Sonographic Target Sign in Neurofibromas

John Lin, MD, Jon A. Jacobson, MD, Curtis W. Hayes, MD

Neurofibromas are the most common tumors of the peripheral nerves. They may be solitary lesions, multiple localized lesions, or large plexiform masses often associated with neurofibromatosis. Relatively few reports discuss the sonographic features of PNST, specifically neurofibromas.[1–7] The typical sonographic description is that of a well defined, homogeneous hypoechoic lesion, which can show posterior acoustic enhancement mimicking a cystic lesion.[1,3,4] We present a case of neurofibromatosis in a 19 year old man, which was initially diagnosed by ultrasonography. We describe the ultrasonographic findings that we believe correspond to the so-called target sign on T2-weighted MR imaging examinations. The appearance on T2-weighted MR images is reported as increased signal intensity peripherally and decreased signal intensity centrally.[8–10] A target sign appearance was seen sonographically in numerous lesions, demonstrating a hyperechoic central region and a hypoechoic periphery.

ABBREVIATIONS

PNST, Peripheral nerve sheath tumors; MR, Magnetic resonance

Received January 12, 1999, from the Department of Radiology, The University of Michigan Medical Center, Ann Arbor, Michigan. Revised manuscript accepted for publication April 4, 1999.

Address correspondence and reprint requests to John Lin, MD, Department of Radiology, The University of Michigan Medical Center, 1500 East Medical Center Dr., TC 2910, Ann Arbor, MI 48109-0326.

CASE REPORT

A 19 year old man was referred to our institution with a 2 year history of right knee discomfort centered in the popliteal fossa. He had a long history of multiple small painless masses in his legs, which were presumed to represent multiple lipomas and followed by his family physician since age 14 years. Because symptoms in the popliteal fossa did not resolve and had recently become slightly more bothersome, the patient was referred to our orthopedic oncology service for further workup.

Clinical examination revealed three small palpable nodules in the anterior thigh of each leg. No mass was palpable in the popliteal fossa region of the right knee, and no soft tissue masses were seen on visual inspection. The patient was referred to radiology for sonographic evaluation of the right lower extremity, specifically to evaluate for the presence of a mass in the popliteal fossa region. The

primary differential diagnostic consideration of the clinician at this juncture was multiple lipomas.

We used a Sonoline Allegra ultrasonographic unit (Siemens Medical Systems, Iselin, NJ), with a 7.5 MHz linear array transducer. We performed the lower extremity examination primarily from a posterior approach, with the patient lying prone. Comparison with the contralateral extremity was also performed. For examination of the upper extremity, we used the same 7.5 MHz linear array transducer, adjusting the depth and focal zones accordingly to optimize for the structures of interest. Longitudinal and transverse scanning were performed along the expected course of the nerves we investigated.

Sonographic examination of the right lower extremity revealed extensive multilobulated soft tissue masses posteriorly in the distribution of the sciatic nerve, extending through the popliteal fossa region into the calf along the course of the tibial nerve (Fig. 1). Separate nerves could not be identified. These lesions involved the entire lower extremity, from the hip to the ankle, representing the bulk of the posterior soft tissues of the leg. The standard of reference to determine relative echogenicity was the adjacent skeletal muscles. Most lesions demonstrated a relatively hypoechoic outer margin, with a central region of increased echogenicity (Figs. 2, 3). The largest individual mass was located deep within the popliteal fossa, measuring 5 by 3 cm in size (Fig. 2). The majority of these lesions measured approximately 2 to 3 cm in diameter. The margins were well defined, with a thin echogenic border outlining each individual mass.

Comparison examination of the contralateral asymptomatic lower extremity showed similar findings along the distribution of the sciatic and tibial nerves. The extent of disease was similar to that of the symptomatic right lower extremity. Questioning of the patient during the examination uncovered complaints of numbness and tingling in the left upper extremity. Examination of the left forearm demonstrated fusiform enlargement of the ulnar and median nerves, measuring 4 to 8 mm diameter in several locations, with normal appearance of the intervening nerves. The fusiform lesions demonstrated a uniform hypoechoic appearance, with distal acoustic enhancement in several of these lesions (Fig. 4).

An outside MR imaging examination of the right knee performed on a 1.5 T Signa magnet (General Electric Medical Systems, Milwaukee, WI) included the following sequences: T1-weighted axial (TR = 500 ms, TE = 16 ms), sagittal (TR = 383 ms, TE = 22 ms), and coronal (TR = 433 ms, TE = 22 ms) views and T2-weighted sagittal (TR = 3000 ms, TE = 102 ms) and coronal (TR = 4166 ms, TE = 102 ms) views. We reviewed this study with the clinician several days after the ultrasonographic examination, confirming these continuous multilobulated mass lesions, which were posteriorly located and which extended beyond the field of view in both proximal and distal directions. These lesions showed a uniform low signal on T1-weighted images (Fig. 5) and an increased signal with a central region of low signal intensity within most individual lobules on T2-weighted images (Fig. 6).

The diagnosis of neurofibromatosis was made based on the sonographic findings. Correlation with the MR imaging examination supported our diagnosis. As a result, the patient was treated symptomatically and responded to conservative therapy.

DISCUSSION

The sonographic features of PNST have been described in prior reports.[1–7] Both neurofibromas and schwannomas are typically well defined, homogeneous hypoechoic lesions. Several reports describe

Figure 1 Longitudinal extended field of view sonogram of the right lower extremity from a posterior approach shows extensive multilobulated soft tissue masses *(white arrows)* extending from the proximal thigh, through the popliteal fossa, and continuing into the distal calf. Note the target sign *(black arrows)* appearance of numerous individual lobules. Posterior femoral and tibial cortices *(curved white arrows)* are echogenic.

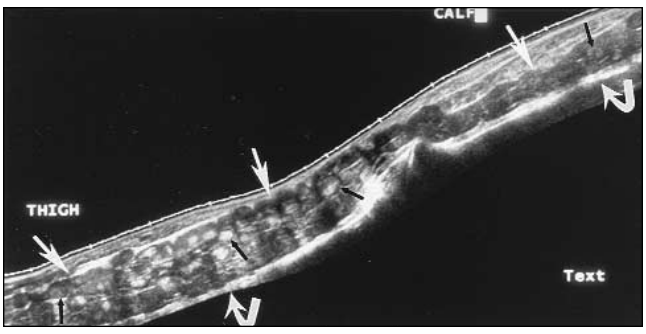

Figure 2 Focused longitudinal sonogram of the right popliteal fossa region reveals an individual mass showing a prominent hyperechogenic central region *(arrowheads)*, with a hypoechogenic periphery *(arrows)* corresponding to the MR imaging equivalent target sign.

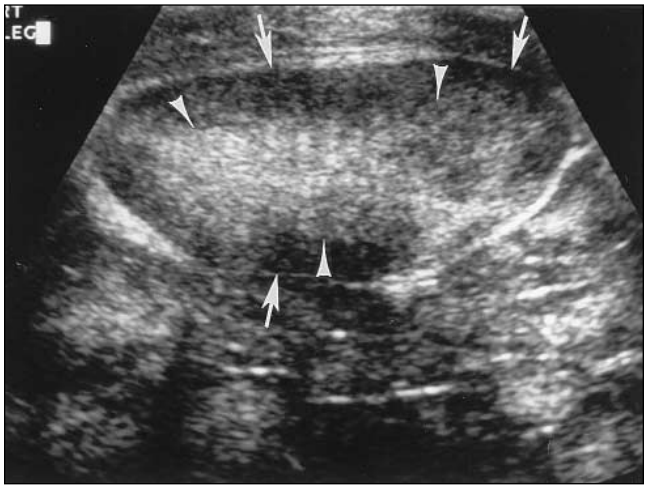

Figure 3 Small field of view longitudinal sonogram of the posterior right thigh shows numerous conglomerate lobulated masses, each demonstrating the target sign *(arrows)* appearance.

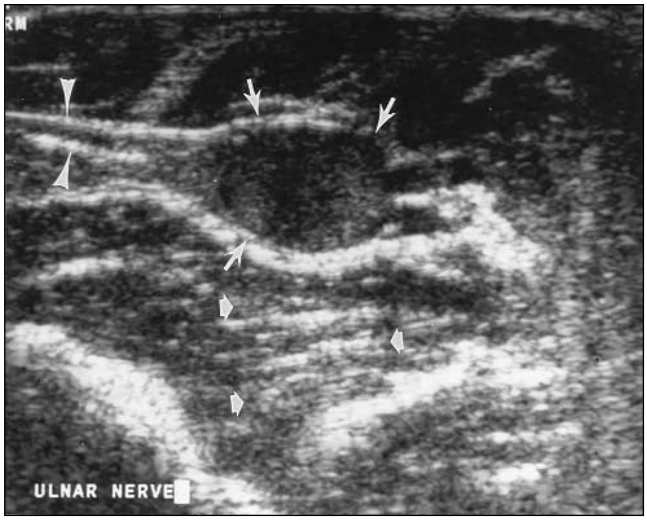

Figure 4 Longitudinal sonogram of the left elbow medially, distal to the cubital tunnel, reveals a solitary ovoid mass *(arrows),* with a tapered appearance proximally in continuity with the ulnar nerve *(arrowheads).* Lesion shows hypoechoic echotexture with well defined borders. Note the distal acoustic enhancement *(short arrows).*

the additional finding of distal acoustic enhancement in some cases, simulating the appearance of a cyst.[1,3,4]

The MR imaging features of PNST are well described.[8–13] Most commonly, neurofibromas demonstrate a homogeneous low signal on T1-weighted images and a variable increased high signal on T2-weighted images. Of particular interest to our case are the few reports on the target sign found in benign PNST, which is seen on T2-weighted images and consists of increased peripheral signal intensity and decreased central signal intensity. Suh and associates found that seven of 10 neurofibromas demonstrated this finding, not seen in their series of neurofibrosarcomas.[8] Bhargava and colleagues reported the target sign in all 12 neurofibromas but in only one of the 11 neurofibrosarcomas, suggesting that the target sign may be useful in differentiating benign PNST from malignant PNST.[9] Varma and coworkers also concluded that the presence of the target pattern indicated a benign nerve sheath tumor (present in 12 of 23 neurofibromas and schwannomas and in zero of nine malignant nerve sheath tumors).[10]

As previously reported, MR imaging–histologic correlation of the target sign[8,10] showed dense fibrous and collagenous central zones corresponding to the low signal center on T2-weighted images. Abundant myxoid material with high fluid content in the outer zones corresponded to the high signal periphery on T2-weighted images.

In this case, the sonogram revealed bilateral, extensive multilobulated soft tissue masses involving the entire distribution of the sciatic and tibial nerves. A target sign appearance was evident within most of the individual lobules (Figs. 1–3). The hypoechoic outer zone corresponded to the high signal peripheral zone on T2-weighted MR imaging examination. The hyperechoic central zone corresponded to the low signal central zone on T2-weighted MR imaging examination. Correlation with previously reported MR imaging findings[9,10] suggests that the presence of the sonographic target sign may also be useful in differentiating benign PNST from malignant PNST.

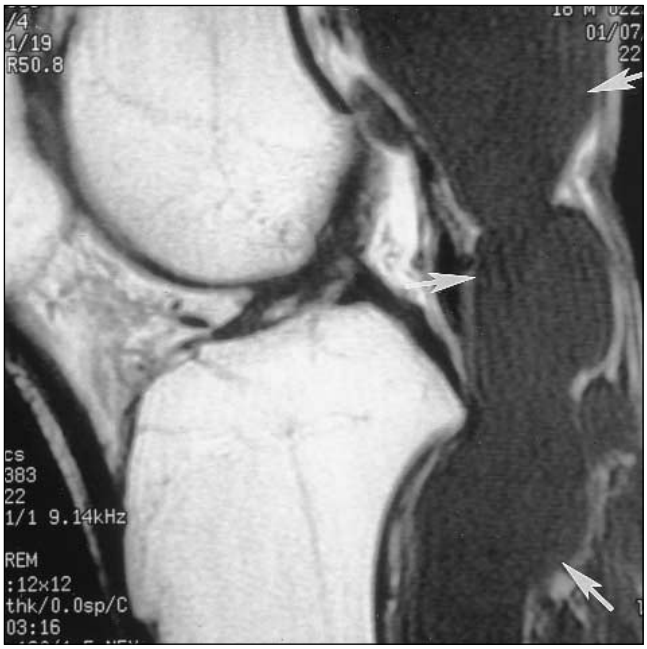

Figure 5 Sagittal T1-weighted MR image of the right knee shows uniform low signal multilobulated mass *(arrows)* extending above and below the level of knee joint posteriorly. Superior and inferior extent of this lesion is beyond the field of view of this examination.

Figure 6 Coronal T2-weighted MR image of the right knee shows multilobulated masses posteriorly *(white arrows)*. Discrete individual lesions can be discerned, showing a high signal intensity periphery, with the majority of lesions demonstrating a central region of low signal intensity *(black arrows)*.

Further studies with histologic confirmation are needed to verify this hypothesis.

As previously mentioned, the target sign appearance seen on MR imaging has been histologically correlated with a dense fibrocollagenous center and a high fluid content myxoid periphery. We speculate that fibrous and collagen tissues centrally demonstrate increased echogenicity due to multiple interfaces present, whereas the myxoid periphery is relatively homogeneous, resulting in a hypoechoic appearance. The target sign was present in the individual lobules within the large plexiform neurofibromas in the lower extremities but was not seen in the smaller lesions in the forearm of the same patient. This may be related to the histologic composition of each individual lesion. The larger lesions may be more apt to consist of specific histologic zones than smaller lesions.[10] Or it may be more difficult to differentiate a tiny central zone in smaller lesions as opposed to a more significant central zone in larger lesions. Previous reports relied upon older equipment with less resolution than the current technology, which may also be a factor.

We showed fusiform soft tissue masses intimately involved with ulnar and median nerves and large lobulated masses in both lower extremities consistent with plexiform neurofibromas, presumably extensively involving and obscuring the sciatic and tibial nerves. Normal peripheral nerves show increased echogenicity relative to adjacent muscle on ultrasonography.[14] Recently, the sonographic appearance of peripheral nerves has been described as fascicular, with parallel hypoechoic and hyperechoic regions, corresponding histologically to neuronal fascicles and connective tissue stroma, respectively.[15] This pattern was demonstrated in our case within the intervening portions of the median and ulnar nerves between the fusiform masses.

The extended field of view feature of the sonogram was useful in showing the relationship of nearby structures and defining the scope of disease.[16] The sonographic examination can be easily modified to the specific needs of each individual patient, and multiple different anatomic regions can be studied as indicated. Sonography can be an accurate, inexpensive, and readily accessible modality for the initial evaluation of suspected soft tissue lesions, including PNST.[14]

Based on our report of the sonographic equivalent of the target sign seen on MR imaging examination,

we speculate that, given confirmation, ultrasonography may be a reliable and expedient method for identification and follow-up of peripheral neurofibromas.

REFERENCES

1. Chinn DH, Filly RA, Callen PW: Unusual ultrasonographic appearance of a solid schwannoma. J Clin Ultrasound 10:243, 1982
2. Reuter KL, Raptopoulos V, DeGirolami U, et al: Ultrasonography of a plexiform neurofibroma of the popliteal fossa. J Ultrasound Med 1:209, 1982
3. Hoddick WK, Callen PW, Filly RA, et al: Ultrasound evaluation of benign sciatic nerve sheath tumors. J Ultrasound Med 3:505, 1984
4. Hughes DG, Wilson DJ: Ultrasound appearances of peripheral nerve tumors. Br J Radiol 59:1041, 1986
5. Fornage BD: Peripheral nerves of the extremities: Imaging with US. Radiology 167:179, 1988
6. Cantos-Melian B, Arriaza-Loureda R, Aisa-Varela P: Tibialis posterior nerve schwannoma mimicking achilles tendinitis: Ultrasonographic diagnosis. J Clin Ultrasound 18:671, 1990
7. Cozzolino F, Tricarico A, Ferrucci D, et al: Echotomographic imaging in a case of plexiform von Recklinghausen neurofibromatosis. Ital J Orthop Traumatol 15:389, 1989
8. Suh JS, Abenoza P, Galloway HR, et al: Peripheral (extracranial) nerve tumors: Correlation of MR imaging and histologic findings. Radiology 183:341, 1992
9. Bhargava R, Parham DM, Lasater OE, et al: MR imaging differentiation of benign and malignant peripheral nerve sheath tumors: Use of the target sign. Pediatr Radiol 27:124, 1997
10. Varma DGK, Moulopoulos A, Sara AS, et al: MR imaging of extracranial nerve sheath tumors. J Comput Assist Tomogr 16:448, 1992
11. Glasier CM, Williamson MR, Lange TA: MRI of peripheral neurofibromas in children. Orthopedics 12:269, 1989
12. Cerofolini E, Landi A, DeSantis G, et al: MR of benign peripheral nerve sheath tumors. J Comput Assist Tomogr 15:593, 1991
13. Stull MA, Moser RP, Kransdorf MJ, et al: Magnetic resonance appearance of peripheral nerve sheath tumors. Skeletal Radiol 20:9, 1991
14. Fornage BD (Ed): Musculoskeletal Ultrasound. New York, Churchill Livingstone, 1995, pp 21, 73
15. Silvestri E, Martinoli C, Derchi LE, et al: Echotexture of peripheral nerves: Correlation between US and histologic findings and criteria to differentiate tendons. Radiology 197:291, 1995
16. Barberie JE, Wong AD, Cooperberg PL, et al: Extended field-of-view sonography in musculoskeletal disorders. AJR 171:751, 1998