Giornale Italiano di Dermatologia e Venereologia
EDIZIONI MINERVA MEDICA

A NGFR+ S100- MYXOID NEUROTHEKEOMA: A NEVER DESCRIBED IMMUNOHISTOCHEMICAL PHENOTYPE

Elena GUANZIROLI, Luigia VENEGONI, Daniele FANONI, Nadia QUIRICI, Emilio BERTI

Giornale Italiano di Dermatologia e Venereologia 2018 Jan 24
DOI: 10.23736/S0392-0488.18.05865-0

Article type: Letter to the Editor

Article first published online: January 24, 2018
Manuscript accepted: January 11, 2018
Manuscript received: November 24, 2017

A NGFR+ S100- MYXOID NEUROTHEKEOMA: A NEVER DESCRIBED IMMUNOHISTOCHEMICAL PHENOTYPE

Elena Guanziroli, MD[1*], Luigia Venegoni, BSc[1], Daniele Fanoni, BSc[2], Nadia Quirici, BSc [3], Emilio Berti MD[1]

[1]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano, IRCCS Fondazione Ca' Granda - Ospedale Maggiore Policlinico, via Pace 9, 20122 Milan, Italy;

[2] Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Unità Operativa di Dermatologia, IRCCS Fondazione Ca' Granda - Ospedale Maggiore Policlinico, via Pace 9, 20122 Milan, Italy

[3] Fondazione Matarelli, Ospedale Fatebenefratelli e Oftalmico, Milan, Italy

CORRESPONDING AUTHOR

Elena Guanziroli, MD

Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano

Unità Operativa di Dermatologia, IRCCS Fondazione Ca' Granda - Ospedale Maggiore Policlinico

via Pace 9 - 20122 Milan, Italy

Phone: +390255034718; Fax: +39025503

Email: elena.guanziroli@hotmail.it

ACKNOWLEDGEMENTS

Financial support: none.

Conflicts of interests: none.

Dear Editor,

neurothekeoma (NTK) was first described in 1980 by Gallagher and Helwig as a dermal tumor with close histologic resemblance to the previously described nerve sheat myxoma (NSM) (1).
This slow-growth neoplasm is usually asymptomatic, does not have a tendency to metastases, and recurrences are very un common.
It mainly affects the face and upper limbs of women between the second and third decades of life and it manifests as a solitary, well-defined, dome-shaped, and firm red papule or nodule (2).
Due to the lack of specific clinical and dermoscopic features, diagnosis is based only on histologic findings (2).
They show a nodular or multinodular lesion, typically composed of fascicles of spindle shaped to epithelioid tumor cells, with abundant eosinophilic cytoplasm and absent or sparse mucinous matrix (3).
Based on the amount of myxoid matrix NTKs are divided into myxoid, intermediate, and cellular subtypes: tumors with 10% or less of myxoid matrix are classified as cellular variants; those with more than 50% are considered myxoid ones; values from 10% to 50% are typical for intermediate NTKs (3).
The myxoid variant of NTKs has been often assimilated to the NSMs(6), even though most authors demonstrated that they are distinct entities for their different immunohistochemical characteristics, particularly for the absence of the expression of markers for neural differentiation in NTK (3).
In fact immunohistochemical staining usually demonstrate positivity for CD68, vimentin, NKI/C3, and CD10 and negativity for S100 protein, glial fibrillary acidic protein (GFAP), and CD57.
Therefore, it is postulated that it originates from fibroblastic cells, able to differentiate into myofibroblasts with the tendency to recruit histiocytes (3).
The negativity of nerve growth factor receptor (NGFR) was rarely discussed as another data to validated this hypotesis (4).
We report a recent case of a myxoid variant of NTK which react with antibodies anti-vimentin, CD68, and CD10; without the expression of antibodies anti-GFAP, and S100 protein (Fig.1).
Surprisingly the tumor was diffusely reactive for NGFR (Fig.2).
NGFR, also known p75 neurotrophin receptor (p75NTR), or CD271, is a low-affinity receptor that belongs to the tumor necrosis factor receptor family and interacts with a variety of ligands and co-receptors to mediate a range of neurotrophin functions.
This transmembrane signaling receptor is involved in negative cell cycle regulation and is specific for neural crest origin .

NGFR is also considered a tumor stem cell marker that is shown to result in tumors when transplanted into nude or immunodeficient mice.

It was recently demostrated that it has an important role in the different stages of melanomagenesis: NGFR-positive melanoma stem cells have shown correlations with higher metastatic potential (4). Asymmetric cell division, label-retention and colony-formation are determinants of stem-like cells, as well as a high cellular plasticity. The last characteristic represents a proposed mechanism leading to intra-tumor heterogeneity for the ability of tumor-initiating cells to enter, exit and to re-enter a stem-cell state while changing their phenotype defined by expression of cell surface markers like NGFR (5).

The expression of NGFR in this benign tumor induces to not exclude a neural origin or, however, to consider the presence of a mixed cellular population of different derivations.

Finally, we must consider that the down-regulation mechanisms of NGFR, which manifests with the decrease or absence of reactivity on immunohistochemical staining, could also promote a cell-lineage switch from neural-like to mesenchymal-like, property highlighted in recent studies and already attributed to melanoma cells (5).

Figure 1. Lack of immunoreactivity for S100 protein in a case of myxoid NTK (10x magnification).

Figure 2. Immunohistochemical results for NTK showing a consistent reactivity for NGFR (10x magnification).

REFERENCES

1) Papadopoulos EJ, Cohen PR, Hebert AA. Neurothekeoma: report of a case in an infant and review of the literature. J Am Acad Dermatol 2004;50:129-34.

2) Fetsch JF, Laskin WB, Hallman JR, Lupton GP, Miettinen M. Neurothekeoma: an analysis of 178 tumors with detailed immunohistochemical data and long-term patient follow-up information. Am J Surg Pathol 2007;31:1103-14.

3) Laskin WB, Fetsch JF, Miettinen M. The "neurothekeoma": immunohistochemical analysis distinguishes the true nerve sheath myxoma from its mimics. Human Pathol 2000;31:1230-41.

4) Guo R, Fierro-Fine A, Goddard L, et al. Increased expression of melanoma stem cell marker CD271 in metastatic melanoma to the brain. Int J Clin Exp Pathol 2014;7:8947-51.

5) Redmer T, Welte Y, Behrens D, et al. The nerve growth factor receptor CD271 is crucial to maintain tumorigenicity and stem-like properties of melanoma cells. PLoS One 2014;9:e92596.