

Neurothekeoma in childhood: a benign tumor mimicking malignant disease

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Neurothekeoma (NT) sometimes extends to subcutaneous adipose tissue, skeletal muscle or epidermis, and thus may imitate some malignant situations.

A 17-year-old female patient was admitted to another medical center with a swelling at her waistline. Plexiform fibrous histiocytoma was diagnosed, and she was referred to our clinic. Total re-excision was performed. The new pathology report indicated features of atypical NT.

A case of atypical NT, which can be misdiagnosed as a malignant mesenchymal tumor, is discussed in this paper.

Key words: child, neurothekeoma, skin neoplasms.

Neurothekeoma (NT) is a very rare, benign tumor of uncertain origin, although it might be considered to arise from a peripheral nerve sheath¹. It was first described as a nerve sheath myxoma by Harkin and Reed¹, but different names have been used since then, such as pacinian neurofibroma, cutaneous lobular neurofibroma and perineural neurofibroma. Recently, this tumor was referred to as NT by Gallager and Helwig². NTs are more common in females and younger patients and generally are seen on the upper limbs, head, and neck². NTs are commonly dermal, but mucosal and submucosal lesions have been described³.

A case of atypical NT, which can be misdiagnosed as a malignant mesenchymal tumor, is discussed in this paper.

Case Report

A 17-year-old female patient was evaluated for a swelling along her waistline that had been present for almost a year, and which had exhibited growth recently; the mass was excised at another center. Plexiform fibrous histiocytoma was diagnosed after histopathological examination of the material, and the patient was referred to our clinic. The patient's physical examination was normal, except for the incision scar at her waistline. There was no pathological finding in laboratory

values or superficial tissue ultrasound. The first pathological examination from the excision material was not suitable for a definite diagnosis, so total excision was planned. Re-excision of the tumor tissue, with a longest diameter of 2 cm, was done, and the material was sent to the Department of Pathology. Macroscopically, the tumoral lesion was grayish-white, with ill-defined margins, on cut sections, measuring 1.6 cm in diameter. On microscopic examination, under low magnification, a dermal tumoral lesion typically having a compartmental micronodular pattern (distinctive multinodular pattern) separated by dense hyaline collagen was observed. The tumor was composed of nests and bundles of variably epithelioid to spindled cells with pale eosinophilic cytoplasm. Pleomorphic cells were present in the tumor tissue, and tumor cells were invading the fatty tissue. The tumor cells were stained with vimentin, CD10, CD68, and smooth muscle actin (SMA); however, they were not stained with S100, glial fibrillary acidic protein (GFAP), CD34, desmin, or CD117. In addition, foreign body reaction, chronic inflammation and fibrosis were observed. The final pathological diagnosis was atypical NT (Figs. 1, 2).

Our patient did not require any extra treatment and remains healthy at this time.

Discussion

Neurothekeoma (NT) is an unusual benign tumor involving the dermis, and is composed of distinct lobules of bland spindle cells separated by fibrous connective tissue with a plentiful myxoid matrix. By immunohistochemistry, protein S100⁴, epithelial membrane antigen (EMA), vimentin, and neuron specific enolase (NSE)⁵ have been found positive. Myelin basic protein, neurofilaments, GFAP, keratin, Leu-7⁶, NK1/C3, and PGP9.5 can also be utilized as useful markers. Our patient is a young adult female, as described in the literature. Tumor cells were stained with vimentin, CD10, CD68, and SMA; however, they were not stained with S100, GFAP, CD34, desmin, or CD117.

The origin of the tumor is unknown. SMA positivity is similar to the epithelioid variant of leiomyoma or myofibroblastic proliferations⁷. GFAP positivity is rare; however, its positivity supports a peripheral nerve sheath origin⁸. Immunoreactivity for NSE and S100 in the myxoid type support Schwann cell origin, but the lack of S100 protein and positive EMA in the cellular type suggest perineural cell lineage⁹.

The immunohistochemical findings and light microscopic features are variable, although there are three subtypes of NT recognized according to the tumor cellularity, growth pattern, amount of stromal mucin, and S100 positivity¹⁰: Myxoid (classic) type (MNT), cellular type (CNT), and mixed type.

Myxoid (classic, MNT) type has been reported in middle-aged adults and is predominant in females. It is most commonly located on the head, neck and upper extremities¹¹. Classic NTs are considered as a variant of nerve sheath tumors, such as neurofibromas. The MNT is characterized by extremely myxomatous changes and less cellularity with well-circumscribed spindle cells in myxoid matrix and multinucleated giant cells; they stain positively for S100, collagen type IV and nerve growth factor receptor and are negative for EMA or markers of histiocytic differentiation¹².

The cellular type (CNT) has been observed in younger adults, more commonly in females, and on the head and neck¹⁰. CNTs have been suggested to be related to plexiform fibrohistiocytic tumors (PFHT) because of the similarities in morphologic and phenotypic

features. PFHT is a more aggressive type because of its localization on the trunk and inferior limbs and its higher capacity for infiltration of the subcutaneous fatty tissue¹³.

Cellular type cells are epithelioid with ample eosinophilic cytoplasm and large “bubbly nuclei” and prominent nucleoli. Atypia and mitotic features are more common in this type. Myxoid material is usually insufficient and present only around the individual burrows¹⁰. CNTs do not stain S100, collagen type IV, or nerve growth factor receptor, but reactivity with NK1C3 (CD57) and the panmonocyte marker Ki-M1p is positive¹².

The cellular type is a benign tumor, but because of hypercellularity, the presence of nuclear atypia, and its extension into fat or skeletal muscle, CNT may be mistaken for a malignant tumor, such as a sarcoma. These atypical forms of CNT have not shown an aggressive behavior¹⁴. Atypical NT has been described as resembling either benign or malignant melanocytic growths such as malignant melanoma, Spitz nevus, and cellular blue nevus, but melanoma is S100-positive, and CNTs do not stain with antibody to S100 protein¹⁵.

Our patient’s lesion was in the waist area, which has not been reported in the literature previously, and the histopathological report

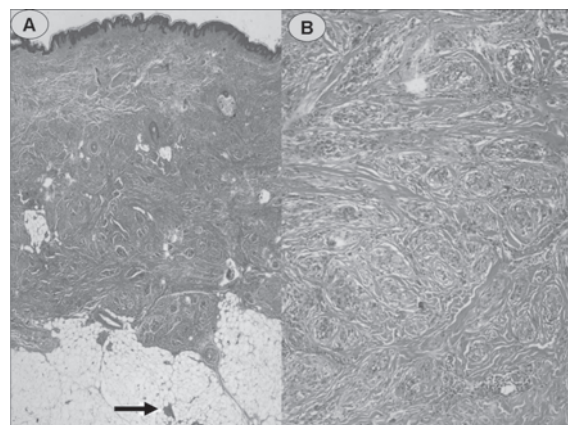


Fig. 1.

A. Tumor tissue showing dermal involvement by a partly lobulated, partly plexiform appearance and infiltration into underlying subcutaneous fat (arrow) (hematoxylin-eosin, original magnification, X20).

B. Bundles and nests of tumor cells infiltrate between dermal collagen bundles (hematoxylin-eosin, original magnification, X100).

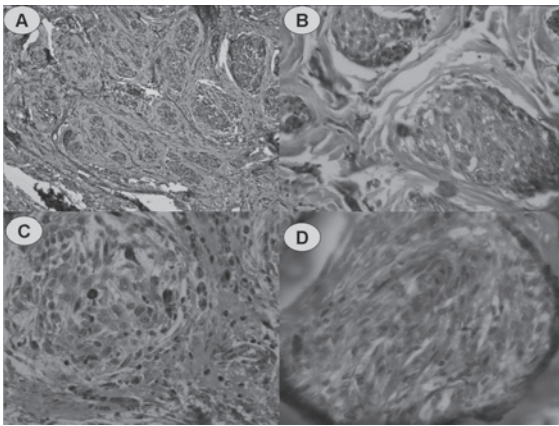


Fig. 2.

- A. Tumor cells showing diffuse staining (vimentin, original magnification, X100).
 B. Tumor cells showing cytoplasmic positivity for SMA (SMA, original magnification, X400).
 C. Focal staining in some tumor cells (CD68, original magnification, X400).
 D. Tumor cells showing cytoplasmic positivity for CD10 (CD10, original magnification, X400).

of the tumor tissue was misdiagnosed as a PFHT in the medical center at which our patient was first examined. The tumor cells were stained with vimentin, CD10, CD68, and SMA; however, they were not stained with S100, GFAP, CD34, desmin, or CD117 after re-excision. Invasion of the lesion was also present in fatty tissue. Therefore, the tumor was accepted as an atypical NT by our Pathology Department.

Mixed type NT shows the properties of both types¹⁶. The immunohistochemical features of these cases are confusing because of an irregular or lack of reactivity to S100 and SMA¹⁴.

Neurothekeomas (NTs) are slow-growing lesions³. They are often solitary, and are either asymptomatic or may present as painful, puffy, skin-colored, well-circumscribed, and less than 3 cm in diameter nodules. The complaint of our patient was also painless swelling, and her tumor exhibited a slow growth pattern over time; she had been admitted with a complaint of swelling.

The diagnosis of tumors is achieved with histopathological evaluation of the tissue sample. The differential diagnosis of dermal nodule in childhood includes fibrous, histiocytic, lymphocytic, melanocytic, and neural tumors¹⁷.

Treatment of NT is total excision. Total excision

is almost invariably curative, but the tumor showed recurrence in some cases¹⁸. This recurrence was thought to be secondary to incomplete excision of the primary tumor¹⁹. We performed re-excision in our patient due to the absence of clear information about the surgical margins in the first intervention, and we followed the patient without additional treatment after detection of clean surgical margins. In our patient, no recurrence has been observed over the nearly one-year follow-up. There is no standard value for the resection margins of this tumor, although a few millimeters from a grossly detectable margin may be sufficient. However, due to the varying features of atypical NTs, a punch biopsy to confirm this atypia may be useful before reconstruction. If atypical or aggressive features are found in the histological analysis, waiting for permanent margins may be useful²⁰. Our patient did not require any extra treatment and remains healthy at this time.

In conclusion, a case of atypical NT, which can be misdiagnosed as a malignant mesenchymal tumor because of atypical mitosis, atypical cells and invasion to the muscle or fatty tissue, has been discussed herein in light of the relevant literature.

REFERENCES

- Harkin JC, Reed RJ. Nerve sheath myxoma: tumors of the peripheral nervous system. In: Rosai J (ed). Atlas of Tumor Pathology (2nd ed) Vol. 3. Washington, DC: Armed Forces Institute of Pathology; 1969: 60-64.
- Gallager RL, Helwig EB. Neurothekeoma: a benign cutaneous tumor of neural origin. *Am J Clin Pathol* 1980; 74: 759-764.
- Bhaskar AR, Kanvinde R. Neurothekeoma of the hand. *J Hand Surg Br* 1999; 24: 631-633.
- Husain S, Silvers D, Halperin A, McNutt NS. Histologic spectrum of neurothekeoma and the value of immunoperoxidase staining for s-100 protein in distinguishing it from melanoma. *Am J Dermatopathol* 1994; 16: 496-503.
- Aronson P. Unmasking myelin proteins in neurothekeoma. *Letter* 1992; 26: 659.
- You TT, Kaiser PK, Netland TP, Jakobiec FA. Neurothekeoma palpebrae: a rare nerve sheath tumor arising in the eyelid. *Ophthal Plast Reconstr Surg* 1999; 15: 448-449.
- Calonje E, Wilson-Jones E, Smith NP, Fletcher CD. Cellular 'neurothekeoma': an epithelioid variant of pilar leiomyoma. Morphological and immunohistochemical analysis of a series. *Histopathology* 1992; 20: 397-404.

8. Katsourakis M, Kapranos N, Papanicolaou SI, Patrikiou A. Nerve-sheath myxoma (neurothekeoma) of the oral cavity: a case report and review of the literature. *J Oral Maxillofac Surg* 1996; 54: 904-906.
9. Schortinghuis J, Hille JJ, Singh S. Intraoral myxoid nerve sheath tumour. *Oral Dis* 2001; 7: 196-199.
10. Argenyi ZB, LeBoit PE, Cruz DS, Swanson PE, Kutzner H. Nerve sheath myxoma (neurothekeoma) of the skin: light microscopic and immunohistochemical reappraisal of the cellular variant. *J Cutan Pathol* 1993; 20: 294-303.
11. Angervall L, Kindblom LG, Haglid K. Dermal nerve sheath myxoma. A light and electron microscopic, histochemical and immunohistochemical study. *Cancer* 1984; 53: 1752-1759.
12. Rudolph P, Schubert C. Myxoid cellular neurothekeoma. *Am J Dermatopathol* 2002; 24: 92-93.
13. Leclerc-Mercier S, Brousse N, Fraitag S. Is plexiform fibro-histiocytic tumor a deep form of cellular neurothekeoma? *J Cutan Pathol* 2009; 36: 1123-1125.
14. Hornick JL, Fletcher CD. Cellular neurothekeoma: detailed characterization in a series of 133 cases. *Am J Surg Pathol* 2007; 31: 329-340.
15. Barnhill RL, Mihm MC. Cellular neurothekeoma. A distinctive variant of neurothekeoma mimicking nevomelanocytic tumors. *Am J Surg Pathol* 1990; 14: 113-120.
16. Yang YW, Shih IH, Huang YH, Kuo TT, Hong HS. Mixed-type neurothekeoma presenting with an unusual clinical appearance of multiple satellite lesions on the back. *Dermatol Surg* 2005; 31: 720-722.
17. Hurwitz S. *Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence*. Philadelphia: Saunders; 1993: 198-241.
18. Busam KJ, Mentzel T, Colpaert C, Barnhill RL, Fletcher CD. Atypical or worrisome features in cellular neurothekeoma: a study of 10 cases. *Am J Surg Pathol* 1998; 22: 1067-1072.
19. Papadopoulos EJ, Cohen PR, Hebert AA. Neurothekeoma: report of case in an infant with a review of literature. *J Am Acad Dermatol* 2004; 50: 129-134.
20. Koumanis DJ, Glickman LT. Facial neurothekeoma in a 10-year-old child. *Can J Plast Surg* 2007; 15: 175-177.