its soft tissue attachments proximally and distally. Ensure a length of specimen > 3 cm.

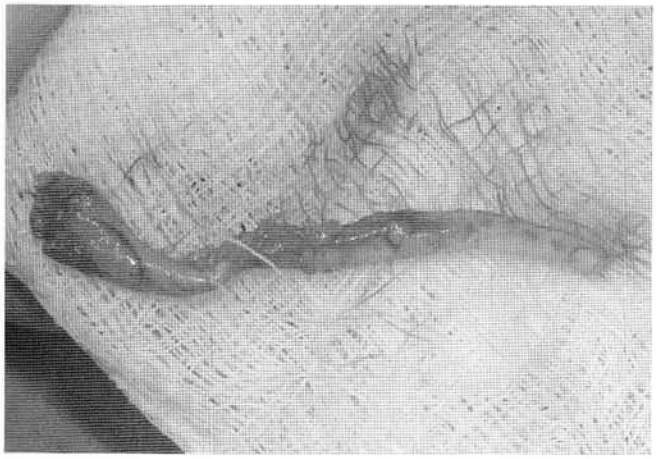

Figure 4. Gently transfer the nerve to a moist sponge.

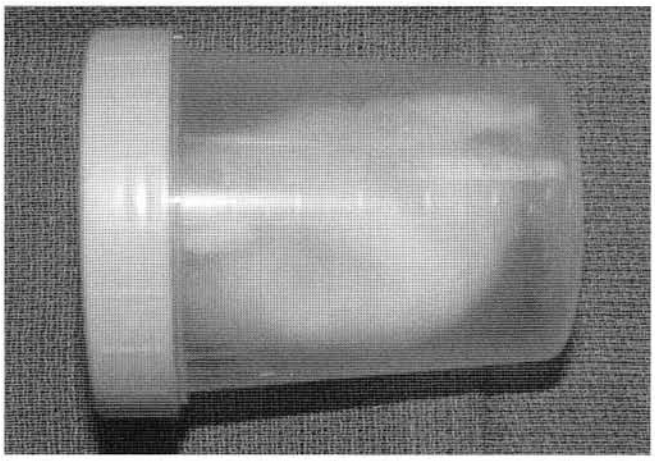

Figure 5. Place specimen (within sponge) into sterile container and transfer immediately to hospital's pathology lab for preparation.

Pathology Results

The nerve histopathology lab will primarily search for specific diagnoses utilizing microscopic analysis of routine and specially stained sections of nerve as well as semi-thin sections under an electron microscope. It is important that the patient understand that the nerve biopsy may not yield any further information as to the cause of their peripheral neuropathy. For example, we have seen that in some cases the peripheral neuropathy had progressed to a point of complete nerve fibrosis such that the underlying disease process could not be delineated.

Depending on the etiology, the results of any specimen may be specific or nonspecific. The nerve biopsy may only serve to distinguish between types of nerve damage, such as demyelination versus axon degeneration (Figure 6). While it would be impossible to cover the histopathologic findings of all peripheral neuropathies in this article, certain neuropathies have diagnostic features evident on microscopic examination worth brief detailing. These include amyloidosis, vasculitis, leprosy, metachromatic leukodystrophy, and various hypertrophic (onion bulb) neuropathies whose characteristics are enumerated in Figures 7-11.[6] Additionally, Fabry's disease is marked by perineural and vascular infiltration of lipid and Krabbe's disease is associated with "globoid cells" (large macrophages in close association).[6]

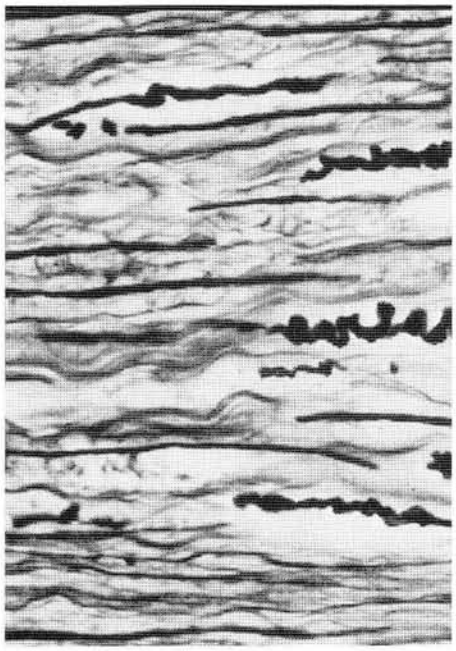

Figure 6. Axonal degeneration, such as seen here, is nonspecific but can be consistent with certain diagnoses. In this case, the patient has a history of alcholism, with Wernicke syndrome and this axonal degeneration would be consistent with peripheral neuropathy secondary to alcoholism.[6]

CONCLUSION

Although a sural nerve biopsy is infrequently required to determine the underlying etiology of a patient presenting with peripheral neuropathy, it is a procedure that the experienced podiatric surgeon is well-equipped to perform and may be a service that the podiatrist can offer to neurology or pathology when a nerve biopsy is deemed an appropriate measure. Keys to the success of the procedure include preoperative coordination between all involved hospitals for proper specimen protocol, harvesting an adequate length of specimen, utilizing the surgical techniques of anatomic dissection and minimal tissue handling, and the appropriate preparation and transfer of the nerve biopsy for microscopic evaluation.

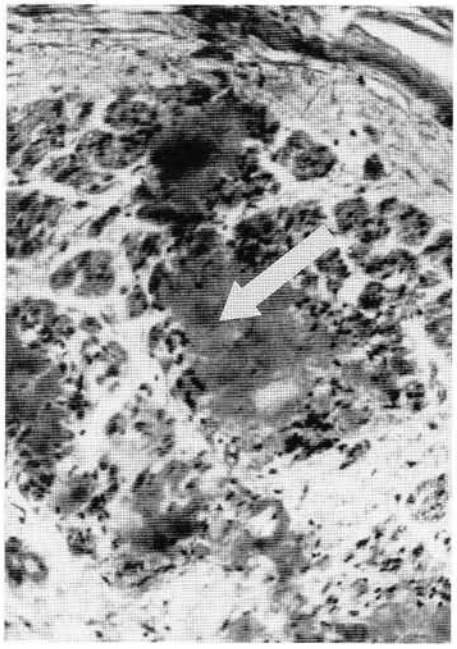

Figure 7. Amyloidosis: Amorphous, eosinophilic amyloid accumulation in nerve evident on H&E stain.[6]

Figure 8. Leprosy: characterized by acid-fast organisms (seen here within large mononuclear cells) and inflammatory tissue reaction.[6]

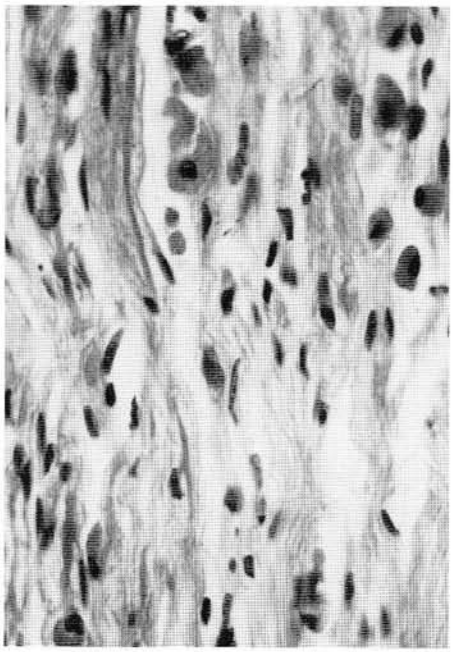

Figure 9. Metachromatic leukodystrophy: diagnostic metachromatic material within nerve on staining with cresyl violet, toluidine blue, or pseudoisocyanine.[6]

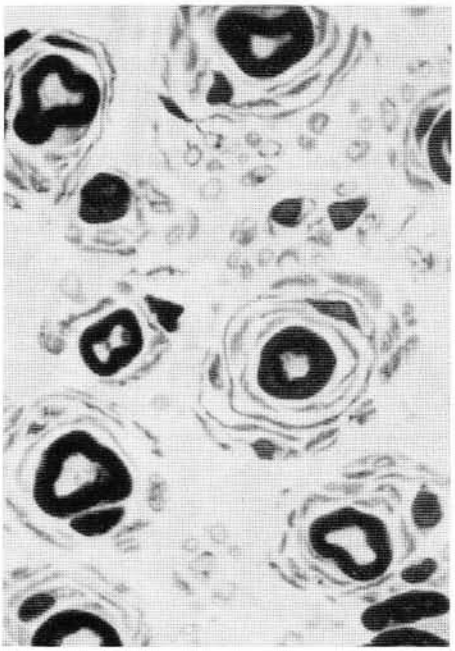

Figure 10. Hypertrophic (onion bulb) neuropathies: "onion bulb" is a nonspecific finding that refers to concentrically-aligned aggregated Schwann cells about large axons that often result in hypertrophy of the nerve. Charcot-Marie-Tooth and Dejerine-Sottas disease exemplify types of hypertrophic neuropathies characterized by, among other things, exuberant onion-bulb formation.[6]

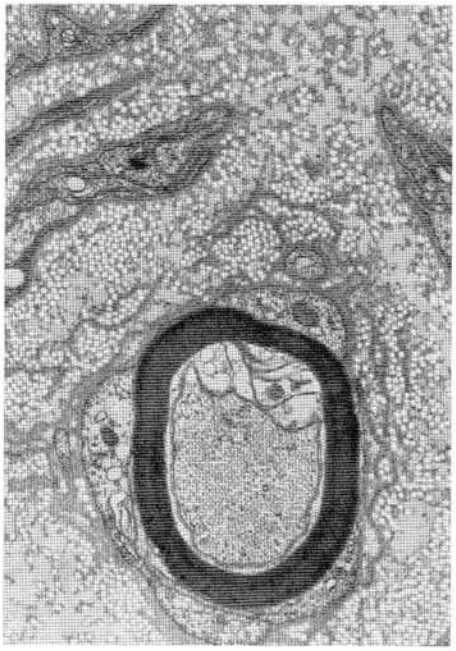

Figure 11. Hypertrophic (onion bulb) neuropathy. Onion bulb under electron microscopy shows a myelinized central axon and alternating collagen and schwann cell layers.[6]

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