PATHOLOGICA 2020;112:210-213;
DOI: 10.32074/1591-951X-104

Case Report

Atypical cellular neurothekeoma (ACN) of the elderly: case report and brief review of the literature

Nicoletta D'Alessandris[1], Andrea Picchetto[2], Maria Gemma Pignataro[1], Bruna Cerbelli[1], Domenico Manzo[3], Carlo Della Rocca[4], Giulia d'Amati[1], Angelina Pernazza[4]

[1] Department of Radiological, Oncological and Pathological Sciences, Sapienza, University of Rome, Rome, Italy;[2] Department of General Surgery and Surgical Specialties "P. Stefanini", Sapienza University of Rome, Rome, Italy; [3] General Surgery Division, Raphael Medical, Rome, Italy; [4] Department of Medico-Surgical Sciences and Biotechnologies, Polo Pontino-Sapienza University, Latina, Italy

Summary

Atypical cellular neurothekeoma (ACN) is an aggressive and rare variant of cellular neurothekeoma. Only few cases have been reported in the literature and the biological behavior seems to be uncertain. We describe the case of an ACN presenting on the scalp of an elderly man, emphasizing the cytologic features of malignancy. In addition, we provide a brief overview of the literature and discuss the differential diagnosis with other entities, and the possible diagnostic pitfalls.

Key words: atypical cellular neurothekeoma, scalp elderly, diagnostic pitfalls

Received: April 3, 2020
Accepted: May 20, 2020

Correspondence
Angelina Pernazza
Department of Medico-Surgical Sciences and Biotechnologies, Polo Pontino-Sapienza University, 04100 Latina, Italy
E-mail: angelina.pernazza@uniroma1.it

Conflict of interest
The Authors declare no conflict of interest.

How to cite this article: D'Alessandris N, Picchetto A, Pignataro MG, et al. Atypical cellular neurothekeoma (ACN) of the elderly: case report and brief review of the literature. Pathologica 2020;112:210-213. https://doi.org/10.32074/1591-951X-104

Introduction

Neurothekeoma (NT), was first described by Harkin and Reed in 1969 with the term of nerve sheat myxoma [1]. A few years later, it was reclassified as NT by Gallager and Helvig in 1980 [2]. In 1986 Rosati et al. coined the term "cellular neurothekeoma" [3], but only in 1990 Barnhill and Mihm described in detail additional cases of CN emphasizing the morphologic similarity to melanocytic lesions [4].

It is now clear that the classical form, myxoid neurothekeoma and cellular neurothekeoma are unrelated. In fact, the former is a true schwannian neoplasm, while the latter probably falls in the spectrum of fibrohistiocytic tumors.

NT typically occurs in young adults, with a peak incidence in the second decade of life (median age: 17 years) and a slight female predominance. This neoplasm involves more frequently the head and neck, upper extremities and shoulder region. Rarely, multiple NTs may occur [5].

Although most NTs are benign tumors, Busam et al. in 1998 first described the morphological profile of atypical cellular neurothekeoma (ACN) [6]. This is an aggressive variant of cellular neurothekeoma with uncertain clinical behavior. To the best of our knowledge, currently, 35 cases have been reported in the literature [6-10].

We report the clinical, histological and immunohistochemical profile of a case of ACN occurring on the scalp of an older patient and provide a review of the published literature on this lesion.

Case report

A 79-year-old man presented to our attention with a painless, palpable mass in the mid parietal area of the scalp that had shown a slow increase in size over 6 months. Surgical excision of the lesion was performed. A hard, whitish mass (cm 2 in diameter) was completely removed.

On microscopic examination we observe an ulcerated dermal based neoplastic proliferation composed of medium to large-size cells (Fig. 1). The neoplastic cells, in the deepest portion, were reminiscent of classic cellular NT (Fig. 2): spindled small-size cells with small, oval nuclei with occasional pinpoint nucleoli and scant cytoplasm, with ill-defined cell borders. In the superficial portion, near to the epidermidis, the cells were larger and more atypical, with an epithelioid appearance, characterized by round nuclei, prominent nucleoli and abundant eosinophilic cytoplasm (Fig. 3). The neoplastic cells were arranged in fascicles and nests, separated by a fibrotic stroma, at least focally myxoid in the deeper portion, and showed an infiltrative growth pattern into the adipose tissue (Fig. 4). Mitotic activity was very high (about 35/10 high power field) in the epithelioid area (Fig. 3). Perineural invasion and tumor necrosis were not observed.

On immunohistochemistry, the neoplastic cells were positive for vimentin, MITF, CD10, NSE and negative for S100, melan-A, HMB45, CD68, smooth muscle actin, desmin, EMA, CKAE1/AE3, CK8/18, Factor XIIIa, CD34, CD56 (Fig. 5). The proliferative index (Ki-67) was 35%. Based on these findings, our final diagnosis was ACN.

The absence of melanocytic markers ruled out the hypothesis of cutaneous melanoma. The differential diagnosis with atypical fibroxanthoma (AF), the cutaneous counterpart of undifferentiated pleomorphic sarcoma (UPS), was difficult, given that AF is a relatively common lesion on sun-damaged elderly skin. Despite the immunohistochemical profile between ACN and AF/UPS partially overlap (Tab. I), the lack of cellular pleomorphism, multinucleation and, specially, the recognition of areas resembling classic NT, supported the diagnosis of ACN [11].

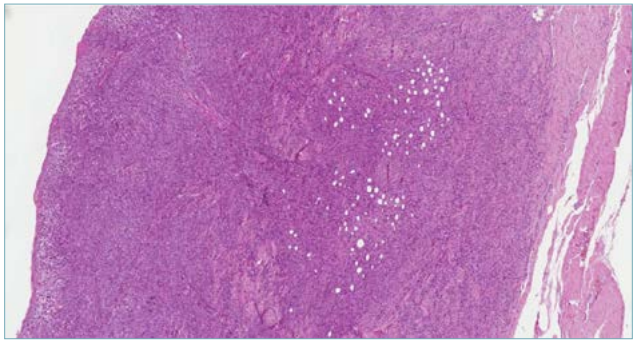

Figure 1. On low-power magnification, a non-polipoid, ulcerated and dermal based proliferation, with fascicles architecture (H-E 2x).

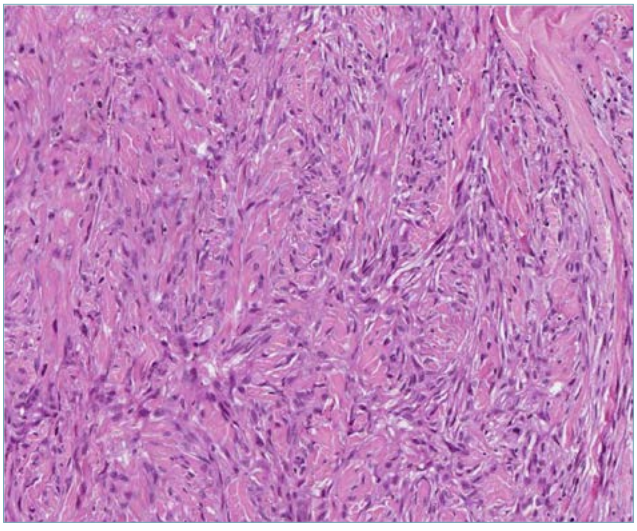

Figure 2. In this side of the tumor, the neoplastic cells appear to be spindle and slender with storiform arrangement, similar to classic NT (H-E, Original magnification 10x).

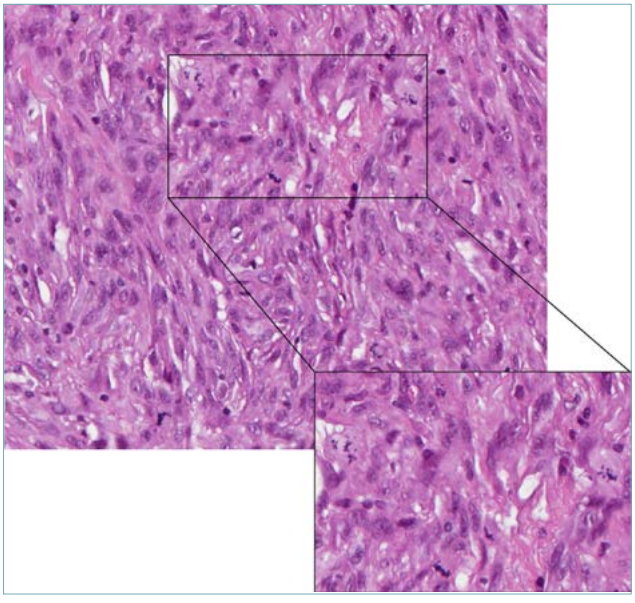

Figure 3. At high magnification, in the superficial portion of the tumor, the cells become epithelioid with a high number of atypical mitotic figures (H-E, Original magnification 20x).

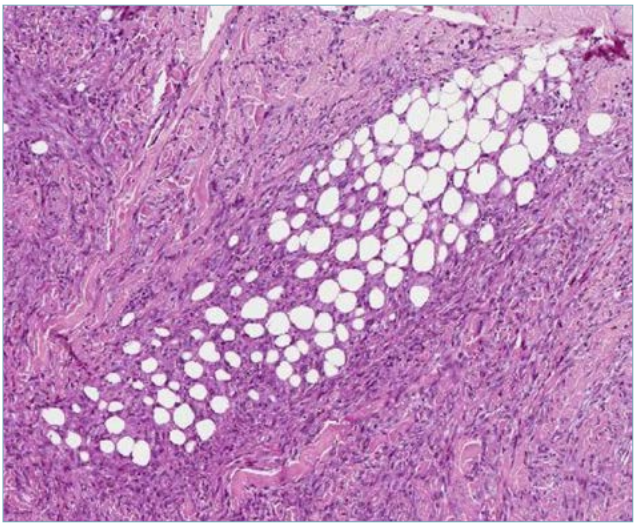

Figure 4. Infiltration of adipose tissue (H-E, Original magnification 4x).

Other entities encountered in the differential diagnosis of ACN were sarcomatoid carcinoma, nerve sheath myxoma and superficial angiomyxoma, that were easily excluded both for morphologic features and immunohistochemical profile (Tab. I).

Discussion

While several cases of classical NT are reported in literature, only few cases of ACN have been documented. Busam et al. first presented 10 cases of ACN, emphasizing the worse clinical behavior and recommending for this reason a surgical complete excision [6]. From 1998 until now, 25 more cases has been reported [7-10], but in only 3 cases the patients were over 70 years old [9].

Our case shows an atypical neurothekeoma in an unusual age of presentation.

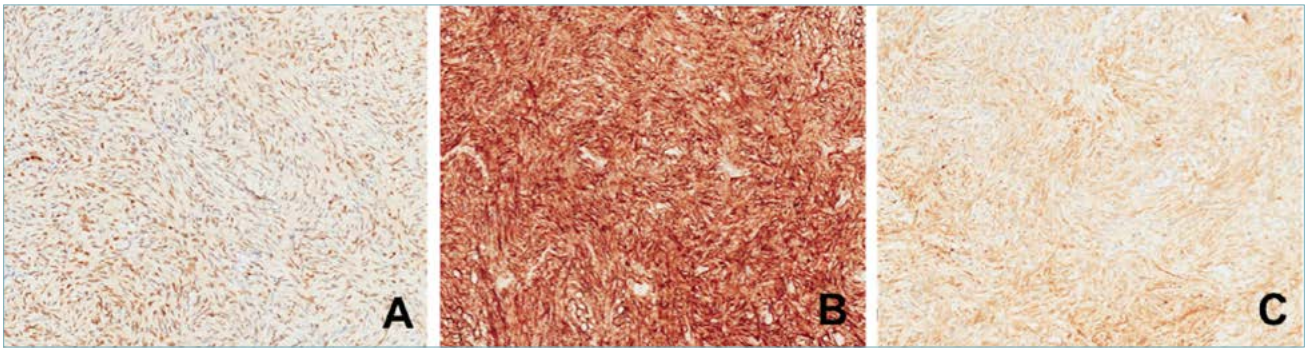

Figure 5. Results of immunohistochemistry: the neoplastic cells are diffusely positive for MITF (A), CD10 (B) and NSE (C) (Original magnification 10X).

Table I. Immunohistochemical profile of ACN compared to other lesions.

	ACN	Melanocytic lesion	UPS	AF	Sarcomatoid carcinoma	Nerve Sheat Myxoma	Superficial angiomyxoma
MITF	+	+	+/-	+/-	-	-	-
CD10	+	-	+	+	-	-	+
NSE	+	-	-	-	-	+	-
S100	-	+	-	-	-	+	-/+
MelanA	-	+	+ *	-	-	-	-
HMB45	-	+	-	-	-	-	-
CD68	-	-	+	+	-	-	-
SMA	-	-	-	-/+	-/+	-	-/+
Desmin	-	-	-	-/+	-	-	-/+
EMA	-	-	-	-	+	+/-	-/+
CKAE1/AE3	-	-	-	-	+	-	-
FactorXIIIa	-	-	+	-/+	-	-	-
CD34	-	-	+	-	-	+/-	+
CD56	-	-	-	-	-	-	-

Legends: *aberrant expression; UPS: undifferentiated pleomorphic sarcoma; AF: atypical fibroxhantoma.

A mitotic rate of >2/10 HPFs represents a criterion to designate a CN as atypical [9]. Nevertheless, to the best of our knowledge, this high level of mitotic activity (35/10 HPF) is not previously reported in literature. The unexpected mitotic activity, the atypical features and the elderly age could suggest alternative diagnoses, such as melanocytic tumors, especially regarding to MITF intense nuclear positivity. However, unlike true melanocytic tumors, ACN is negative for S-100 protein and other melanocytic markers of differentiation. AF/UPS was also considered as possible differential diagnosis both for the clinical presentation and for nuclear MITF expression, that shows high prevalence in these tumors [11]. However, our lesion displayed a lower degree of cellular atypia than could be expected for AF/UPS. These findings and the recognition of areas of conventional NT, confirmed our hypothesis.

About the lineage of differentiation, D'Antonio et al. described strong positive staining for neuroendocrine markers, such as NSE, chromogranin, synaptophysin and CD56, suggesting possible neuroendocrine differentiation of tumor cells. In our case, in line with most of the reported cases, the lesion was positive for NSE only [12]. For this reason it was categorized it in the spectrum of fibro-histiocytic differentiation, as is currently accepted [9].

In contrast to the histologic features suggestive of an aggressive clinical behavior, there are no cases of recurrent or metastatic disease reported in the literature. However, due to the scarcity of reports, we cannot exclude that the clinical progression of this disease could be underestimated. For this reason, complete surgical excision, with negative margins, associated to a close follow-up is recommended. Nowadays, this treatment is considered curative.

In conclusion, the pathologist must keep in mind this entity despite the presence of cytological atypia, unexpected mitotic rate and even in case of atypical clinical presentation, in order to avoid diagnostic pitfalls.

References

1 Harkin JC, Reed RJ. Atlas of Tumor Pathology: Tumors of the peripheral nervous system. Washington, D.C.: Armed Forces Institute of Pathology 1969. https://doi.org/10.1002/bjs.1800570721

2 Gallager RL, Helwig EB. Neurothekoma: a benign cutaneous tumor of neural origin. Am J Clin Pathol 1980;74:759-64. https://doi.org/10.1093/ajcp/74.6.759

3 Rosati LA, Fratamico FCM, Eusebi V. Cellular neurothekeoma. Appl Pathol 1986;4:186-91. https://doi.org/10.2336/nishinihonhifu.52.879

4 Barnhill RL, Mihm MC. Cellular neurothekeoma. A distinctive variant of neurothekeoma mimicking nevomelanocytic tumors. Am J Surg Pathol 1990;14:113-20. https://doi.org/10.1097/00000478-199002000-00002

5 Gill P, Abi Daoud MS. Multiple cellular neurothekeomas in a middle-aged woman including the lower extremity: A case report and review of the current literature. J Cutan Pathol 2019;46:67-73. https://doi.org/10.1111/cup.13366

6 Busam KJ, Mentzel T, Colpaert C, et al. Atypical or worrisome features in cellular neurothekeoma: a study of 10 cases. Am J Surg Pathol 1998;22:1067-72. https://doi.org/10.1097/00000478-199809000-00004

7 Mertz KD, Mentzel T, Grob M, et al. A rare case of atypical cellular neurothekeoma in a 68-year-old woman. J Cutan Pathol 2009;36:1210-4. https://doi.org/10.1111/j.1600-0560.2009.01261.x

8 Gullett AE, Jimenez-Quintero LP, Prieto VG, et al. Atypical cellular neurothekeoma in a pregnant woman. Arch Dermatol 2011 https://doi.org/10.1001/archdermatol.2011.333

9 Stratton J, Billings SD. Cellular neurothekeoma: analysis of 37 cases emphasizing atypical histologic features. Mod Pathol 2014;27:701-10. https://doi.org/10.1038/modpathol.2013.190

10 Tran P, McLemore M. Atypical cellular neurothekeoma: a potential diagnostic pitfall for benign and malignant spindle cell lesions in skin. J Cutan Pathol 2018;45:619-22. https://doi.org/10.1111/cup.13274

11 Choy B. et al. High prevalence of MiTF staining in undifferentiated pleomorphic sarcoma: caution in the use of melanocytic markers in sarcoma. Histopathology 2017;70:734-45. https://doi.org/10.1111/his.13139

12 D'Antonio A, Cuomo R, Angrisani B, et al. Cellular neurothekeoma with neuroendocrine differentiation. Dermatol Online J 2011;17:2.