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Neurothekeoma located in the hallux and axilla: Two case reports

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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

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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

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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/ μ L) and bacterial (1014.5/ μ L) 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).

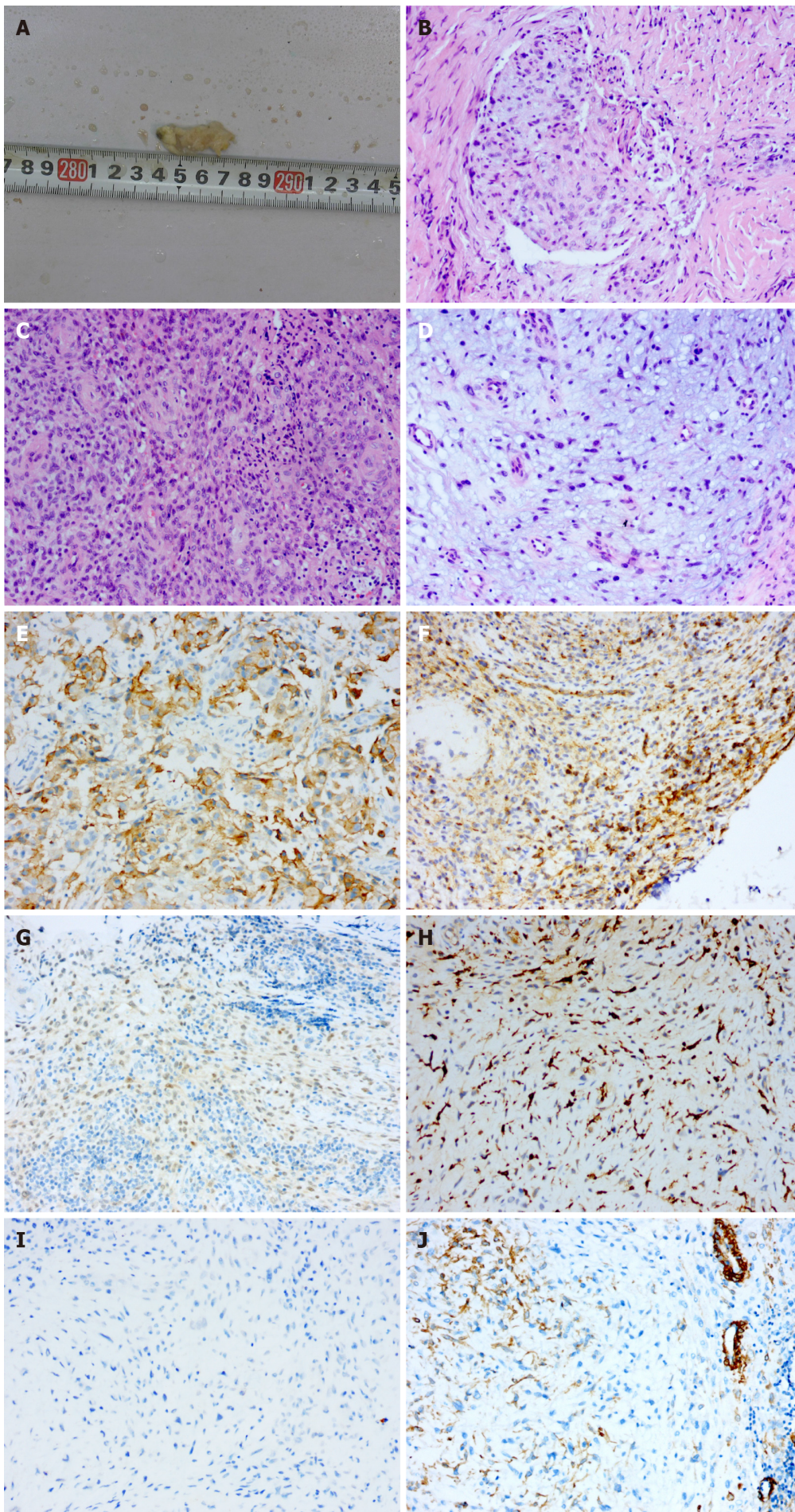
Case 2

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



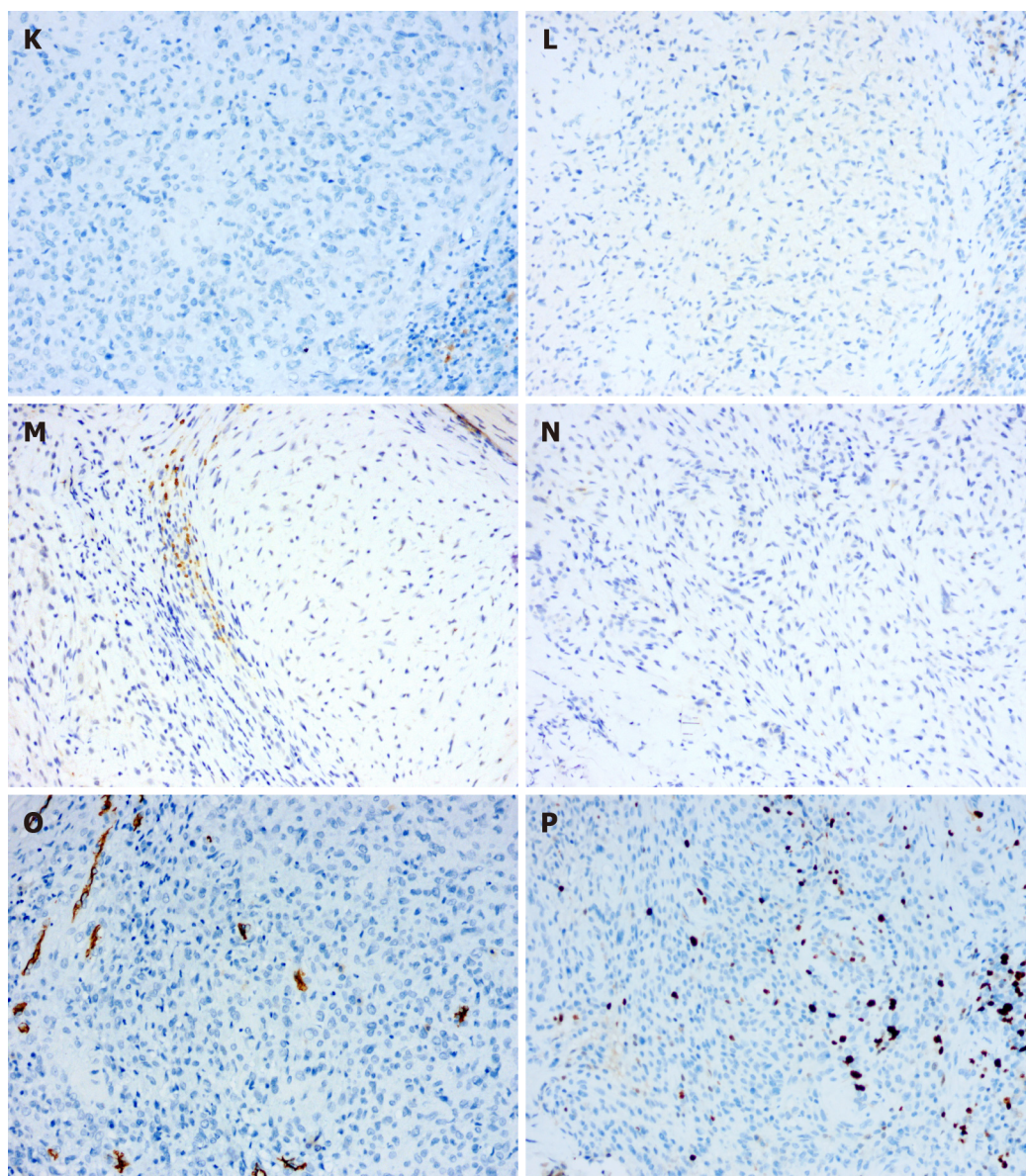


Figure 1 Macropathological and histological analyses of the tumour tissue in case 1. A: Macroscopic image of the verrucous bulge; B-D: Haematoxylin and eosin staining showing the tumour cells ($\times 200$); E-H: Positive immunohistochemical staining for CD10, CD99, transcription factor binding to IGHM enhancer-3 and CD163 ($\times 200$); I-N: Negative immunohistochemical staining for S-100, cytokeratin, EMA, smooth muscle actin, Desmin, Stat6, ALK and NSE ($\times 200$); O and P: Immunohistochemical staining for CD34 and Ki-67 ($\times 200$).

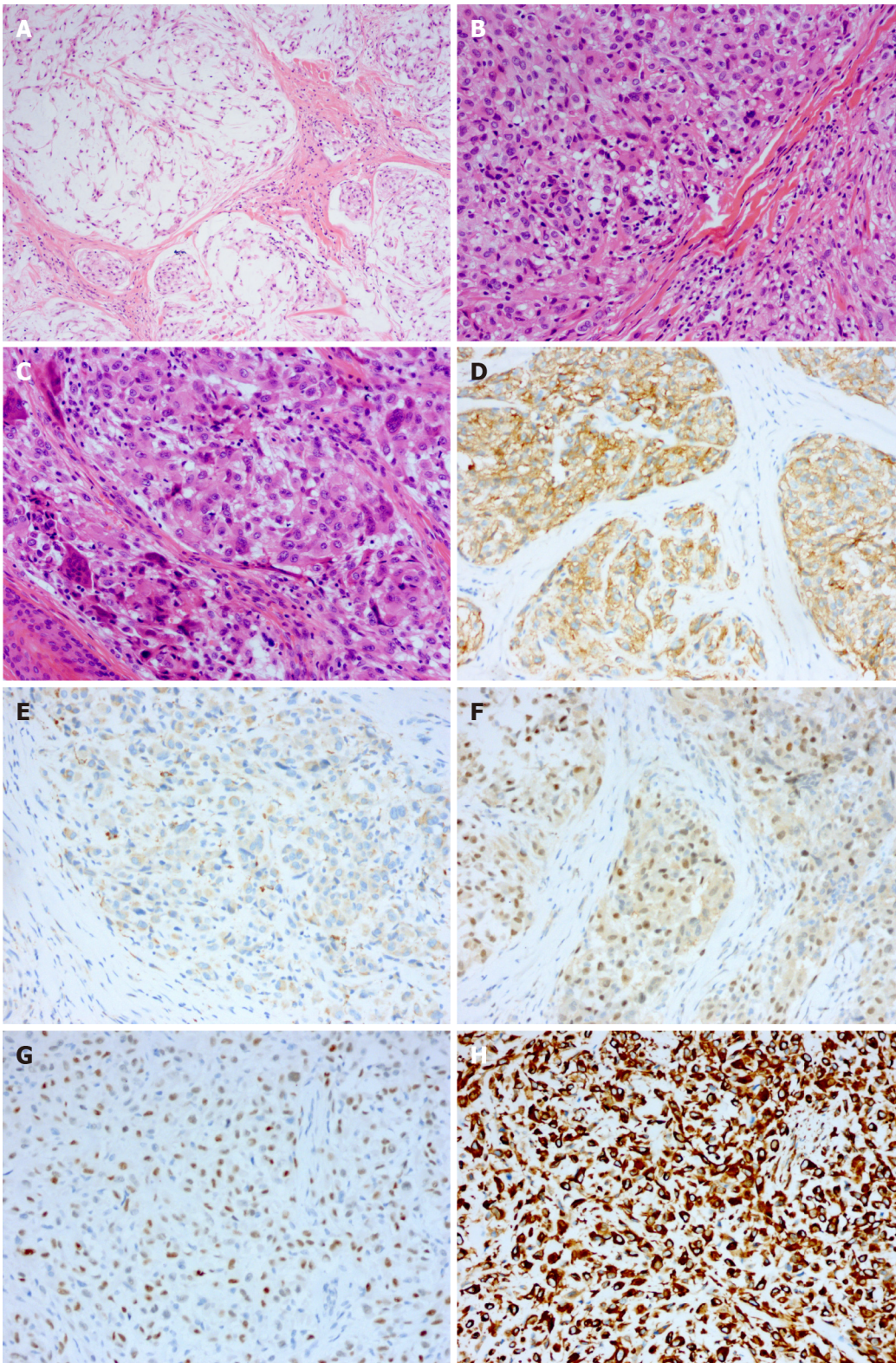
examination.

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.



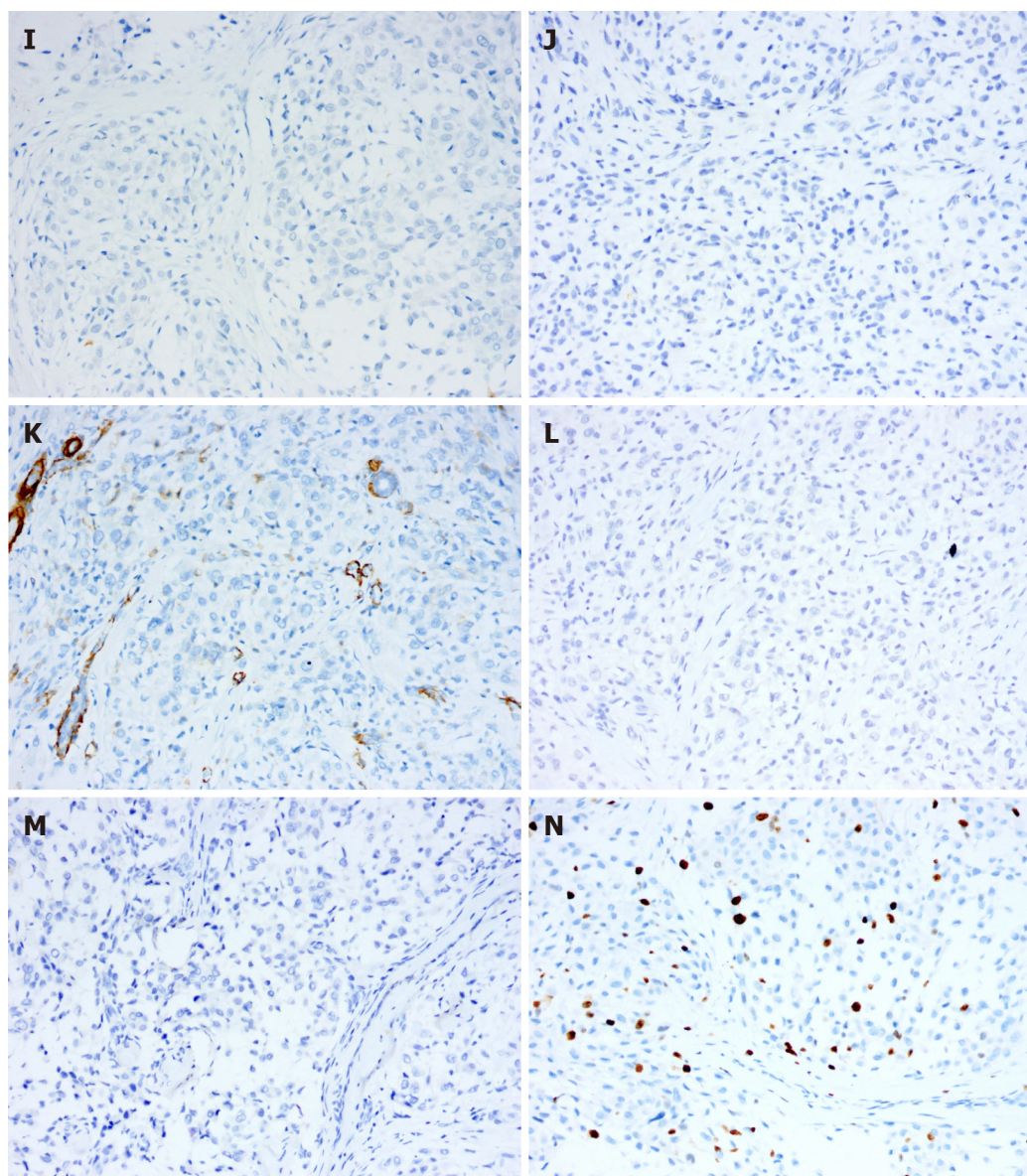


Figure 2 Histological analysis of the tumour tissue in case 2. A-C: Haematoxylin and eosin staining showing the tumour cells ($\times 200$); D-H: Positive immunohistochemical staining for CD10, CD68, transcription factor binding to IGDM enhancer-3, p63 and vimentin ($\times 200$); I-M: Negative immunohistochemical staining for S-100, cytokeratin, smooth muscle actin, glial fibrillary acidic protein and CD1a ($\times 200$); N: Immunohistochemical staining for Ki-67 ($\times 200$).

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

Table 1 Main points in the differential diagnosis between neurothekeomas and several other diseases

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

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.

rich in the cytoplasm and arranged in a nodular or plexiform pattern; spindle-shaped cells are arranged in bunches or swirls and have a benign morphology. The stroma is composed of hyalinized collagen fibres often accompanied by mucoid degeneration. Depending on the amount of myxoid matrix, NTKs have been subclassified into three types: myxoid (myxoid matrix > 50%), mixed (10% < myxoid matrix ≤ 50%) and cellular (myxoid matrix < 10%). The myxoid matrix can occasionally superficially infiltrate skin or muscle tissue. The nuclei can show mild to moderate atypia, and approximately 0-25 mitotic nuclei per high power field can be observed.

Immunohistochemical examination demonstrates that tumour cells express CD10, CD63 (NKI/C3), and mitf. Most tumours also express CD99. A few tumours express SMA and are negative for S-100, cytokeratin, Melan-A, and SOX-10 staining[11,12], indicating that NTKs are associated with scattered histiocytes.

Accurate diagnosis of NTKs is essential given that these lesions can be mistaken for malignancies, leading to unnecessary treatment. The differential diagnosis includes mainly various types of cysts, DNSMs, plexiform fibrous histiocytomas (PFHs), EFHs, Spitz nevi, *etc.* The clinical manifestations of these diseases are similar, but the pathological characteristics are different: subcutaneous cysts contain keratinized or necrotic material without tumour cells; DNSMs express S-100, GFAP and SOX10, as assessed by immunohistochemistry[13]; PFHs have spindle-shaped fibroblasts around the nodular-arranged tumour cells[14]; EFH tumour cells are mostly diffusely arranged and do not express CD63[15]; and Spitz nevi are composed of epithelioid or spindle-shaped pigment cells and express S-100[16]. The differential diagnosis of these diseases is shown in Table 1.

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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