

Case Report

Unusual Recurrent Lateral Canthus Mass in a 16-Year-Old Male Patient: Neurothekeoma

Azza M.Y. Maktabi^a Hailah Al-Hussain^b Hatim Khoja^c
Hind Manaa Alkatan^{d, e}

^aPathology and Laboratory Medicine Department, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia; ^bOculoplastic Division, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia; ^cAnatomic Pathology Department, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; ^dDepartment of Ophthalmology, King Saud University, Riyadh, Saudi Arabia; ^eDepartment of Pathology, King Saud University, Riyadh, Saudi Arabia

Keywords

Ocular · Lateral canthus · Cellular neurothekeoma · Mixed neurothekeoma · Myxoid · Immunohistochemistry

Abstract

Neurothekeoma (NTK) is a specific benign soft tissue tumor, typically involving the skin of the head and neck area as well as the upper part of the body in young age with female predominance. It has a typical lobular pattern of growth but often displays atypical features such as myxoid stroma or fascicular pattern, which makes the diagnosis more difficult and may necessitate the use of immunohistochemical staining to differentiate NTK from nerve sheath tumor. Ocular NTK in general is very rare with only 11 cases previously reported. We are presenting a case of recurrent mixed cellular/myxoid NTK involving the lateral canthal area of a 16-year-old-boy and we demonstrate the diagnostic challenge in such cases to attract the attention of ophthalmologists and pathologist to the rare occurrence of NTK in the ocular region.

© 2019 The Author(s)
Published by S. Karger AG, Basel

Introduction

Neurothekeoma (NTK) is benign soft tissue tumor, often confused with nerve sheath tumors, therefore constitutes diagnostic challenge, especially when the diagnosis is not expected by the ophthalmologists. The term itself was first introduced by Gallager and Helwig in 1980 [1]. It was referred at that time as a benign superficial cutaneous neoplasm of peripheral nerve sheath origin, with cellular, myxoid, or mixed histopathological variants [2]. Typically, the tumor involves the skin of the head and neck in young adults with female predominance. 11 cases of ocular/periorcular NTK have been reported indicating the rarity of this type of neoplasm. Our case is the first reported NTK in the lateral canthal area. Even though the tumor is classified as mixed (cellular/myxoid), it exhibited the immunohistochemical characteristics of cellular NTK.

Case Report

A 16-year-old Saudi young male presented at King Khaled Eye Specialist Hospital with a recurrent painless slowly growing right lateral canthus mass that was first noticed 10 months prior to his presentation. The mass was excised by a local ophthalmologist 5 months earlier with no definitive tissue diagnosis. The mass was painless, firm, measured 15 × 15 mm, and was pushing the globe upwards. The overlying adjacent skin was intact with no ulceration. His ophthalmologic examination of both eyes was unremarkable. Excisional biopsy was performed, and the specimen grossly was described as a piece of skin measuring 25 × 10 × 4 mm with a nodular mass in the center. The cut surface of the mass was smooth and tan in color. The histological sections revealed a multinodular tumor composed of nests of epithelioid/spindle cells separated by fibrous septae within a myxoid background (Fig. 1A). Colloidal Iron stain highlighted the focal myxoid changes (Fig. 1B). Frequent multi-nucleated giant cells were noted. Focally, tumor cells showed moderate to severe dysplasia with few mitotic figures of 2 in 25 HPF (40×). Using immunohistochemical (IHC) staining, the tumor cells expressed CD68, Vimentin, D2-40, with MiTF focal nuclear staining (Fig. 1C, D). The cells also showed weak patchy expression of smooth muscle actin (SMA). The cells did not express S-100 staining. Based on the histopathological features and the IHC properties, the diagnosis of Neurothekeoma (mixed pattern) was established.

Discussion

NTK has been linked to the family of nerve sheath tumors with nerve sheath myxoma (NSM), being classified as a subtype of NTK in 1969. Laskin and his group in 2000, studied 22 soft tissue tumors that were coded at the Armed Forces Institute of pathology (AFIP) as either NSM or NTK and demonstrated that they were actually two separate entities based on consistent differences in their clinical, histological, and IHC features [3]. This was specially noted when all tumors labeled as cellular or myxoid NTK were consistently negative with S-100 with further staining indicating a possible “fibro-histiocytic” origin [3].

The pathogenesis of this tumor is not clear and might be triggered by high estrogen levels and trauma [4]. The tumor appearance is typically described as a solitary, slow-growing, commonly painless dome-shaped pink-tan to reddish-brown colored nodule of soft to firm consistency, which is similar to the mass characteristics in our case. The history of presentation

may vary from few weeks to many years. The Age ranges from 20 months to 85 years, however NTK tends to occur in younger age around the second or third decades with a slight female predominance. The majority of tumors were located on the face, shoulder, or arm. The trunk, pelvic girdle, legs, hands, and feet were less commonly affected. Based on one of the largest series in literature reported by Fetsch and his group in 2007 where they studied 178 cases from the AFIP archives, the tumors were found to be non-capsulated, dermal in location, and typically forming multiple small to medium-sized nodules. Subcutaneous involvement was documented in almost 85% of the cases [5]. The tumors had variable amounts of myxoid matrix and were sub-classified as cellular neurothekeomas (<10% myxoid matrix), mixed-type (10–<50%), and myxoid neurothekeomas (>50%) [5]. In most cases, the tumor was composed of spindle cells that predominated over the epithelioid cells. In their series, 85% lacked fascicular pattern, in contrast to the characteristic whorled growth in NSM and there was also no tendency to form discrete cords or closely packed syncytial-like aggregates, as in true NSM [5]. All their cases showed some degree of atypia ranging from minimal to generalized moderate atypia and mitotic activity was variable ranging from 0–20/WHPFs. Osteoclast-like giant cells were found in 39% of cases. Inflammatory cells were often encountered, but they were not a prominent feature. The most common inflammatory cells were lymphocytes [5]. Tumors did not contain a distinctive stroma, but dermal collagen bands, which frequently sclerotic were found [5]. Despite the aggressive looking cells and the presence of atypia and mitotic figures, the tumor was found to behave in a benign fashion, with no invasion, progression or metastasis. Recurrence is very rare, and it is reported with incomplete excision, which is suspected in our case since it has been performed by a local ophthalmologist [5]. It has been interesting to confirm that all previously mentioned histopathological features since 1980 when the terminology of NTK has been first introduced by Gallager and Helwig were still observed [1, 5]. Different reports have shown that NTK is consistently negative with S-100 in comparison to the NSM cases [6, 7]. Page in 2004 studied 11 cases to characterize the combination of MiTF and NKI/C3 expression in cellular NTK. Nine out of 11 tumors expressed both NKI/C3 and MiTF, while were all negative to S-100 [8]. He concluded that immunoreactivity for these antibodies may be positive in a number of other lesions, so the interpretation should be made within the context of accurate histopathological appearance. IHC stains for NKI/C3 and CD-10 are useful ancillary tests for the diagnosis of cellular NTK if used in combination to histopathological features. Also, in cases of S-100 negative neurothekeoma of the myxoid type, fibro-histiocytic markers are to be considered such as CD-68 [6, 9, 10]. The differential diagnosis in the reviewed cases included neurothekeoma (23%) melanocytic tumor variants (especially a Spitz nevus), neurofibroma, schwannoma/neuroma variant, fibro-histiocytic tumor, and NSM. Interestingly, malignancy was suspected in 21% of the cases [5].

Ocular/Periocular NTK is rare. In a recent excellent review of 11 cases of NTK involving the ocular region including the eyelids, NTK was reported in the cornea in a 39-year-old Caucasian female presented with left corneal white opaque and elevated pannus-like mass, which persisted for 3 months despite treatment with antibiotics. There was no associated pain, irritation, photosensitivity, or acute changes in vision. The clinical diagnosis was Salzmann's nodular degeneration [11]. Excisional biopsy revealed cells with round to oval vesiculated nuclei, prominent nucleoli, and a moderate amount of eosinophilic cytoplasm. The cells expressed the following IHC stains: microphthalmia transcription factor (MITF), CD-68, CD-10, NSE, SMA, and HAM56, but were negative with S-100, Melan A, HMB45, Desmin, CK7, CK20, EMA, CD-34, and CD1a. All above-mentioned pathologic features were diagnostic for cellular NTK [11]. The reviewed cases of NTK included one orbital case, and their corneal case had similar

histopathological features to ours, however our present case had a mixed rather than cellular pattern NTK and it is the first case involving the lateral canthus.

Conclusion

Cellular NTK is a benign tumor that may rarely involve the ocular adnexa. The presence of atypical features does not appear to impact its behavior. Therefore, recognition of this entity is important to avoid the pitfall of mislabeling it as something more sinister. The cellular origin of NTK is still not clear, since histologic and IHC findings are neither specific nor conclusive and further studies might be needed.

Statement of Ethics

The case report has been prepared according to the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. It has been approved by the HEC/IRB at KKESH, where the patient has presented. An informed General Consent has been taken, which includes using patient's anonymous information.

Disclosure Statement

The authors have no financial or conflict of interest related to this work.

Author Contributions

A.M.Y.M.: Literature search and drafting of the manuscript.

H.A.-H.: Clinical data of the case and management.

H.K.: Pathological diagnosis consultation.

H.M.A.: Critical correction, review of the manuscript and update of the literature (senior author).

References

- 1 Gallagher RL, Helwig EB. Neurothekeoma—a benign cutaneous tumor of neural origin. *Am J Clin Pathol*. 1980 Dec;74(6):759–64.
- 2 Misra RP. Neurothekeoma palpebrae. *Plast Reconstr Surg*. 2004 Dec;114(7):1975–6.
- 3 Laskin WB, Fetsch JF, Miettinen M. The “neurothekeoma”: immunohistochemical analysis distinguishes the true nerve sheath myxoma from its mimics. *Hum Pathol*. 2000 Oct;31(10):1230–41.
- 4 Navarrete-Dechent C, Curi-Tuma M, Marín C, González S, Sandoval-Osses M. Cellular neurothekeoma: case report and its (un) relation with nerve sheath myxoma. *An Bras Dermatol*. 2015 May-Jun;90(3 Suppl 1):156–9.
- 5 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 Jul;31(7):1103–14.
- 6 Abuawad YG, Saraiva MI, Westin AT, Valente NY. S-100 negative myxoid neurothekeoma: a new type of neurothekeoma? *An Bras Dermatol*. 2017 Jan-Feb;92(1):153–5.
- 7 Fullen DR, Lowe L, Su LD. Antibody to S100a6 protein is a sensitive immunohistochemical marker for neurothekeoma. *J Cutan Pathol*. 2003 Feb;30(2):118–22.

- 8 Page RN, King R, Mihm MC Jr, Googe PB. Microphthalmia transcription factor and NKI/C3 expression in cellular neurothekeoma. *Mod Pathol*. 2004 Feb;17(2):230–4.
- 9 Yun SJ, Park HS, Lee JB, Kim SJ, Lee SC, Won YH. Myxoid Cellular Neurothekeoma: A New Entity of S100-Negative, CD68-Positive Myxoid Neurothekeoma. *Ann Dermatol*. 2014 Aug;26(4):510–3.
- 10 Stratton J, Billings SD. Cellular neurothekeoma: analysis of 37 cases emphasizing atypical histologic features. *Mod Pathol*. 2014 May;27(5):701–10.
- 11 Naguib MM, Craven C, Kozarsky A, Grossniklaus HE. Neurothekeoma of the Cornea. *Ocul Oncol Pathol*. 2016 Oct;2(4):212–7.

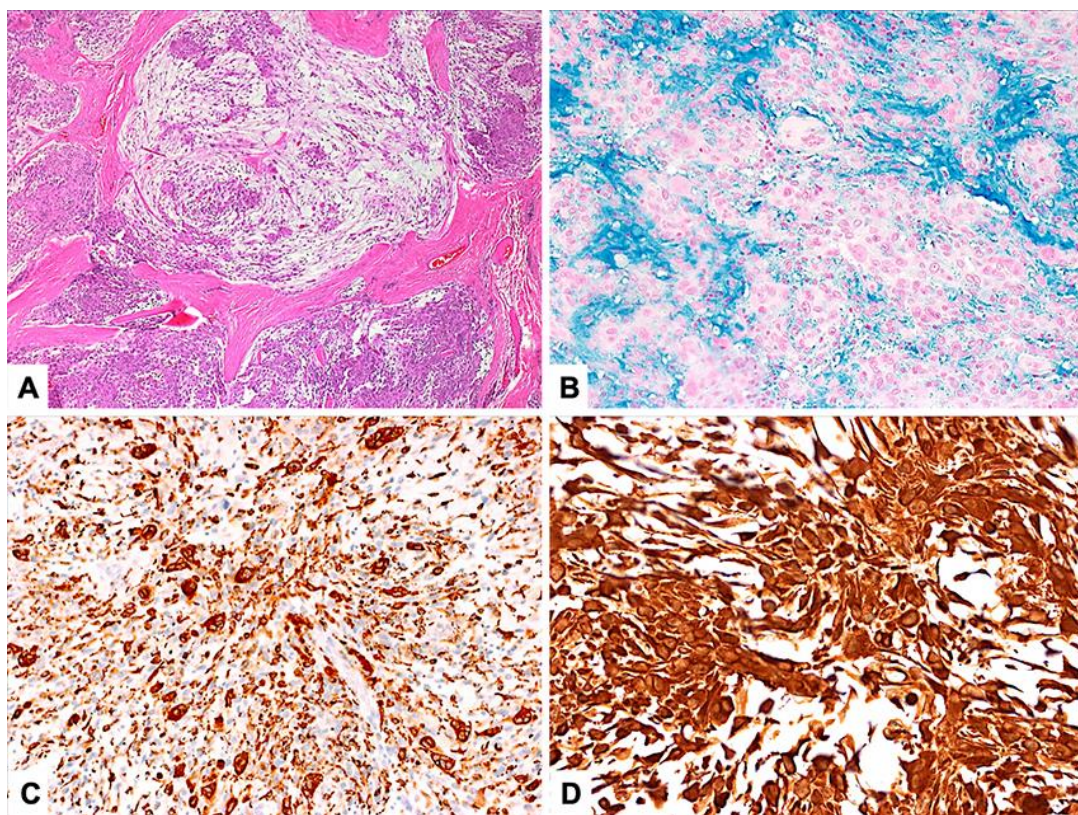


Fig. 1. **A:** The histopathology of this tumor showing nests of epithelioid and spindle cells separated by fibrous septae within a myxoid background (Original magnification $\times 50$ Hematoxylin and eosin). **B:** Myxoid areas highlighted by Colloidal iron stain. (Original magnification $\times 200$). **C:** The cellular area of the tumor expressing CD68 (Original magnification $\times 200$). **D:** The mixed area with cells expressing positive staining for Vimentin marker (Original magnification $\times 400$).