Nerve Sheath Myxoma in the Lower Extremity: A Rare Case with Description of Magnetic Resonance Imaging and Sonographic Findings

**Patient:** Male, 36-year-old

**Final Diagnosis:** Nerve sheath myxoma

**Symptoms:** Pain

**Medication:** —

**Clinical Procedure:** —

**Specialty:** Radiology

**Objective:** Rare disease

**Background:** This report is of a nerve sheath myxoma presenting as a slow-growing mass in the back of the left ankle of a 36-year-old man that was investigated by ultrasound and magnetic resonance imaging (MRI) before the diagnosis was confirmed by histopathology.

**Case Report:** We report a nerve sheath myxoma of the ankle in a 36-year-old man. The palpable abnormality was falsely assumed to be a ganglion cyst prior to advanced imaging. Magnetic resonance imaging demonstrated a lobular mass with high T2 and intermediate T1 signal as well as moderate enhancement. T2 sequences also demonstrated distinctive internal septae. These internal septae were also noted on sonographic evaluation prior to biopsy. The patient was treated with surgical excision, and pathologic analysis showed myxoid nodules with loose arrangements of spindled cells separated by fibrous septae. S-100 protein and glial fibrillary acidic protein positivity by immunohistochemistry staining was demonstrated. Follow-up imaging at 12 months showed no evidence of tumor recurrence.

**Conclusions:** This case highlights that while nerve sheath myxomas are rare tumors, they should be considered in cases of cutaneous soft-tissue masses with myxoid imaging features. Ultrasound and magnetic resonance imaging features of thin internal septae may be present and correspond well with the unique histopathological characteristics of these lesions. This report shows the importance of imaging of peripheral soft-tissue masses, including ultrasound and MRI, which can identify localized and benign features and the solid, cystic, and myxoid areas, which were characteristic in this case of benign nerve sheath myxoma.

**Keywords:** Nerve Sheath Neoplasms • Neurothekeoma • Peripheral Nervous System Neoplasms

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Background

First described in 1969 by Harkin and Reed, neurothekeomas and nerve sheath myxomas (NSM) are rare cutaneous neoplasms of peripheral nerve origin and are characterized as benign soft-tissue tumors according to current guidelines [1-3]. In 2020, the World Health Organization (WHO) classified nerve sheath myxomas as one of 12 subtypes of soft-tissue tumors [3]. Although previously used interchangeably, neurothekeomas and NSMs are now described as unique entities, with the later exhibiting S100-positivity [4,5]. In addition to diffuse immunoreactivity to S100, NSMs also demonstrate moderate to diffuse reactivity to GFAP and CD57 and show strong immunoreactivity to collage IV around tumor cells [3].

Surgical excision is usually the treatment of choice in symptomatic patients, with a high recurrence rate in cases of incomplete excision [3,13]. We present a case report of a NSM occurring in the subcutis of the ankle, a somewhat rare location for these tumors. We also describe the sonographic and magnetic resonance imaging (MRI) features of this tumor. To our knowledge there have been only 4 other reported cases of a NSM at the ankle, and no case reports have published ultrasound images [5]. Ultrasound and MRI provide excellent anatomic detail in the characterization of soft-tissue tumors, and identifying the unique imaging features of NSMs can help in their diagnosis when surgical excision is not an option [14].

Case Report

A 36-year-old man presented to an outpatient primary care clinic for evaluation of a left posterolateral ankle palpable mass. Past medical history was notable for shin splints. The patient had no history of prescription medication and he used over-the-counter naproxen occasionally for lower-extremity pain. The patient denied a current history of tobacco, alcohol, or drug use. The patient reported that the ankle mass had existed for the past 14 years and was previously diagnosed as a ganglion cyst. The mass was treated conservatively until it started to become symptomatic, exhibiting “stinging” pain, pressure, and gradual increase in size for 8 months prior to the patient’s presentation. Physical exam showed a firm, palpable, flesh-colored nodule measuring 1×1 cm located at the posterolateral ankle, distal to the lateral malleolus. There were no skin discolorations or neuromuscular deficits.

The patient was prescribed naproxen, 500 mg by mouth, twice daily for the pain associated with the lesion. An initial radiograph performed of the ankle demonstrated a nonspecific soft-tissue density posterior to the talus (arrow). The mass showed a firm, palpable, flesh-colored nodule measuring 1×1 cm (anteroposterior×transverse×craniocaudal) in size. Given the nonspecific imaging features of the mass and inability to exclude soft-tissue sarcoma, the patient was referred to orthopedic oncology and then to the musculoskeletal radiology service for ultrasound-guided biopsy. Pre-biopsy sonographic evaluation of the mass showed a well-circumscribed, hypoechoic mass without internal vascularity and with posterior sonographic enhancement (Figure 3). Corresponding to the MRI findings, there were scattered isoechoic internal septae within the mass. Ultrasound-guided biopsy was performed with a 14-gauge spring-loaded needle device.

Figure 1. Lateral radiograph of the left ankle demonstrating radiographic features of a benign nerve sheath myxoma prior to resection. This radiograph demonstrates a nonspecific soft-tissue density posterior to the talus (arrow).
The patient was scheduled for a surgical excision, which was performed without complications. The excisional specimen consisted of a yellow-tan, fibrofatty, firm mass measuring 2×1.9×2 cm. Serial sectioning revealed a white-tan to yellow-tan, rubbery cut surface with multiple lobulations. Sections of the initial biopsy and excisional specimens showed large, irregular, myxoid nodules containing loose arrangements of spindled cells with small nuclei and few scattered bland fibrohistiocytic cells. The nodules were separated by internal thick fibrous bands (Figure 4). No high-grade features, such as nuclear enlargement, hyperchromasia, nuclear membrane irregularities, or mitotic figures, were identified. The tumor displayed diffuse and strong staining for S-100 protein and glial fibrillary acidic protein (GFAP) by immunohistochemistry (Figure 5). The histology and staining patterns were confirmatory for a nerve sheath origin tumor and were consistent with a dermal NSM.

One month following resection, the patient stated that his symptoms had significantly improved, with mild occasional numbness and “tingling” along the left lateral malleolus. Follow-up MRI 6 months after resection demonstrated residual non-masslike T2 hyperintense signal and mild non-masslike enhancement in the surgical bed. Follow-up MRI at 12 months demonstrated resolution of T2 signal abnormality and no enhancement consistent with absent tumor recurrence (Figure 6). No treatment complications were recorded on follow-up clinical visits.

Discussion

NSMs are rare, benign nerve sheath tumors that primarily occur in superficial locations [5]. Although usually asymptomatic, pain can be a presenting symptom [5]. Until recently, the terms NSM and neurothekeoma have been used interchangeably; however, these tumors are now differentiated by immunohistochemistry with NSMs exhibiting S100-positivity [4,5]. Reported NSMs are more common in the upper extremities,
especially the hands. When occurring in the lower extremities, the knee and foot are the most common locations [5,8,9]. To our knowledge, there have been only 4 other reported cases of a NSM at the ankle [5].

In 2005, Fetsch et al published the largest clinicopathologic NSM case series, with 57 cases [5]; imaging features of NSMs were not reported, 86% of their cases occurred in the extremities, and most lesions were present for many years prior to surgical resection. They had follow-up data for 34 cases and 47% of these had local recurrence, highlighting the importance of performing a resection with margins clear of disease. Histology features of these lesions common to our case include multinodular/multilobular masses in dermal and/or subcutis locations with abundant myxoid matrix and a peripheral fibrous border. Correlating with our findings of internal septae on imaging, their specimens showed fibrous connective tissue bordering the multinodular tumor architecture. Dominant cellular tumor components were epithelioid Schwann cells in corded, nested, and/or syncytial-like aggregates [5].

Fetsch et al were the first to suggest that NSMs are a subset of peripheral nerve sheath tumors and are distinct from neurothekeomas based on the latter lacking S-100 and GFAP staining and a fibrous border. Neurothekeomas also have less myxoid matrix, more cellular spindling, and more nuclear variability than NSMs [5]. Pathologic differential diagnosis for NSM includes neurothekeoma, superficial angiomyxoma,
neurofibroma, schwannoma, perineurial tumors, chondroma of soft parts, and superficial acral fibromyxoma [5].

Sonographic and MRI features of NSMs have been infrequently described in the literature, especially in cases occurring in the extremities. This is likely due to the typical dermal and subcutis locations of these lesions, with physicians opting for surgical excision without imaging. The imaging features for many soft-tissue masses are very nonspecific as most benign soft-tissue masses cannot reliably be distinguished from malignant sarcomas or metastatic disease on imaging. Most soft-tissue cases require histopathologic evaluation; however, consideration of the imaging features remains important for assessing lesion imaging and pathologic correlation.

This case of NSM highlights some important imaging features reflected in the histopathology of these lesions. First, the background T2 signal of these lesions are very bright, in keeping with the myxoid components (extracellular mucin). Lesions with myxoid components sharing this bright T2 MRI signal characteristic include benign lesions such as myxomas and peripheral nerve sheath tumors [21-27], but also include malignant lesions such as myxoid liposarcomas and chondrosarcomas, among others. Similar to NSMs, benign myxomatous lesions show more homogeneous T2 bright myxoid signal whereas malignant myxomatous lesions tend to have more heterogeneous components and are likely to show features related to their cell of origin [28].

Bright T2 myxoid-like signal shown in the present case report is consistent with MRI features described in prior NSM case

Figure 6. Axial T2 magnetic resonance images of a nerve sheath myxoma of the ankle 6 (A) and 12 months (B) after resection, demonstrating gradual resolution of signal abnormality. (A) Axial T2 fat saturation MR image 6 months after resection with bright surface vitamin E marker shows subtle non-masslike increased T2 signal representative of post-excision granulation tissue (arrow). (B) Axial T2 fat saturation MR image performed 12 months after resection with bright surface vitamin E marker shows no resection bed signal abnormality.
**Table 1.** Table of case reports of nerve sheath myxomas with descriptions of magnetic resonance imaging characteristics. Features listed include T1 and T2 signal characteristics, enhancement, as well as other noteworthy features.

| Case Report | T1 | T2 | Enhancement | Other Characteristics |
|-------------|----|----|-------------|-----------------------|
| This case report (ankle) | Isointense to muscle | Bright | Present | Internal septations |
| O’Rourke et al [18] (forearm) | Isointense | Bright | Present | Heterogeneous enhancement |
| Vij et al [19] (CPA angle) | Hypointense | Bright | Present | Extension into internal auditory meatus |
| Malkoc et al [29] (paravertebral space) | Mildly hyperintense | Moderately hyperintense | Present | Lesion heterogeneity; Post-gadolinium figure shows probable septations |
| Khashaba et al [30] (hand) | Hypointense | Hypointense | Not reported | Lesion heterogeneity; STIR figure shows probable septations |
| Bulduk et al [31] (middle cranial fossa) | Hypointense | Bright and intermediate portions | Present | Solid and cystic components |
| Sanchez-Orgaz et al [32] (orbit) | Hypointense | Bright | None on CT | Conjunctival congestion |

reports in the upper extremities, orbital, and intracranial locations (Table 1) [18,19,30-32]. Myxoid components with high water content also promote ultrasound features of hypoechogeticity and posterior acoustic enhancement. This case report is the only known case report in the literature to show NSM ultrasound figures. A recent case report in the hand reported ultrasound features of a lobulated, circumscribed, and hyper-echoic mass but did not publish the images [30].

The current authors believe that internal dark signal septae shown in this case report are an important feature which could be characteristic of NSMs, and this finding should be evaluated in future NSM studies. Internal septae are most evident on T2-weighted and post-contrast sequences. On ultrasound, septae may be isoechoic on a hypoechoic lesion background, as in this case report. Internal septae seen at imaging correlate with the fibrous septae seen on NSM histopathology. Including this case report, dark signal septations were present in 3 of 7 NSMs case reports with MR imaging (Table 1). Older case reports might have not been able to demonstrate internal septations as current MRI techniques allow for better tissue contrast and spatial resolution. Understanding the imaging characteristics of soft-tissue lesions of the ankle and foot are important considering MRI plays an important role in the management of these tumors when greater than 2 cm. A thorough physical exam and imaging features help differentiate between determinate and indeterminate lesions, which subsequently guides biopsy and surgical excision [33].

**Conclusions**

A case of benign nerve sheath myxoma in the back of the left ankle of a 36-year-old man was presented. This report has shown the importance of imaging of peripheral soft-tissue masses, including ultrasound and MRI, which can identify localized and benign features and the solid, cystic, and myxoid areas, which were characteristic in this case of benign nerve sheath myxoma. Nerve sheath myxomas are a rare soft-tissue mass most often encountered in the dermis of the upper extremities or to a lesser extent in the lower extremities. Specimen staining with S100 positivity can differentiate these tumors from previously associated neurothekeomas. This case report describes a rare case in the ankle, with discussion of infrequently reported ultrasound and MRI features that correlate to histopathological findings in these tumors. When a dermal-based, solid mass is encountered with imaging showing bright T2 myxoid signal and internal septae, nerve sheath myxoma should be considered in the differential list of possibilities.

**Disclaimer**

The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its components.
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