CASE REPORT

Atypical cellular neurothekeoma: A lamb in wolf’s clothing*

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Key words: CD10; cellular neurothekeoma; fibrohistiocytic; neurothekeoma; NKI-C3 (CD63).

INTRODUCTION

Cellular neurothekeoma (CN) is a benign neoplasm of uncertain histogenesis, but is most often described as a fibrohistiocytic tumor. Subject to misdiagnosis, atypical CN (ACN) is an uncommon variant of an uncommon neoplasm, and so is unfamiliar to many clinicians and pathologists. We present an ACN that had worrisome cytologic features but ultimately had a favorable prognosis.

CASE REPORT

A 24-year-old woman complained of a dorsal forearm lesion, present for a year and slowly enlarging. The dermatologist noted an 8 mm, pink to violaceous, very tender nodule and performed a punch biopsy through its center (Fig 1).

Tissue sections revealed a hypercellular, infiltrative, epithelioid neoplasm involving the entire dermis, with epidermal sparing. At medium power, a nested or fascicular pattern could be appreciated, with cellular aggregates surrounded by thin layers of connective tissue (Fig 2).

Many neoplastic cells showed severe cytologic atypia and pleomorphism (Fig 2, B). There were 2 mitotic figures per 10 high power field, with several atypical mitoses (Fig 3, A). Immunohistochemical stains showed diffuse positive staining for CD63 (NKI/C3; Fig 3, B), MITF (Fig 4, A), NSE, CD68, CD163, and ERG (Fig 3).

Atypical cells were negative for S100, SOX-10, Melan-A, SMA, EMA, AE1/3, CK 8-18, CK 5/6, p63, CD34, and desmin (Fig 4). We did not find evidence of neural or vascular invasion; this was confirmed by examination of S100 and CD34 immunohistochemical stains. The combination of clinical features, nested/fascicular architecture, and distinctive immunohistochemical staining pattern established a diagnosis of ACN. Our patient was treated with conservative resection to ensure complete removal.

DISCUSSION

Neurothekeomas, also known as CN, are uncommon neoplasms, but Fetsch et al.1 were able to study 178 lesions affecting 176 individuals. They found a female:male ratio of 112:64, and patients were primarily young adults. 24% of their patients were younger than 11 years old and only 20% were older than 29 years of age. Thus the condition primarily affects young adults who are 20-30 years old; 75% of the CN involved the head, upper extremities, and shoulder girdle. All cases studied had spindled and epithelioid mononuclear neoplastic cells with copious cytoplasm and indistinct cell borders. There was a strong tendency for the neoplastic cells to show a whorled growth pattern and often focal fascicular growth.1

Dr A. Bernard Ackerman wrote that “differentiation of malignant from benign neoplasms by conventional microscopy is accomplished best by noting features that concern their architectural pattern…rather than

Abbreviations used:
ACN: atypical cellular neurothekeoma
CN: cellular neurothekeoma
HPF: high power field

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their nuclear details.\textsuperscript{2} The ACN is an excellent example of this concept, and a nested or fascicular pattern of neoplastic cells when viewed at low power is an important clue for establishing the correct diagnosis. However, our case showed a nested/fascicular growth pattern in combination with MITF\textsuperscript{1} staining, which might suggest the possibility of malignant melanoma. Additionally, the distal extremity location in a young patient, severe cytologic atypia with marked pleomorphism, and a fascicular growth pattern is consistent with epithelioid sarcoma. Therefore, several immunohistochemical stains may be required to establish a confident diagnosis of ACN. Depending on cellular and stromal morphology, the microscopic differential diagnosis might also include dermal nerve sheath myxoma, schwannoma, neurofibroma, Spitz nevus, pilar leiomyoma, fibrous histiocytoma, plexiform fibrohistiocytic tumor, and clear cell sarcoma.\textsuperscript{3} Despite its name, CN dependably lacks expression of many nerve sheath markers such as S100 protein.\textsuperscript{4-6} CN is positive for NKI-C3 (CD63) and
CD10 in almost all cases. In most cases, and there is variable staining for CD68, smooth muscle actin, and PGP9.5, all markers which are not sufficiently specific to be of much assistance.

CN becomes "atypical" when one or more of the following features is present: large size (up to 6 cm), deep penetration extending into skeletal muscle and/or subcutaneous tissue, diffusely infiltrative borders, high mitotic activity (greater than 3 mitotic figures per 10 high power fields), marked cytologic pleomorphism, and signs of vascular invasion. In our patient, atypical features include severe cytologic atypia with marked pleomorphism and several atypical mitoses. When reviewing 37 cases of ACN, Stratton and Billings found severe cytologic atypia in only 3 cases, and only 1 case had atypical mitotic figures. Therefore, our case is quite unusual in terms of cytologic features, but fortunately is typical in terms of architectural pattern.

CNs seldom recurs and does not metastasize, even those with atypical features. Recurrences have been attributed to incomplete removal, and so complete surgical excision is the recommended treatment.

**Conflicts of interest**
None disclosed.

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