Dermatology Reports

Atypical cellular neurothekeoma: report of a case

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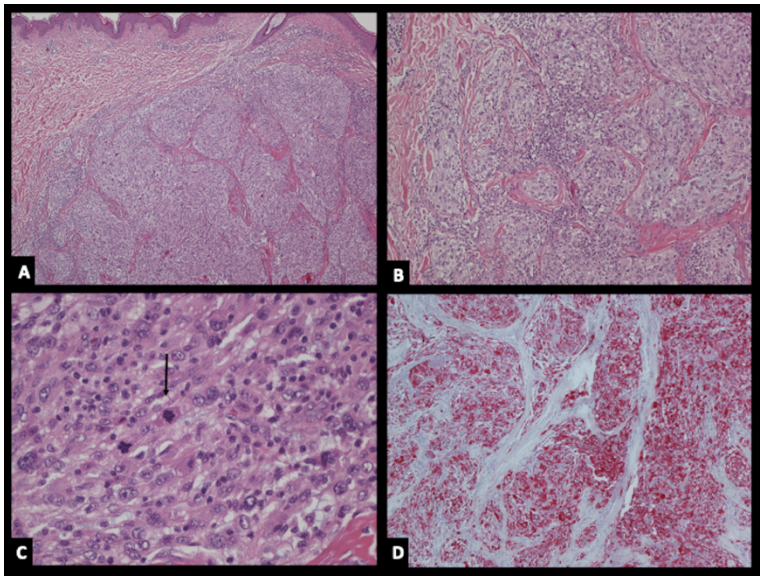
TO THE EDITOR

Cellular neurothekeomas (CNTs) are extremely rare soft-tissue neoplasms first described in 1980. Initially thought to arise from nerve sheats, CNT is now universally recognized as deriving from fibroblast-like cells (1). CNTs often present as skin-colored papules or nodules with no specific dermoscopic features. Classical CNT typically involves head, neck or trunk of young adults, with a slight female predominance (1, 2).

The diagnosis is particularly challenging because of the rarity and the non-specific clinical appearance of this entity. Histopathological evaluation is mandatory and remains the gold standard.

Recently, a 15-year-old boy referred to our center for a 2-year history of a slowly growing nodule on the volar surface of left forearm, suspicious for pilomatricoma. The lesion was slightly tender and no previous trauma was reported. Ultrasound of the nodule showed a solid nodular formation with regular margins. Histologically, cells with pleomorphic nuclei and epithelioid or spindle shape were present in the dermis, focally extending into the subcutaneous tissue (Figure 1). Multinucleated cells and atypical mitotic figures were also present. Immunophenotyping revealed diffuse positivity for NKI/C3, with focal expression of CD68, SMA, MITF, D2-40 and NSE. Staining for S100, desmin, HMB-45 and CAM5.2 was negative. The lesion was also characterized by significant cytoproliferative activity (Mib-1 15%). These findings were consistent with the diagnosis of atypical CNT (ACNT). A 4-year-old boy came to our clinic few weeks later for the presence of a nodule of the left calf. As in the previous case, it was misdiagnosed as pilomatricoma and surgically excised. Pathology findings were comparable to the ones described above and also suggested a diagnosis of ACNT.



Possible differential diagnoses of CNTs include pilomatricoma, fibrohistiocytic tumors, neurofibromas, and melanocytic lesions (1,3). Immunohistochemistry is mandatory for the diagnosis of CNT, since specific surface molecules (NKI/C3, NSE, CD10) are generally present on neoplastic cells (3), while the expression of nerve sheath markers such as S100 protein are constantly lacking.

The presence of atypical histologic features in the context of CNTs is not uncommon and can pose a great diagnostic challenge. Possible atypical findings include infiltrative growth, cytologic atypia, marked proliferative activity, vascular or perineural invasion, myxoid stroma, fascicular and plexiform growth patterns (3). In markedly atypical cases, immunostaining is not sufficient for differentiating CNT from atypical fibroxanthoma or undifferentiated pleomorphic sarcoma, since those entities can be positive for NKI/C3 and CD10, giving reason of the great difficulties encountered by pathologists in the diagnostic process (3). ACNT was first described by Busam et al. as a distinct variant of CNT with uncertain clinical behavior (4). To date, no metastases or malignant transformation have been reported. However, recurrent ACNT have been described in literature, but recurrences were associated to incomplete surgical resection of the lesion nearly in all cases, with present data suggesting that complete surgical excision of these lesions should be curative (2,3). Unfortunately, only short-term follow-up data are available in literature (1-5 years) (2).

Interestingly, we report two cases of described ACNTs occurring in children, localized on the extremities, therefore being characterized by uncommon clinical and demographic data for such

diagnosis. It is important to bear in mind that CNTs are benign neoplasms, even in the presence of atypical features (3,5). Complete surgical resection represents the treatment of choice and, despite the absence of official guidelines, few-millimeter excision margins are considered safe in most cases (5). However, ACNTs can represent a diagnostic pitfall, and research for new markers is needed to avoid the risks of both over- and under-treatment. Further data on patient follow-up should also be collected, considering the lack of consensus and the paucity of evidence-based findings in this scenario.

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FIGURE LEGENDS

Figure 1. Pathology specimens showing a non-capsulated neoplastic proliferation with medium-large size cells with both nodular and plexiform growth patterns and clear edges, mainly located in the dermis (A: H&E 40x; B: H&E 100x). Nuclear pleomorphism and atypical mitotic figures (red arrow) were also present (C: H&E 200x). Immunoreactivity for NKI-C3 (panel D).