

# Multilobulated tumor located on the ankle: a diagnostic dilemma

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## INTRODUCTION

Nerve sheath myxoma (NSM) is a rare, benign tumor originating from perineural Schwann cells. It typically presents as a slow-growing, asymptomatic dermal or subcutaneous nodule or plaque, most commonly affecting the fingers and the infrapatellar pretibial region. Early diagnosis and complete surgical excision are essential to prevent recurrence. This report highlights novel dermoscopic features and underscores the critical role of immunohistochemistry in differentiating NSM from neurothekeoma (NTM).

## CLINICAL PRESENTATION

A 23-year-old woman presented with a three-year history of an asymptomatic, slowly growing mass over her right ankle. Physical examination revealed a solitary, firm, non-tender, multilobulated, freely mobile, exophytic growth measuring  $1.8 \times 1.6 \times 1.2$  cm with a smooth surface, located 3 cm posterior to the medial malleolus of the right ankle (Figure 1).

## What is your diagnosis?

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**Figure 1.** Multilobulated exophytic growth with a smooth surface located posterior to the medial malleolus of the right ankle.



## Diagnosis

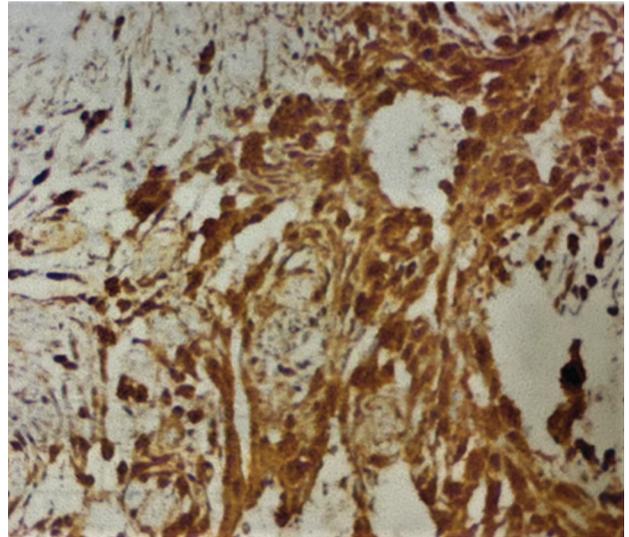
Nerve sheath myxoma

## Microscopic findings

Excisional biopsy revealed an unencapsulated, multilobulated tumor with irregular myxoid nodules separated by fibrous bands. The cells were spindle-shaped with elongated, wavy nuclei and scant eosinophilic cytoplasm. A few stellate cells and congested blood vessels were also observed (Figures 2a and 2b). Immunohistochemical staining showed strong positivity for S100 (Figure 3) and glial fibrillary acidic protein (GFAP), while epithelial membrane antigen (EMA) was negative.

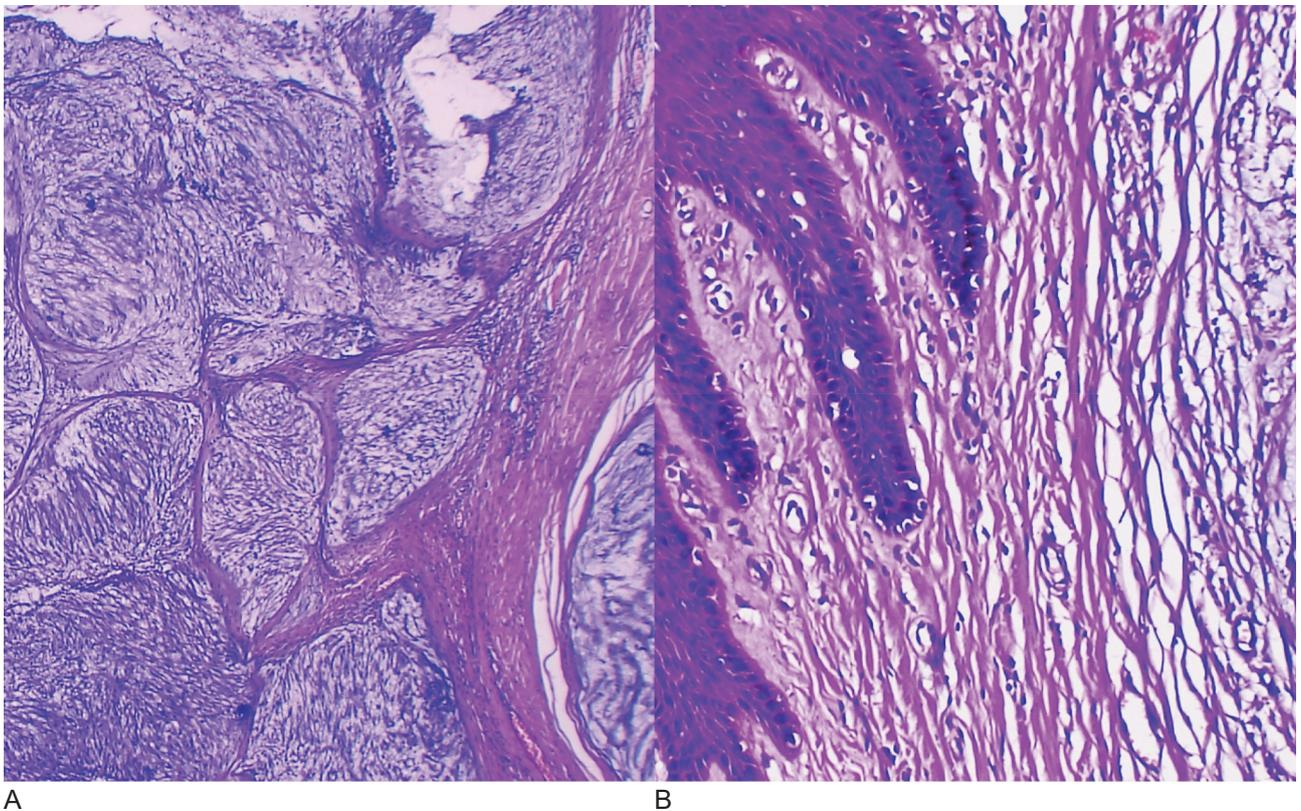
## DISCUSSION

NSM is a rare benign tumor originating from the perineural Schwann cells of peripheral nerves. It was initially described by Harkin and Reed as a micronodular, myxoid, and loosely cellular benign tumor of neural origin. NSM is more common in females in their fourth decade of life<sup>1</sup>. The youngest reported case involved a 4-month-old



**Figure 3.** Immunohistochemistry showing strong positivity for the S100 marker.

girl<sup>2</sup>. Typically, NSM presents as a longstanding, gradually enlarging, asymptomatic dermal and/or subcutaneous nodule or plaque, measuring up to 3 cm in diameter. The extremities—particularly the fingers and the infrapatellar pretibial region—are



**Figure 2.** (A) Multilobulated tumor with irregular myxoid nodules separated by fibrous bands. (B) A few stellate cells (black circle) are visible.

the most frequently affected sites. Rarely, the head and neck region or the trunk may be involved <sup>1,3</sup>.

Classical histopathology reveals a well-defined multinodular tumor composed of myxoid nodules separated by fibrous septae. The nodules contain stellate-shaped, ring-shaped, and epithelioid Schwann cells arranged in cords or grouped into syncytial-like aggregates. The histopathological differential diagnosis includes NTM, superficial angiomyxoma, myxoid schwannoma, myxoid neurofibroma, soft tissue chondroma, perineuroma, myxoid liposarcoma, and myxofibrosarcoma <sup>3,4</sup>. These features predict immunoreactivity for S-100 protein and GFAP, with limited activity for EMA and neuron-specific enolase (NSE) <sup>3</sup>. Stellate-shaped Schwann cells within a myxoid stroma are the hallmark of NSM. Ring-shaped Schwann cells contribute to its distinctive architectural pattern, while epithelioid Schwann cells, characterized by their rounded, epithelial-like morphology, are diagnostically significant in

distinguishing NSM from other neoplasms.

Immunohistochemistry plays a crucial role in diagnosing NSM. S-100 protein is a sensitive marker for Schwann cells and melanocytes, showing strong positivity in NSM and confirming its neural crest origin. GFAP highlights glial differentiation, further supporting the presence of Schwannian components. NSE, a marker of neuronal and neuroendocrine differentiation, also aids in identifying Schwannian lineage. In contrast, EMA is typically negative in NSM but positive in perineuroma, making it an important marker for distinguishing between these two entities.

Previously, NSM was considered a myxoid variant of NTM. However, recent reports suggest that NSM is a distinct entity, unrelated to NTM <sup>4</sup>. The differentiating features between NSM and NTM are summarized in Table 1.

Non-invasive diagnostic methods, such as MRI, reveal the presence of a well-defined, lobulated

**Table 1.** Differentiating features between Nerve sheath myxoma and neurothekeoma

Factors	Nerve sheath myxoma	Neurothekeoma
Origin	Neural	Fibrohistiocytic
Age	Fourth decade	Young adults
Sex	Female	Female
Morphology	Solitary/multilobulated	Solitary
Site	Extremities	Head, neck, and upper body
Onset	Gradual	Gradual
Dermoscopy	Greyish background with yellow septae Cobblestone areas Hairpin vessels Pigment network Pale red area Linear vessels Focal area of white scales and adjacent yellow sero-crusts Numerous linear brown streaks	Pink ovoid areas with whitish halo and yellowish background Homogenous pinkish-white background White areas on a dull pink background Irregular linear and arborizing vessels
Cytology	Stellate and epithelioid cells in clusters, groups or whorls Bland nuclei Metachromatic myxoid background	Mesenchymal proliferation with moderate cellularity Abundant metachromatic myxoid matrix Fusiform and epithelioid cells in groups or whorls Bi- or multinucleated cells with hyperchromatic nuclei
HPE	Multilobulated Excess myxoid matrix Fibrous septae Stellate/spindles cells in clusters Cells with elongated nuclei	Single lobule Relatively less myxoid matrix Thick collagen bands Spindle cells in a whorled pattern Cells with round nuclei
Immunohistochemistry (IHC)	S100 strongly positive GFAP, NSE, and EMA may be positive	S100, GFAP, and EMA negative NSE may be positive
MRI	Well-defined lobulated mass septations + No infiltration	Smooth bordered ovoid mass Homogenous density Minimal septations + No infiltration
Recurrence	47%	Uncommon

soft-tissue mass with multiple thin septae and no underlying infiltration<sup>3</sup>. This tumor requires complete resection with clear margins. Recurrence has been reported in approximately 47% of cases, according to a study conducted by Fetsch *et al.*<sup>4</sup>. In our patient, no recurrence was observed after six months of follow-up.

#### **Informed consent**

The authors certify that they have obtained the patient's consent for her images and other clinical information to be published in the journal. The patient understands that her name and initials will not be published, and reasonable efforts will be made to protect her identity; however, complete anonymity cannot be guaranteed.

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None.

#### **Authors' contributions**

AS and VP were involved in patient evaluation,

data collection, literature review, and manuscript preparation, while **KK** supervised the work, critically revised the manuscript, and approved the final version.

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None.

**Conflict of interest:** None declared.

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