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TECHNICAL REPORT

Technically successful ultrasound-guided percutaneous sural nerve needle biopsy in a patient with indeterminate peripheral neuropathy

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Abstract

Objective To determine whether ultrasound-guided percutaneous sural nerve needle biopsy yields sufficient tissue for analysis in a patient with suspected vasculitis-related peripheral neuropathy.

Materials and methods With real-time ultrasound guidance, a hydrodissection of the sural nerve from the adjacent small saphenous vein was first performed. A 14-gauge biopsy needle was then manipulated under real-time ultrasound guidance to obtain two transverse samples of the sural nerve at the lateral distal calf.

Results The biopsy was technically successful and yielded adequate tissue for routine processing. The specimen showed mild epineurial perivascular chronic inflammation with marked loss of myelinated axons. These histologic findings are not diagnostically definitive for vasculitis-related peripheral neuropathy but were supportive of the diagnosis in combination with the patient's physical examination, laboratory, and electromyography findings. The patient suffered no immediate complications after the procedure.

Conclusions This ultrasound-guided sural nerve needle biopsy, like many surgical biopsies, did not yield a definitive result in a patient with suspected vasculitis-related peripheral neuropathy; however, the procedure was technically successful. Given that percutaneous needle procedures offer many advantages over surgical procedures, we believe that this procedure warrants further investigation.

Keywords Ultrasound · Sural nerve · Biopsy · Peripheral neuropathy · Percutaneous

Introduction

Among patients with systemic vasculitis, 60 to 70% demonstrate peripheral nerve involvement [1]. Patients with vasculitis-related peripheral neuropathy present with weakness and a painful loss of sensation. These symptoms are seen in multiple peripheral nerve distributions and demonstrate a stepwise progression, usually over weeks or months [2]. The diagnosis of vasculitis-related peripheral neuropathy in these patients can be inferred without a nerve biopsy if vasculitis is confirmed in another organ and the patient has consistent laboratory, electromyogram, and physical examination data [3]. In many cases, however, a nerve biopsy is requested because peripheral nerve epineurial arterioles can demonstrate signs of disease [4]. The sural nerve is an optimal target for biopsy because it has a very reliable, superficial location and provides only sensory innervation [5]. Sural nerve biopsy for indeterminate peripheral neuropathy (not limited to vasculitis-related peripheral neuropathy) was first described by Dyck and Lofgren more than 50 years ago [5, 6]. The procedure is performed through an incision made under local anesthesia with removal of a full-thickness segment of nerve without grafting or anastomosis [7]. Fascicular nerve biopsy has also been described; in this procedure, a small number of nerve fascicules are microscopically dissected and removed so that the nerve is not completely transected. However, this technique has a lower success rate in the setting of vasculitic neuropathy compared with full-thickness nerve biopsy [6, 8]. Unfortunately, even with good surgical technique, a definitive

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histologic diagnosis of vasculitic neuropathy is not consistently achieved. The definitive diagnostic rate for surgical biopsies varies greatly, ranging from 20 to 62% [9, 10]. Combined nerve and muscle biopsy has been reported to improve yield in some but not all studies [2, 9, 11, 12].

With the high-frequency linear ultrasound transducers currently available, high-resolution, real-time imaging of superficial structures can be achieved. The sural nerve is one such structure that can be well visualized on ultrasound images despite its small size. Ultrasound guidance is currently used routinely in a wide range of soft tissue and even some focal nerve lesion biopsies. Therefore, it would seem that the use of ultrasound guidance may allow for less-invasive percutaneous sampling of the sural nerve when indicated. In the setting of indeterminate peripheral neuropathy, ultrasound has been used to assist in localizing the sural nerve for surgical biopsy [13]; however, to the authors' knowledge, there are no previous reports of ultrasound-guided percutaneous sural nerve needle biopsy in the setting of indeterminate peripheral neuropathy. Therefore, we sought to explore the use of this procedure in a patient with suspected vasculitis-related peripheral neuropathy.

Methods

We attempted an ultrasound-guided percutaneous sural nerve needle biopsy in a 67-year-old man with a slender body habitus (height, 1.8 m; weight, 65 kg; body mass index, 20 k/m^2) who presented to our tertiary care center with pain, weakness, and significant weight loss (> 30 pounds over 6 months). Based on physical examination, electromyogram, and laboratory studies, the consulting neurology service suspected vasculitis-related peripheral neuropathy and requested a sural nerve biopsy.

Given the growing experience with real-time ultrasound-guided musculoskeletal interventions at our institution, the musculoskeletal imaging team agreed to attempt an ultrasound-guided core biopsy of the sural nerve at the time of the peroneus brevis muscle biopsy in an effort to spare the patient a surgical biopsy. The nature of the procedure was discussed in detail with the patient, including the risk, benefits, and alternatives, and informed consent was obtained and documented in the electronic medical record.

We used a 14-MHz linear ultrasound probe (Acuson X700 machine; Siemens, Erlangen, Germany) with an image resolution of 1024 × 768 pixels to identify the sural nerve 3 to 4 cm proximal to the fibular tip between the fibula and Achilles tendon. The nerve was imaged and the procedure was performed entirely in the short axis of the nerve, transverse plane. A sterile site was prepared, and local anesthesia was achieved with 1% lidocaine. The sural nerve runs immediately parallel to the small saphenous vein at this level of the lower extremity. Therefore, in an attempt to isolate the nerve from the adjacent small saphenous vein, we used a 22-gauge needle to hydrodissect around the nerve using 5 cc of lidocaine (Fig. 1). Next, a 13-G introducer was advanced just superficial to the nerve and vein. A 14G Bard Mission (Tempe, AZ, USA) core biopsy needle was then advanced to the level of the nerve. Under real-time ultrasound guidance, the biopsy needle tray was deployed and manipulated such that the tray was superficial to the small saphenous vein but contained a cross section of the sural nerve (Fig. 2). Immediately before the biopsy needle was fired, the apparatus was angulated superficially to help prevent injury to the adjacent vein and better capture the nerve. Two core samples centered about the nerve were obtained and sent to the pathology laboratory (Fig. 3).

Results

The samples retrieved from the biopsy needle were 20 mm in length and approximately 1.6 mm in diameter. Although small, the samples were large enough to contain a full cross section of the sural nerve. The maximum thickness of the cross section of sural nerve removed in this case was 1.6 mm per sample. Because we were able to obtain a sample of the entire cross section of the sural nerve and the sample was able to be processed in the routine manner by the pathology department, the samples were felt to be technically adequate. Slides of the specimen demonstrated mild epineurial perivascular chronic inflammation with marked loss of myelinated axons (Fig. 4). The specimen was negative on Congo red stain. These histologic findings are not definitive for peripheral nerve-related vasculitis; however, the pathologist

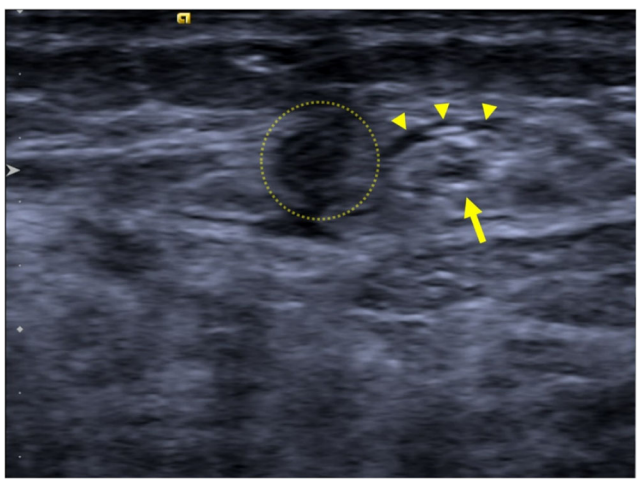

Fig. 1 Transverse ultrasound image showing the small saphenous vein (*circled*) adjacent to the more oval-appearing sural nerve (*arrow*). There is fluid (*arrowheads*) surrounding the nerve from hydrodissection performed before the biopsy attempt

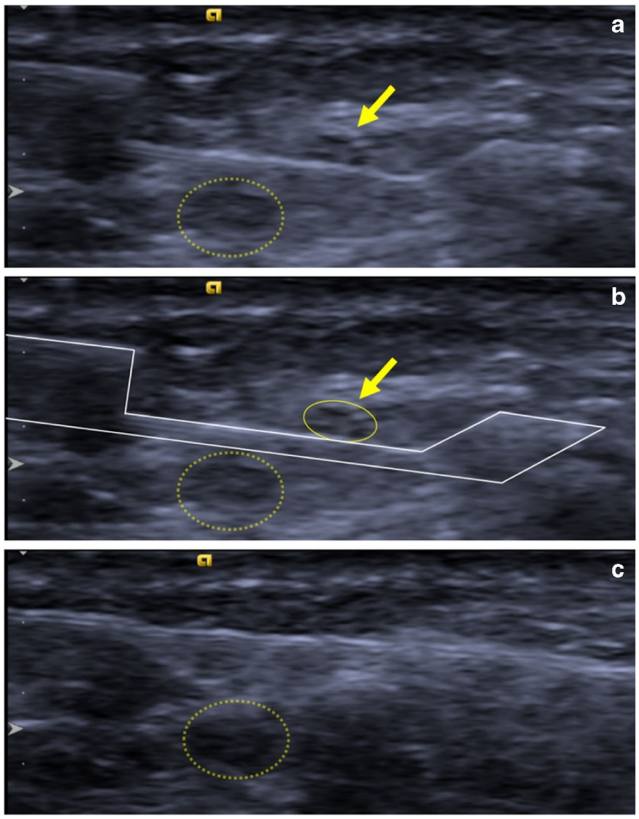

Fig. 2 **a, b** Transverse ultrasound images show the sural nerve (*arrow, solid circle*) positioned within the biopsy needle tray excluding the adjacent small saphenous vein (*dashed circle*). **c** The needle was angled slightly superficially and fired

commented that the result was similar to what is seen for many surgical specimens given this indication. Therefore, the procedure was considered technically successful, although not able to yield a definitive diagnosis. When combined with the patient's physical examination, laboratory, and electromyography findings, the histologic findings, although nonspecific, supported the diagnosis of antineutrophil cytoplasmic antibodies-associated vasculitis with predominant peripheral nerve involvement.

The patient tolerated the procedure well. He had mild initial discomfort during lidocaine administration into the skin and around the sural nerve. However, during the procedure, he reported no pain. It is unclear whether this was attributable to the local anesthetic, the neuropathy, or both. Immediately following the procedure and for the remainder of his hospital stay (4 days), he did not report symptoms at the site of the biopsy. The patient did not undergo a surgical biopsy.

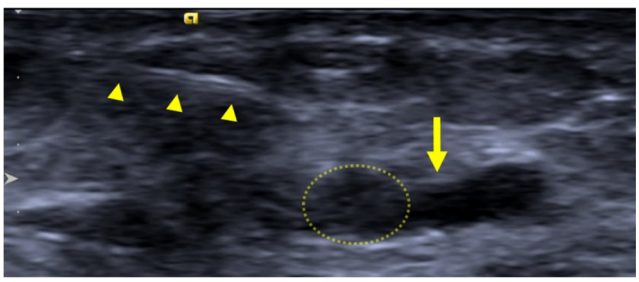

Fig. 3 Transverse ultrasound image shows an anechoic defect in the area of the sural nerve after biopsy (*arrow*). The adjacent small saphenous vein appears intact (*dashed circle*). The needle introducer is seen more superficially (*arrowheads*)

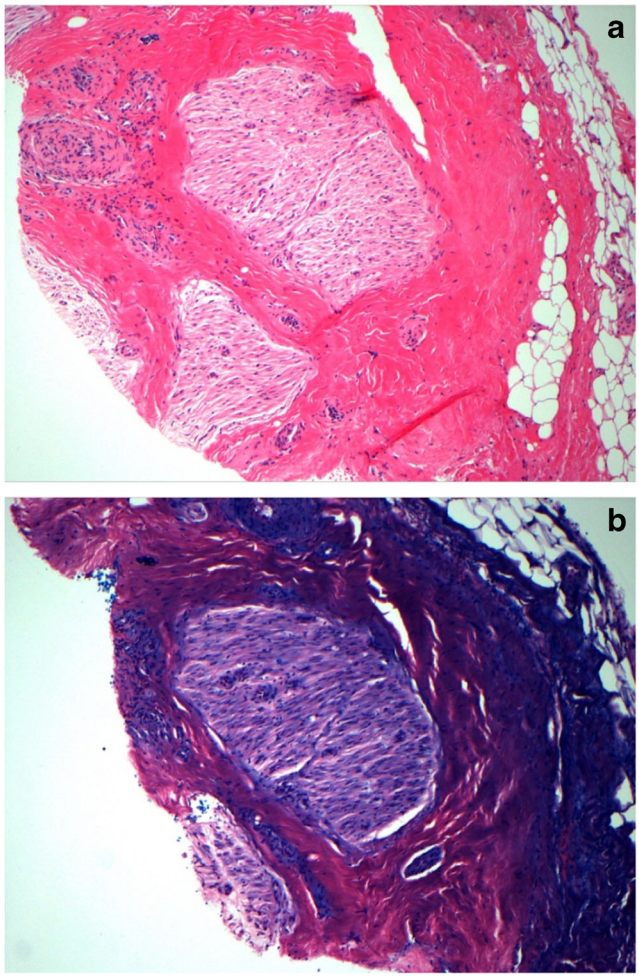

Fig. 4 **a** Hematoxylin and eosin-stained section showing nerve fascicles with adjacent fibrovascular and adipose tissue. Rare perivascular chronic inflammatory cells consisting of benign-appearing lymphocytes are present around small epineurial blood vessels (original magnification, 100×). **b** Luxol fast blue-stained section of peripheral nerve tissue highlighting a marked loss of myelinated axons (original magnification, 100×)

Discussion

Most cases of peripheral neuropathy do not require a tissue diagnosis. However, for conditions such as vasculitis-related peripheral neuropathy, a nerve biopsy is often needed. In such cases, the sural nerve is a preferred biopsy target because it is an easily accessible pure sensory nerve frequently involved in vasculitic peripheral neuropathy. The risk of sensory deficit from sural nerve biopsy is relatively low, and biopsy of this

nerve is unlikely to lead to pressure ulceration given its dorsal innervation [7]. A surgical biopsy usually involves a 6-cm-long incision and removal of a 2- to 7-cm length of full-thickness sural nerve. Biopsy samples as short as 1 cm have been reported; however, because disease can be patchy, 2- to 7-cm samples are typically obtained [7, 10]. The transected nerve ends are not routinely anastomosed, and the incision is typically closed with sutures.

Despite the low risk of significant morbidity with sural nerve biopsy, complications do occur. Postprocedural pain has been reported to occur in up to 33% of patients (range, 5–33%), dysesthesia in up to 60% of patients (range, 30–60%), and infection/delayed wound healing in 15–22% of patients [8, 10, 14, 15]. Sensory deficits appear to be more common when longer biopsy specimens are harvested, as has been reported for fascicular nerve biopsy [5, 16]. The risk of postprocedural pain also appears to be related to the length of nerve resected. For instance, Hilton et al. [15] reported that 29% of patients had persistent pain after a 3-cm biopsy was taken, whereas Rappaport et al. [10] reported that only 5% of patients had pain after a 2-cm (average length) biopsy was obtained. At 5 or more years after biopsy, dysesthesia in the sural nerve distribution has been reported to be the only residual symptom for either whole or fascicular nerve biopsy [8, 17].

Peripheral nerves can heal after transection. Neurotrophins secreted by the distal stump of the nerve help guide sprouting activity from the proximal stump to generate a scaffold and subsequently allow axonal regrowth. Axonal regeneration can span gaps up to 1.5 to 2.5 cm [18, 19]. Given that the typical surgical sural nerve specimen is 2 to 7 cm in length, axonal regeneration after a sural nerve biopsy is theoretically limited. For larger nerve defects, collateral sprouting can occur, providing some re-innervation; however, primary microsurgical reunion and axonal regeneration are superior [20–22].

In this report, the ultrasound-guided percutaneous needle biopsy of the sural nerve was technically successful, but like many surgical biopsies, was unable to demonstrate definitive histologic findings of vasculitis-related peripheral neuropathy. A total of 38 to 80% of surgical whole nerve or fascicular biopsies also yield nonspecific findings [9, 10]. Even when surgical sural nerve biopsy is combined with muscle biopsy, there are conflicting data regarding whether muscle biopsy improves overall diagnostic yield [2, 9, 11, 12]. Fortunately, for our patient, the resulting sural nerve defect was tiny, only 2–3 mm long, an order of magnitude shorter than a typical surgical defect and well within range for spontaneous axonal regeneration. Long-term sensory deficits and dysesthesia therefore seem theoretically less likely after percutaneous needle biopsies. A percutaneous needle biopsy requires only a tiny puncture wound(s) and therefore carries a very low risk for infection. Additionally, after percutaneous needle procedures, scarring is typically minimal or possibly undetectable. Unlike alternative imaging guidance modalities, ultrasound offers real-time cross-sectional visualization of the nerve and surrounding structures, so the biopsy needle can be manipulated to eliminate or minimize injury to surrounding tissues and optimize sample collection.

This technically successful ultrasound-guided sural nerve needle biopsy met a fate similar to that seen with many surgical biopsies, yielding a nonspecific result. However, because percutaneous needle procedures have so many advantages over surgical procedures and have replaced many surgical biopsies, we believe that ultrasound-guided percutaneous needle biopsy of the sural nerve for indeterminate peripheral neuropathy warrants further investigation. More study is needed to determine whether such a technique can provide a definitive diagnosis for an acceptable number of patients. Given the known patchy disease distribution, taking multiple biopsies along the sural nerve may improve yield, and because each individual needle biopsy specimen is small, even taking multiple needle biopsy samples should allow for better nerve healing than is seen with long-segment surgical biopsy. Therefore, although ultrasound-guided percutaneous sural nerve needle biopsy may never replace surgical biopsy, it may offer an alternative for patients with a high surgical risk or compromised wound healing, such as patients with obesity or diabetes. Nevertheless, more study is needed before ultrasound-guided sural nerve biopsy is considered for routine clinical application.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Gwathmey KG, Burns TM, Collins MP, Dyck PJ. Vasculitic neuropathies. Lancet Neurol. 2014;13(1):67–82.
2. Gorson KC. Vasculitic neuropathies: An update. Neurologist. 2007;13(1):12–9.
3. Schaublin GA, Michet CJ Jr, Dyck PJ, Burns TM. An update on the classification and treatment of vasculitic neuropathy. Lancet Neurol. 2005;4(12):853–65.
4. Wees SJ, Sunwoo IN. Oh SJ. Sural nerve biopsy in systemic necrotizing vasculitis. Am J Med. 1981;71(4):525–32.
5. Dyck PJ, Lofgren EP. Nerve biopsy. Choice of nerve, method, symptoms, and usefulness. Med Clin North Am. 1968;52(4):885–93.
6. Dyck PJ, Lofgren EP. Method of fascicular biopsy of human peripheral nerve for electrophysiologic and histologic study. Mayo Clin Proc. 1966;41(11):778–84.

7. Bevilacqua NJ, Rogers LC, Malik RA, Armstrong DG. Technique of the sural nerve biopsy. J Foot Ankle Surg. 2007;46(2):139–42.
8. Pollock M, Nukada H, Taylor P, Donaldson I, Carroll G. Comparison between fascicular and whole sural nerve biopsy. Ann Neurol. 1983;13(1):65–8.
9. Vital C, Vital A, Canron MH, et al. Combined nerve and muscle biopsy in the diagnosis of vasculitic neuropathy. A 16-year retrospective study of 202 cases. J Peripher Nerv Syst. 2006;11(1):20–9.
10. Rappaport WD, Valente J, Hunter GC, et al. Clinical utilization and complications of sural nerve biopsy. Am J Surg. 1993;166(3):252–6.
11. Collins MP, Mendell JR, Periquet MI, et al. Superficial peroneal nerve/peroneus brevis muscle biopsy in vasculitic neuropathy. Neurology. 2000;55(5):636–43.
12. Prayson RA, Sedlock DJ. Clinicopathologic study of 43 patients with sural nerve vasculitis. Hum Pathol. 2003;34(5):484–90.
13. Chen CH, Shen CC, Lan HHC, Lee SK. Ultrasound-assisted sural nerve biopsy: technical note and correlation of ultrasound imaging with operative findings. J Med Ultrasound. 2013;21(1):43–5.
14. Dahlin LB, Eriksson KF, Sundkvist C. Persistent postoperative complaints after whole sural nerve biopsies in diabetic and non-diabetic subjects. Diabet Med. 1997;14(5):353–6.
15. Hilton DA, Jacob J, Househam L, Tengah C. Complications following sural and peroneal nerve biopsies. J Neurol Neurosurg Psychiatry. 2007;78(11):1271–2.
16. Solders G. Discomfort after fascicular sural nerve biopsy. Acta Neurol Scand. 1988;77(6):503–4.
17. Gabriel CM, Howard R, Kinsella N, et al. Prospective study of the usefulness of sural nerve biopsy. J Neurol Neurosurg Psychiatry. 2000;69(4):442–6.
18. Sahni V, Qi Y, Frostick S. Peripheral nerve regeneration. Eur Surg. 2005;37(4):187–92.
19. Lundborg G, Dahlin LB, Danielsen N, et al. Nerve regeneration in silicone chambers: influence of gap length and of distal stump components. Exp Neurol. 1982;76(2):361–75.
20. Theriault M, Dort J, Sutherland G. Zochodne DW. A prospective quantitative study of sensory deficits after whole sural nerve biopsies in diabetic and nondiabetic patients. Surgical approach and the role of collateral sprouting. Neurology. 1998;50(2):480–4.
21. Schoeller T, Huemer GM, Shafighi M, Gurunluoglu R, Wechselberger G, Piza-Katzer H. Microsurgical repair of the sural nerve after nerve biopsy to avoid associated sensory morbidity: a preliminary report. Neurosurgery. 2004;54(4):897–901.
22. Kennedy WR, Navarro X, Kamal H. Reinnervation of sweat glands in the mouse: axonal regeneration versus collateral sprouting. Muscle Nerve. 1988;11(6):603–9.