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Neurothekeoma located in the hallux and axilla: Two case reports

Wan-Ying Huang, Yi-Qi Zhang, Xiang-Hong Yang

Abstract

BACKGROUND
Neurothekeomas (NTKs) are rare benign soft tissue tumours that typically occur in the head, trunk, and upper limbs and are rare in other parts of the body.

CASE SUMMARY
Herein, we present two rare cases in which primary NTKs were located in the hallux and axilla. A 47-year-old woman complained of a verrucous bulge on the plantar side of the left hallux. The surface skin of the tumour was abraded due to poor wound healing. A 6-year-old boy complained of a gradually growing subcutaneous mass in the axilla. The tumours of both patients were completely resected, and the diagnosis of NTK was confirmed by histopathology. At the one-year follow-up, both patients had a good prognosis without local recurrence.

CONCLUSION
To date, NTKs located in the hallux and axilla have rarely been reported in the literature. We describe NTKs that occurred in unconventional areas and summarize the challenges in their diagnosis and differential diagnosis.

Key Words: Neurothekeoma; Hallux; Armpit; Histopathological examination; Immunohistochemical staining; Case report

Core Tip: In these patients, the lack of specificity of clinical symptoms and imaging examination findings as well as the unusual location of neurothekeomas increased the difficulty in diagnosis and treatment. Histopathological examination and immunohistochemical staining may help confirm the diagnosis, but there are still many challenges...
INTRODUCTION

Neurothekeomas (NTKs) are rare, benign, superficial soft tissue tumours that typically present as solitary nodules with a predilection for the head, neck, and upper limbs of females[1,2]. Due to the low prevalence and undefined clinical symptoms of NTKs, it is difficult to accurately distinguish them from other skin tumours. NTKs rarely occur in the lower limbs or axillae and have been reported only once in the areas of the toes and axillae[3,4]. In this report, we describe two different types of NTKs arising in the hallux of a 47-year-old female and the axilla of a 6-year-old boy. Both patients underwent surgical resection, and the final diagnosis was confirmed through histopathological examination.

CASE PRESENTATION

Chief complaints
Case 1: A 47-year-old woman complained of a painless, verrucous bulge on the plantar side of the left hallux for 3 years.
Case 2: A 6-year-old boy visited our hospital and complained of a gradually increasing subcutaneous mass in the axilla for 2 years.

History of present illness
Case 1: The verrucous mass appeared on the plantar side of the left hallux three years previously, and the surface skin of the tumour was abraded due to poor wound healing. Inflammatory granulation tissue formation was observed in the wound. The patient intermittently adhered to conservative treatment, but her condition was not relieved.
Case 2: The subcutaneous mass was found in the axilla two years previously, and the colour of the mass was the same as that of the normal skin. The mass was only 1 cm in diameter when it was first discovered but gradually grew to 2 cm within two years.

History of past illness
Case 1: The patient was diagnosed with tuberculous pleurisy 20 years previously and was cured, and she underwent uterine fibroid surgery 1 year previously.
Case 2: The patient did not complain of any prior specific symptoms.

Personal and family history
Cases 1 and 2: Both patients denied any history of smoking, drinking, or drug abuse. Underlying systemic disease and family genetic history were denied.

Physical examination
Case 1: The patient's general condition was stable with normal vital signs (body temperature 36.8 °C, blood pressure 140/80 mmHg, pulse 110 bpm). A red solid mass with a diameter of 0.8 cm was found on the plantar side of the left hallux with a tough texture, normal skin temperature, and good dorsal artery pulsation.
Case 2: The patient's general condition was stable with normal vital signs (body temperature 36.7 °C, blood pressure 95/65 mmHg, pulse 103 bpm). A subcutaneous mass with a diameter of 2 cm was observed in the left armpit with good mobility, normal surface skin colour and temperature, and mild palpable pain. The superficial
lymph nodes were not enlarged.

**Laboratory examinations**

**Case 1:** Laboratory tests revealed signs of inflammation in the urinary system, and the percentage of neutrophils (73.9%) in blood and white blood cell (99.6/μL) and bacterial (1014.5/μL) counts in urine were slightly elevated.

**Case 2:** No obvious abnormality was noted in the laboratory examination results.

**Imaging examinations**

**Case 1:** An ultrasound from the local hospital showed a solid nodule on the plantar side of the left hallux with abundant blood supply.

**Case 2:** An ultrasound from the local hospital showed a round, well-demarcated soft tissue mass in the left armpit with no significant alterations in the surrounding tissue.

**Histopathological examination**

**Case 1:** In general, the red, solid, verrucous mass was approximately 0.8 cm in diameter and had a tough texture (Figure 1A). Histopathological examination of the specimen showed that the tumour tissue was in the form of multiple small nodules or clusters. The nodules, which were composed of oval and spindle tumour cells, were abundant in some areas and sparse in other areas. In the cellular area, oval cells were relatively uniform in size with a rich and eosinophilic cytoplasm, a visible nucleolus, and a mild to moderate degree of mitotic activity. In the intermediate area, spindle cells were arranged in bundles and exhibited a benign morphology. Myxoid matrix could be observed in the nodules or interstitium (approximately 40%) (Figure 1B-D). Immunohistochemical examination revealed positive staining for CD10, CD99, transcription factor binding to IGHM enhancer-3 (TFE3) and CD163, indicating NTK (Figure 1E-H). Negative staining for S-100, cytokeratin (CK), epithelial membrane antigen, smooth muscle actin (SMA), desmin, Stat6, anaplastic lymphoma kinase (ALK), and neuron-specific enolase (NSE) can be helpful in differential diagnosis, as this profile distinguishes NTKs from other soft tissue tumours such as dermal nerve sheath myxomas (DNSMs), smooth muscle cell-derived tumours, solitary fibrous tumours, epithelioid fibrous histiocytomas (EFHs), and neuroblastomas (Figure 1I-N). CD34 staining suggested vascular hyperplasia, and the Ki-67 proliferation index was approximately 20% (Figure 1O and P).

**Case 2:** Histopathological examination of the specimen showed that the tumour tissue was composed of multiple small nodules, and the nodules were separated by hyalinized collagen fibres (Figure 2A). The nodules were composed mainly of uniformly sized eosinophilic oval cells, in which nucleoli and mitosis were observed. A small number of multinucleated giant cells infiltrated the nodules, and no myxoid matrix was observed in the interstitium (Figure 2B and C). Immunohistochemical examination revealed positive staining for CD10, CD68, TFE3, p63 and vimentin (Figure 2D-H) and negative staining for S-100, CK, SMA, glial fibrillary acidic protein (GFAP) and CD1a (Figure 2I-M). The Ki-67 proliferation index was approximately 15% (Figure 2N).

**FINAL DIAGNOSIS**

**Case 1**
NTK, mixed subtype (left hallux).

**Case 2**
Cellular NTK (left axilla).

**TREATMENT**

**Case 1**
Surgical treatment was performed with local infiltration anaesthesia. The 0.8-cm tumour was located in the superficial layer of the flexor tendon and had an incomplete capsule. The tumour was completely resected and submitted for pathological
Figure 1 Macropathological and histological analyses of the tumour tissue in case 1. A: Macroscopic image of the verrucous bulge; B-D: Haematoxylin and eosin staining showing the tumour cells (× 200); E-H: Positive immunohistochemical staining for CD10, CD99, transcription factor binding to IGHM enhancer-3 and CD163 (× 200); I-N: Negative immunohistochemical staining for S-100, cytokeratin, EMA, smooth muscle actin, Desmin, Stat6, ALK and NSE (× 200); O and P: Immunohistochemical staining for CD34 and Ki-67 (× 200).

Case 2
Surgical treatment was performed with local infiltration anaesthesia. The solid, well-defined, 2-cm tumour was located in the subcutaneous soft tissue of the armpit and seemed to lack a defined capsule. After complete removal of the tumour and complete haemostasis, the incision was sutured.

OUTCOME AND FOLLOW-UP
At the 12-mo follow-up, both patients had maintained a favourable postoperative clinical evolution without local pain or motion limitation. The surgical incisions had healed well, and neither patient showed signs of recurrence or metastasis.
Huang WY et al. Neurothekeoma in the hallux and axilla

**DISCUSSION**

NTKs are rare, benign soft tissue tumours that were first described by Gallager and Helwig in 1980[5]. NTKs were initially considered to be neurogenic tumours originating from Schwann cells, and NTKs were diagnosed and reported for many years as one of the subtypes of dermal nerve sheath myxomas[6]. Recently, studies have shown that, unlike DNSMs, NTKs do not express the S-100 protein[7]. Further analysis of gene expression profiles shows that DNSMs are similar to schwannomas, while NTKs show evidence of myofibroblastic differentiation and possible relation to dermatofibromas[8]. Therefore, NTK was classified as an independent disease for diagnosis. NTKs clinically manifest primarily as painless, slow-growing subcutaneous nodules with good mobility. Clinical diagnosis of these rare neoplasms is challenging because NTKs are not distinctive in physical examinations and imaging examinations. NTK is often mistaken for a sebaceous cyst, a Spitz naevus, a fibrous histiocytoma, a basal cell carcinoma, or a skin adnexal tumour (mainly pilomatricoma)[9,10], and an accurate diagnosis depends on histopathological and immunohistochemical examination.

Histopathologically, NTK is a poorly circumscribed nodule typically composed of fascicles of spindle-shaped and epithelioid tumour cells with a sparse or no mucinous matrix[10]. Epithelioid cells, which present as oval or polygonal eosinophilic cells, are

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**Figure 2** Histological analysis of the tumour tissue in case 2. A-C: Haematoxylin and eosin staining showing the tumour cells (× 200); D-H: Positive immunohistochemical staining for CD10, CD68, transcription factor binding to IGHM enhancer-3, p63 and vimentin (× 200); I-M: Negative immunohistochemical staining for S-100, cytokeratin, smooth muscle actin, glial fibrillary acidic protein and CD1a (× 200); N: Immunohistochemical staining for Ki-67 (× 200).
Table 1 Main points in the differential diagnosis between neurothekeomas and several other diseases

<table>
<thead>
<tr>
<th></th>
<th>NTK</th>
<th>DNSM</th>
<th>PFH</th>
<th>EFH</th>
<th>Spitz nevus</th>
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</thead>
<tbody>
<tr>
<td>Average age</td>
<td>Adult/teenager</td>
<td>Adult</td>
<td>Teenager</td>
<td>Adult/teenager</td>
<td>Teenager/adult under 35</td>
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<tr>
<td>Sex</td>
<td>Female</td>
<td>Both</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
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<tr>
<td>Predilection site</td>
<td>Head/upper limbs/trunk</td>
<td>Finger/lower limbs</td>
<td>Upper limbs/trunk</td>
<td>Lower limbs</td>
<td>Face/head/lower limbs</td>
</tr>
<tr>
<td>Tumour boundary</td>
<td>Blurred</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
<td>Clear</td>
</tr>
<tr>
<td>Arrangement of tumour cells</td>
<td>Lobular/nodular/clump/whirlpool like</td>
<td>Lobular/nodular</td>
<td>Nodular/clump</td>
<td>Mosaic or whirlpool-like</td>
<td>Nested</td>
</tr>
<tr>
<td>Tumour cell morphology</td>
<td>Round/oval/spindle</td>
<td>Round/oval/spindle</td>
<td>Round/oval/spindle</td>
<td>Round/oval</td>
<td>Polygon/spindle</td>
</tr>
<tr>
<td>Atypia of tumour cells</td>
<td>Mild-moderate</td>
<td>Rare</td>
<td>Rare</td>
<td>Rare</td>
<td>Rare</td>
</tr>
<tr>
<td>Mitosis of nucleus</td>
<td>0-25/WHPF</td>
<td>-</td>
<td>Rare</td>
<td>Rare</td>
<td>Rare</td>
</tr>
<tr>
<td>Immunohistochemical phenotype</td>
<td>CD10(+); CD63(+); mitf(+)</td>
<td>S-100(+); GFAP (+); SOX10 (+)</td>
<td>S-100 (+); vimentin (+); lysozyme (+)</td>
<td>ALK (+); TFE3 (+); S-100 (+)</td>
<td>S-100 (+); HMB-45 (+)</td>
</tr>
</tbody>
</table>

WHPF: Wide high-power field eyepiece 22 mm, sp 40x objective; NTK: Neurothekeoma; DNSM: Dermal nerve sheath myxoma; PFH: Plexiform fibrous histiocytoma; EFH: Epithelioid fibrous histiocytoma; GFAP: Glial fibrillary acidic protein.

CONCLUSION

Herein, we report two rare NTKs; both were completely resected after clinical evaluation, and an accurate diagnosis was obtained after the histopathological and immunohistochemical examination. In addition, we provide a summary of the differential diagnosis and the possible diagnostic pitfalls. The diagnostic and therapeutic experience reported here can be used as a reference for other surgeons and pathologists.

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