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Neurothekeoma: a pediatric case report and literature review

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Dear Editor,

Neurothekeoma is a rare, benign, soft tissue tumor that primarily affects the dermis. Initially described as a variant of nerve sheath myxoma, it was later recognized as a distinct entity because of its histopathological and immunohistochemical differences, as it is thought to be derived from fibroblast.[1] It is most commonly observed in children and young adults, is more frequent in females, and typically arises in the head, neck, and upper extremities.[1,2]

Clinically, neurothekeomas present as slow-growing, painless, solitary dermal nodules ranging in color from flesh-toned to reddish. Their size varies between 0.3 and 2 cm, although larger lesions have been reported.[2,3]

Histologically, neurothekeomas are composed of nests and lobules of epithelioid or spindle-shaped cells with eosinophilic cytoplasm and are embedded in a variable fibromyxoid stroma. Some cases of neurothekeoma have atypical histological features, such as increased mitotic rate (*i.e.*, 4 mitosis/25 high power field [HPF]), infiltrative growth, and nuclear pleomorphism.[3] Based on cellularity and the presence of myxoid material, they are classified into myxoid, mixed, and cellular subtypes.[1-4] While myxoid neurothekeomas resemble nerve sheath myxomas and can express S-100 protein, the cellular neurothekeoma (CN) is characterized by high cellularity, a collagenous rather than myxoid stroma, and a distinct immunohistochemical profile; moreover, it has the ability to differentiate into myofibroblasts and to recruit histiocytes.[1,5]

Immunohistochemical analysis is essential for distinguishing neurothekeomas from melanocytic and neural tumors. CN typically expresses CD10, microphthalmia transcription factor (MiTF), smooth muscle actin (SMA), vimentin, and neuron-specific enolase (NSE) but is negative for melanocytic markers such as S-100, HMB45, and MART-1/MelanA.[2,3,5,6]

This feature is crucial for differentiating CN from desmoplastic melanomas and other melanocytic spitzoid lesions. Clinical and histological differential diagnoses include Spitz nevus and melanoma, which express melanocytic markers; peripheral nerve sheath tumors, typically S-100 positive; plexiform fibrohistiocytic tumors, which exhibit a biphasic appearance and plexiform growth; and cutaneous leiomyoma, which is desmin-positive with intersecting fascicular growth.[7]

Neurothekeomas are benign tumors with low recurrence rates when completely excised. While no formal guidelines exist for surgical margins, excision with clearance of a few millimeters is generally recommended; in cases with atypia, wider surgical margins may be warranted. Surgical excision remains the treatment of choice, with a favorable prognosis in the vast majority of cases.[2] Although rare, neurothekeomas should be considered in the differential diagnosis of dermal nodules, particularly in young patients.

Herein, we report a case of a 10-year-old girl presenting with a slowly growing dermal nodule, emphasizing the role of dermoscopy, histopathology, and immunohistochemistry in achieving a definitive diagnosis.

A 10-year-old girl presented with a 2-year history of an asymptomatic, growing lesion over the last 2 months on her back. Physical examination revealed a pinkish-reddish nodule on the right back, with a diameter of 1 cm (Figure 1A). The patient had no significant past medical history. Contact non-polarized dermoscopic examination revealed a non-specific homogeneous pattern (Figure 1B). Contact polarized dermoscopic examination showed polymorphic vessels in the central portion of the lesion, along with whitish areas on an erythematous structureless background (Figure 1C). The dermoscopic features observed in our case, including polymorphous vessels and white structureless areas on a reddish background, are consistent with the few previously reported cases of CN dermoscopy.[8,9] Nonetheless, recognizing these features can prompt clinicians to consider CN within the differential diagnosis, especially compared to Spitz nevi, which typically present dotted vessels regularly distributed across the lesion, or dermal nevi, which usually exhibit a more uniform appearance without significant vascular structures. Thus, although limited, dermoscopy can still provide valuable diagnostic clues that highlight the need for timely histopathological confirmation.

Histopathology (Figure 2) showed a nodular dermal infiltrative proliferation, extending focally into the hypodermis, composed of nests of predominantly epithelioid cells, occasionally spindle-shaped, with vesicular nuclei, small nucleoli, and eosinophilic cytoplasm, interspersed within a dense collagenous stroma and a mild lymphocytic inflammatory infiltrate. Mild to moderate atypia and occasional mitotic figures (0-1 mitosis/10 HPF) without evidence of higher-grade cytonuclear atypia were observed. No perineural invasion was identified. Immunohistochemically, CD10, MiTF, NSE, vimentin, and SMA were expressed. Conversely, the lesion was negative for MART-1, HMB45, p16, PRAME, S100, SOX10, BAP1, P80, BRAF V600E, CD117, CD25, CD34, PR, epithelial membrane antigen (EMA), and glial fibrillary acidic protein (GFAP). Based on the immunophenotypic profile and morphological features, a diagnosis of cellular neurothekeoma was made. The lesion was removed with 3 mm of surgical margins, and after one year of follow-up, no local recurrence was observed.

Our case is consistent with previously reported CNs, which typically present as slow-growing, painless nodules in young females. As described by Fetsch *et al.* and Hornick *et al.*, most cases show mild atypia and low mitotic activity, while only a minority exhibit prominent pleomorphism or elevated mitoses.[2,3] Consistently, our case showed mild atypia and rare mitoses, supporting its benign nature.

In conclusion, neurothekeoma represents a rare benign neoplasm of the skin, predominantly affecting pediatric and young adult patients. Despite its indolent clinical behavior, its presentation is often

nonspecific, and a definitive diagnosis relies on histopathological and immunohistochemical evaluation. The cellular variant may raise diagnostic challenges due to its dermal localization, variable morphology, and lack of expression of classic melanocytic or neural markers. However, its immunohistochemical profile – characterized by CD10, MiTF, and NSE positivity but negativity for S100 and GFAP – allows a reliable differentiation from melanoma, nerve sheath tumors, and other spindle cell neoplasms. This distinct immunohistochemical signature, together with the absence of aggressive features and the excellent prognosis after complete excision, supports the notion that cellular neurothekeoma, despite its histologic peculiarity, is a tumor with an excellent clinical outcome. This case contributes to the literature by highlighting the dermoscopic approach to a pediatric CN and emphasizes the diagnostic clarity provided by immunohistochemical profiling, underscoring its utility particularly in young patients presenting with ambiguous dermal nodules.

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Figure 1. A) Pinkish-reddish nodule on the back; **B)** contact non-polarized dermoscopy of the lesion; **C)** contact polarized dermoscopy of the lesion.

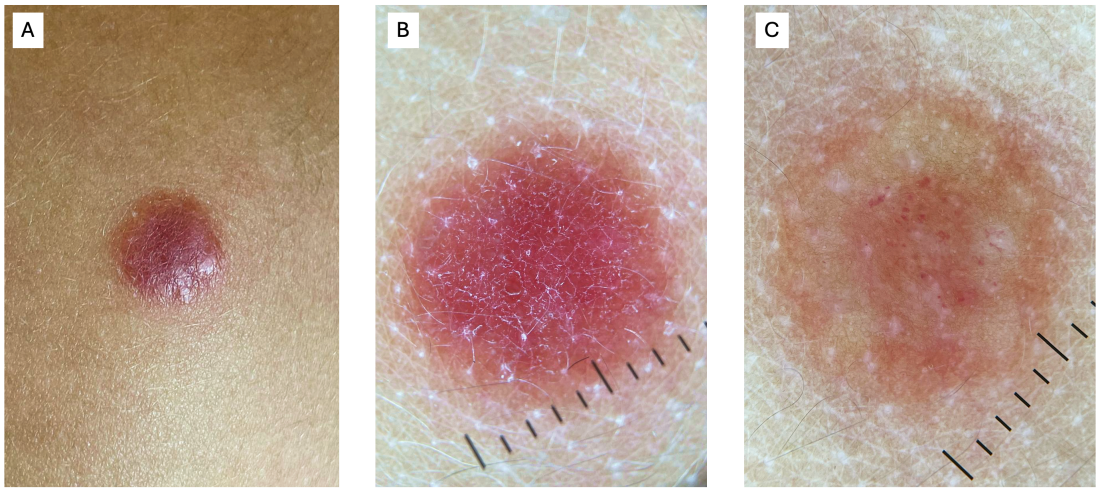

Figure 2. A) Nodular infiltrative proliferation in dermis, interspersed within a dense collagenous stroma and a mild lymphocytic inflammatory infiltrate; **B, C)** nests of epithelioid cells, with vesicular nuclei, small nucleoli, and eosinophilic cytoplasm, with mild to moderate atypia and occasional mitotic figures (0-1 mitosis per 10 HPF); **D)** immunohistochemical expression for CD10.