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Case Letter

Cellular neurothekeoma ☆,☆☆,★

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What is known about this subject in regard to women and their families?

- Cellular neurothekeoma is a rare, benign neoplasm with a female preponderance.

What is new from this article as messages for women and their families?

- Cellular neurothekeoma can mimic both benign and malignant neoplasms; thus, an accurate diagnosis and awareness of the condition is important to optimize care.

Dear Editor,

Cellular neurothekeoma (CNT) is a rare, benign, dermal neoplasm that most commonly occurs on the head and neck during the first 2 decades of life. Historically, CNTs were considered nerve sheath myxomas (NSMs), but they have since been shown to exhibit distinct histologic and immunophenotypic features and likely represent a separate entity with fibrohistiocytic lineage rather than nerve or nerve sheath cellular differentiation, despite the persistence of the probably erroneous neurothekeoma terminology in the current literature. We present a case of CNT in a young girl, with discussion of the diagnosis, treatment, and prognosis.

A 12-year-old girl presented with a painless, slowly growing, cutaneous plaque on her right knee, which had been present for 3 months. She denied preceding trauma to the affected site and was generally well and developing normally. She had applied a moderate-strength topical corticosteroid for 2 weeks without effect. On examination, she had a firm, nontender, violaceous plaque on the right anterior knee (Fig. 1A). There were no other cutaneous lesions evident. The patient was referred to a dermatologist, who performed a punch biopsy. This showed a poorly circumscribed, dermal, lobulated mass composed of whorled epithelioid cells set within a myxoid matrix without significant stromal desmoplasia. Epidermis and subcutis were not involved (Fig. 1B). The tumor cells were predominantly mononuclear and showed only mild variation in nuclear size and shape. These had a uniform open nuclear chromatin pattern, small but frequently multiple nucleoli, and moderately abundant pale cytoplasm with indistinct cell membranes. Mitotic figures numbered up to five per square millimeter. Occasional interspersed osteoclast-like multinucleate giant cells were also present (Fig. 2A). Immunostaining was positive for CD10, neuron-specific enolase, NKI-C3 (clone CD63; Fig. 2B) and focally for factor XIIIa, but negative for S100 protein, HMB45, smooth muscle actin, and the neuroendocrine markers chromogranin and synaptophysin. A diagnosis of CNT was made based on the combination of morphologic and immunohistochemical features, and excision was undertaken with 2-mm clinical margins. The postoperative course was uneventful.

CNT is a rare, benign, dermal tumor of postulated fibrohistiocytic differentiation, rather than nerve sheath lineage as origi-

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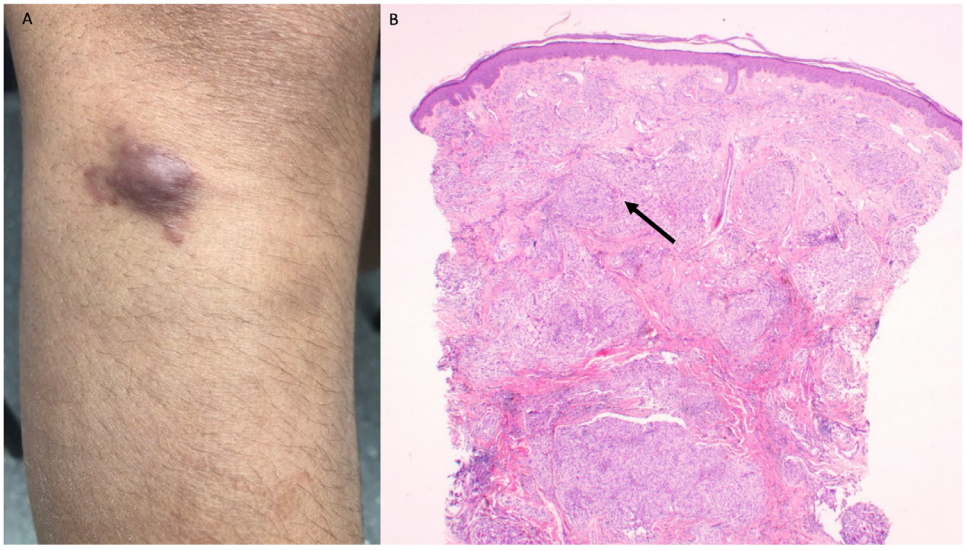

Fig. 1. (A) Clinical presentation: an ill-defined violaceous nodule with peripheral palpable extensions inferior to the right anterior knee. (B) Lobulated dermal neoplasm; arrow corresponds to area of high power cellular detail in Figure 2 (hematoxylin and eosin stain; original magnification × 20).

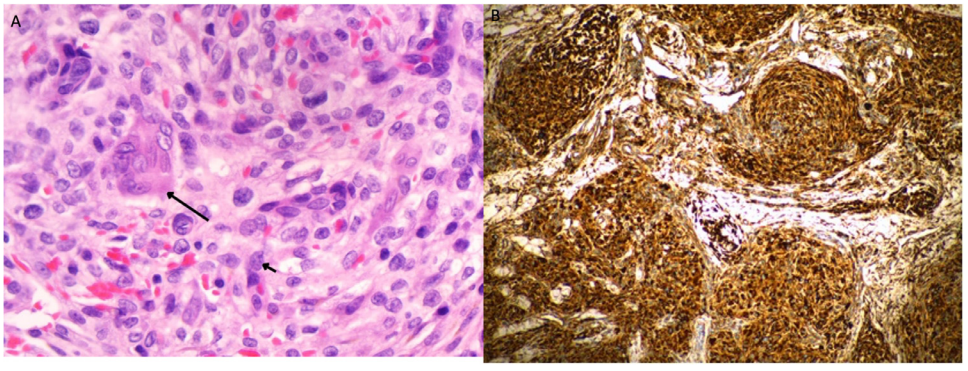

Fig. 2. (A) Tumor cell detail. Dominant mononuclear population has fine, open chromatin pattern with small but frequently multiple nucleoli (short arrow), with interspersed multinucleate giant cells (long arrow; hematoxylin and eosin stain; original magnification × 400). (B) Immunohistochemical staining for NKI-C3 demonstrating positive staining, supporting the diagnosis of cellular neurothekeoma.

nally proposed based on the presence of myxoid stroma (Fetsch et al., 2007). It usually presents as a solitary, painless, slow-growing, pink-tan to reddish-brown papule or nodule, predominantly on the head and neck or upper trunk. It is most commonly seen in children and young adults, with a female predominance (Fetsch et al., 2007).

CNTs are lobulated, micronodular, or occasionally plexiform, composed of nests of epithelioid to spindled cells with pale cytoplasm, surrounded by a variably collagenous or myxoid matrix. Mild nuclear pleomorphism is common, and the mean mitotic rate is two per square millimeter. Osteoclast-like giant cells occur in approximately 40% of cases (Fetsch et al., 2007).

Consistent with continuing uncertainty as to its cellular lineage, CNT lacks any entirely specific immunophenotype. However, it almost always stains positively with NKI-C3 (clone CD63) and CD10 and negatively for epithelial membrane antigen. S-100 protein and Melan-A are not expressed, unlike melanocytic lesions that also enter into diagnostic consideration (Fetsch et al., 2007). Positive immunohistochemical staining for protein gene product 9.5 is common but often eschewed for lack of specificity. S100 calcium-binding protein A6 is often positive. Factor XIIIa may be focally positive (Fetsch et al., 2007). Microphthalmia-associated transcription factor may be positive, but in one study more than two-thirds of cases tested negative for this antigen (Stratton and Billings, 2014). Diagnosis therefore relies on a combined assessment of morphologic and immunohistochemical features.

The most challenging differential diagnoses are with NSM and plexiform fibrohistiocytic tumor (PFT). NSM is typically seen in older individuals and on the distal extremities. It has generally more pronounced myxoid stroma and stains positively with S-100 protein (Fetsch et al., 2007; Laskin et al., 2000). PFT also favors the extremities and is usually situated deeper in the dermis and subcutis. However, like CNT, PFT typically affects children, displays a biphasic population of mononuclear histiocytoid cells and osteoclast-like giant cells, and has a very closely overlapping immunohistochemical profile. These two lesions may therefore be closely related (Fetsch et al., 2007; Stratton and Billings, 2014).

Treatment of CNT is by surgical excision, with a 1- to 2-mm clinical margin generally considered adequate. Local recurrence of up to 15% has been reported; however, it is rare in the setting of complete excision (Hornick and Fletcher, 2007). Atypical features, such as size >2 cm, pleomorphism, and high mitotic rate (>20 mitoses per wide high power field), do not affect the rate of local recurrence (Hornick and Fletcher, 2007; Stratton and Billings, 2014). There has been a single reported case of locoregional metastasis (Zenner et al., 2019).

In conclusion, because CNT can mimic several benign and malignant tumors, both clinically and histologically, it is important for dermatologists and pathologists to be aware of this tumor to make

an accurate and timely diagnosis and institute appropriate treatment.

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Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

Conflicts of interest

Mr John Frew has conducted advisory work for Janssen, Boehringer-Ingelheim, Pfizer, Kyowa Kirin, LEO Pharms, Regeneron, and UCB; participated in trials for UCB, Pfizer, and Eli Lilly; and received research support from Ortho Dermatologics.

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