CASE REPORT

Cellular neurothekeoma: case report and its (un) relation with nerve sheath myxoma*

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Abstract: Neurothekeoma is an uncommon, benign neoplasm presenting in young adults, primarily on the head and neck. It was initially related to nerve sheath myxoma but with the advent of immunohistochemistry, new insights into its cellular differentiation and origin have emerged, unlinking Neurothekeoma and nerve sheath myxoma. Herein we describe a 19-year-old male who had had a frontal, flesh-colored, asymptomatic papule for 2 years. Histology showed a dermal fusocellular-spindle cell tumor, including an eosinophilic cytoplasm with mild cellular pleomorphism and moderately dense fibrous stroma. IHQ was positive for CD10 and negative for S100 and Claudin-1. These findings were compatible with cellular Neurothekeoma. The lesion was completely extirpated and at the 6-month follow-up, the patient was asymptomatic and had experienced no recurrences.
Keywords: Myxoma; Neoplasms, adnexal and skin appendage; Neurothekeoma

INTRODUCTION

Neurothekeoma (NT) is an uncommon, benign, dermal tumor. It was described by Harkin and Reed[1] in 1969 as a cutaneous tumor of neural origin named "nerve sheath myxoma". NT manifests as pink-erythematous, dome-shaped, solitary papules, generally of under 1 cm in diameter; with slow growth, firm consistency and usually asymptomatic. It is mainly located on the face, neck, arms and shoulders of young adults, and is more frequent in females.[1-4]

Nerve sheath myxoma (NSM) has often been regarded as falling within the spectrum of NT, though this is currently a source of discussion among most authors, in light of the advent of immunohistochemistry (IHQ).[2, 5]

CASE REPORT

A 19 year-old, otherwise healthy male presented with a 2-year history of an asymptomatic frontal lesion. A firm, erythematous, non-tender, frontal papule was found (Figure 1). Definitive diagnosis was uncertain with physical examination and the differential diagnosis included a dermal nevus, a Spitz nevus, an adnexal tumor and a spontaneous keloid. Complete excision and microscopic examination was performed, showing a non-capsulated, dermal, fusocellular-spindle cell tumor with eosinophilic cytoplasm, including mild, cellular pleomorphism and moderately dense fibrous stroma without myxoid matrix (Figure 2). No atypical cells or mitotic figures were seen. IHQ was positive for CD10 and negative for S100 and Claudin-1 (Figure 3).

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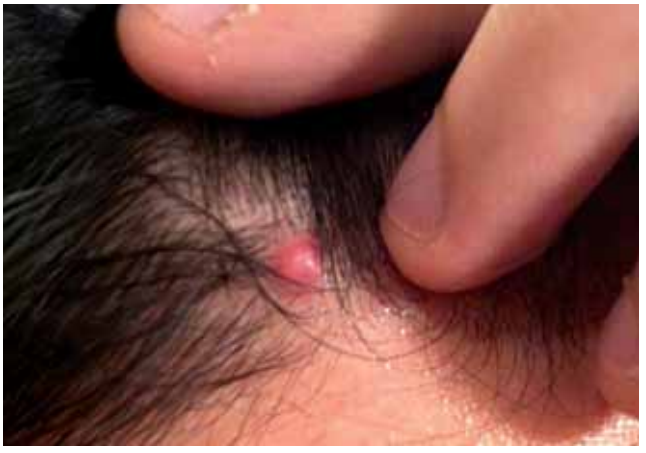


Figure 1: Firm, erythematous, dome-shaped, frontal papule

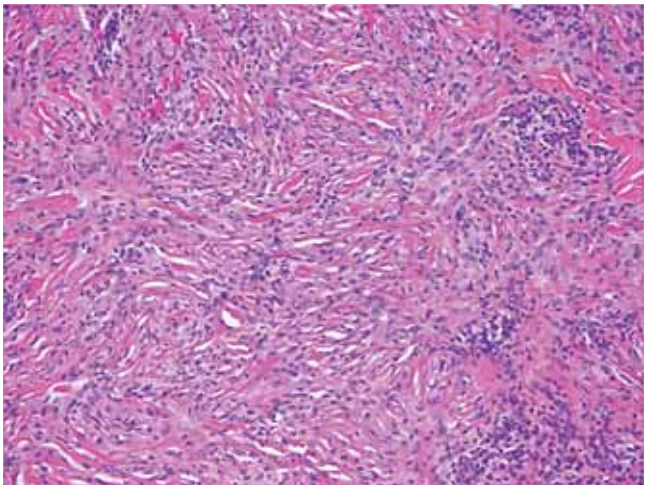
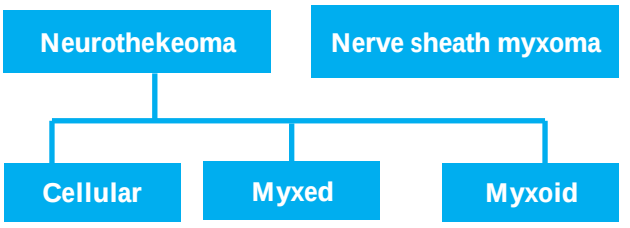


Figure 2: Higher magnification showing grouped spindle cells with round to oval nuclei, no atypia, and moderately dense collagenous stroma. H&E, 200X



Adapted from: Fetsch JF, 2007.[2]

Figure 4: Classification scheme of Neurothekeoma according to myxoid matrix in cellular, myxoid or mixed, Neurothekeoma. Nerve sheath myxoma has been intentionally placed outside

This was compatible with cellular NT. At the 6-month follow-up, the patient was asymptomatic without recurrence signs and excellent healing process.

DISCUSSION

NT is an infrequent, dermal tumor with a two-fold female predominance.[1,2,6-8] It is more common in the second decade of life. The mean age at diagnosis is 17 years: 25% occur in patients aged under 10, 59% in individuals under 20, and 80% in patients under 30.[2,3,9] However, diagnosis should also be suspected in older patients.[1,2] Local trauma and estrogen use have been identified as triggering factors, which may explain the 2:1 ratio in females. [9,10]

Clinically, it manifests as an asymptomatic, pink-erythematous, dome-shaped, solitary papule, with a slow growth rate (mean time 7 months).[2] Differential diagnosis is broad, including benign and ma-

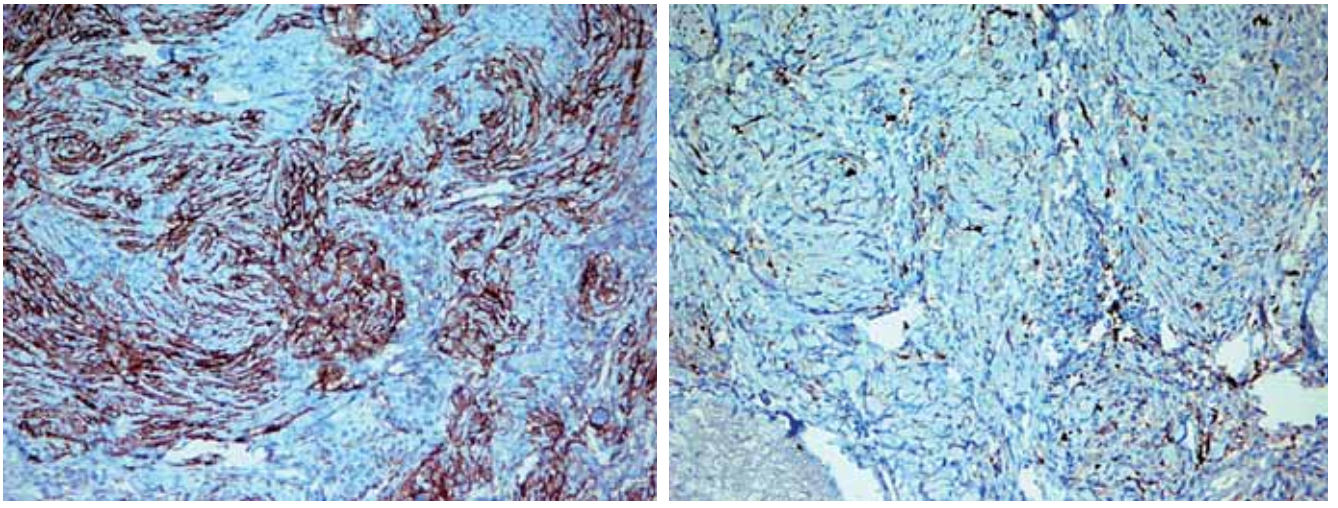


Figure 3: A. Immunohistochemistry panel. A: Highly positive for CD10; **B.** Negative for S100. It was also negative for Claudin-1

Chart 1: Differential (clinical and histological) diagnosis of Neurothekeoma. We placed the conditions in descending order of frequency

Physical exam:	**Histology:**
Epidermal cyst	Melanocytic tumor variants (e.g. Spitz Nevus)
Nevus	Neurofibroma, Schwannoma or neurnoma variants
Dermatofibroma	
Adnexal tumor (e.g. pilomatricoma)	Fibrohistiocytic tumor
Basal cell carcinoma	Nerve sheath myxoma
Insect bite/Arthropod assault	
Granulomatous reaction	
Keloid/scar	
Hemangioma	
Amelanotic melanoma	
Cutaneous metastasis	

Adapted from: Fetsch JF, 2007.[2]

lignant neoplasms, as well as inflammatory reactions (Chart 1). It is remarkable that in a series conducted by Fetsch *et al.*, the diagnosis of NT was not suspected in any of the 176 patients.[2] Hence, NT is mainly a histologic/retrospective diagnosis.

It is commonly located (70%) on the head (34%), arms (20%) and shoulders (15%). On the head, it affects the nose (27%) and scalp (24%) mainly.[2]

The presence of spindle and epithelioid cells with abundant granular-eosinophilic cytoplasm and a tendency to be grouped in whorled nodules spared by collagen bundles in the dermis and subcutaneous area, constitute the presumptive diagnosis. There may be sclerotic collagen and osteoclastlike cells.[2] Depending on the amount of myxoid matrix, NT can be classified into cellular NT (≤ 10% myxoid matrix), mixed NT (10 – 50% myxoid matrix) and myxoid NT (> 50% myxoid matrix). IHQ of NT almost always shows a reaction to NK1/C3 and CD10. S-100, HMB-45, Melan-A and CD56 are usually negative (Figure 4).[2,3]

The cell of origin for NT is still unknown. NSM has been linked to myxoid NT repeatedly. It has been argued that NT has nerve sheath differentiation and is part of NSM. Although this remains controversial due to the lack of positive reaction to S-100 in all NT variants, we agree with Fetsch *et al.* and consider a neural differentiation very improbable (Figure 4). We also recognize the possibility of fibro-hystiocitic lineage.[2]

Few studies have evaluated the prognosis of NT. After adjusting confounding variables, the real recurrence of NT is somewhere around 3%.[2] Risk factors for recurrence are: myxoid type, being female, facial location, younger age at diagnosis, positive margins, and absence of fat-tissue in the sample.[2] The presence of cellular atypia and the number of mitoses were not associated with an increased recurrence rate.[2] For these reasons, we perform 1 – 2 mm margins elliptic deep excisions for NT.

An atypical variant of NT (ANT) has recently been described. Some authors define ANT as entailing larger tumors (up to 6cm) of deep penetration (skeletal muscle and subcutaneous fat involvement), diffuse infiltrative borders, vascular invasion, a high mitotic index (>3 mitosis per 10 high power fields) and pleomorphism.[7] This variant has been incompletely characterized and its clinical behavior is not entirely understood because of the scarcity of reports.[1,6,7] In a series involving 10 ANT patients, no local recurrence or metastasis was found in 1 to 5 years of follow-up. It seems that this "histologic aggressiveness" is not correlated with a "clinical aggressiveness".[6] Still, it is preferable to perform a complete excision of ANT with free margins, until they are more accurately characterized.

Our case confirms the non-specific, clinical appearance of NT and underlines the importance of the biopsy for definitive diagnosis of NT. We do agree with the authors who favor a likely fibro-hystiocitic differentiation for this lesion.❑

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