



Neural or Fibro Histiocytic - Neurothekeoma

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Short Communication

Preface neurothekeoma is an infrequently discerned, distinctive, benign soft tissue neoplasm. The neoplasm can be superficial or dermal and predominantly arises within head and neck, shoulder or upper extremities. Cellular neurothekeoma demonstrates an uncertain histogenesis although it is presumably derived from fibroblastic/myo-fibroblastic or fibro-histiocytic cellular lineage [1]. On account of coincidental clinical and histological representation, nerve sheath myxoma was contemplated as a neoplasm concurrent with myxoid variant of neurothekeoma. Nevertheless, nerve sheath myxoma displays a typical immune profile, possible emergence from diverse locations and proportionately enhanced reoccurrence, in contrast to neurothekeoma [1,2]. Gallager and Helwig in 1980 initially categorized neurothekeoma as a dermal tumour of neural origin displaying characteristic clinical features and a distinctive histology. As the tumour cells recapitulate Schwann cells on ultrastructural evaluation and are denominated as spindle-shaped cells encompassed within a basement membrane devoid of myofilament or melanosomes, a terminology of neurothekeoma is proposed, akin to the Greek phrase “sheath” [1,2]. Rosati [3] in 1986 introduced the category of cellular neurothekeoma, contemplated as a cellular variant of previously described myxoid neurothekeoma. Barnhill and Mihm in 1990 denominated cellular neurothekeoma appearing to be similar to melanocytic tumors and being immune nonreactive to S100 protein. Albeit, neurothekeoma as described by Barnhill and Mihm in 1990, appears to be a distinct entity, disparate from true nerve sheath myxoma [1,2]. Thus, cellular neurothekeoma represents a definitive sub-category or an entirely distinct category of neurothekeoma [2,3].

Disease characteristics originally, neurothekeoma was hypothesized to arise from a nerve sheath. Currently, the neoplasm is considered to delineate fibroblastic derivation with possible differentiation into myo-fibroblasts and concomitant recruitment of histiocytes [3]. Neurothekeoma frequently appears as a soft, flesh colored or mildly erythematous nodule situated upon the head and neck, upper extremity, shoulder girdle or trunk. In contrast to peripheral nerve sheath genesis, neurothekeoma is hypothesized to exemplify a fibro histiocytic derivation. A female preponderance is observed with a female to male proportion of 2:1. The neoplasm is common within the second or early third decade although no age of disease emergence is exempt [3,4]. An estimated 60% of females are implicated between 2 to 85 years with a mean age of 17 years, although around 80% incriminated subjects are below <30 years at preliminary discernment [3,4]. Clinical Elucidation Neurothekeoma is clinically asymptomatic. Typically, a solitary, superficial, gradually progressive, indolent, pink-tan or reddish brown, dome shaped papule or nodule beneath <2-centimeters magnitude is exhibited. Lesions are frequently delineated upon superficial cutaneous surfaces or dermis whereas incrimination of deep-seated skeletal muscle, subcutaneous adipose tissue or mucosal surfaces is exceptional [3,4]. Commonly, young, female subjects typically represent an asymptomatic, indolent, solitary, dermal nodule below <2 cm diameter situated upon the head and neck, shoulder or upper extremities [4]. Histological Elucidation Neurothekeoma is classically denominated as a benign, superficial, cutaneous tumor demonstrating diverse histological configurations such as myxoid, cellular or mixed-type. Aforesaid variants of neurothekeoma are contingent to quantifiable myxoid matrix. Macroscopically, a multinodular mass is exemplified with enveloping myxoid matrix and peripheral fibrosis [4,5]. On histology, spindle-shaped cells are arranged in cellular nests and cords intermingled within a mucinous or myxoid stroma with a concurrence of dermal fascicles of collagen. An admixture of spindle-shaped and epitheloid cells are disseminated within a variably myxoid stroma [4,5].

As previously described, neurothekeoma is subcategorized as myxoid, cellular or mixed-type, contingent to quantifiable myxoid matrix wherein the classical variant, cellular neurothekeoma is a lobular, moderately circumscribed, dermal lesion with an infiltrative periphery. Typically, the tumor is comprised of discreetly whorled nests and cellular aggregates of epitheloid to mildly spindle-shaped cells. Tumor cells demonstrate an abundant, eosinophilic cytoplasm, spheroidal to

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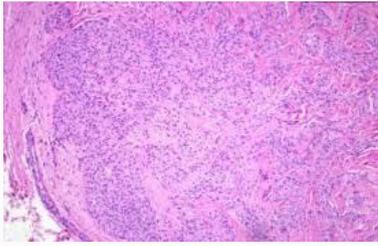


Figure 1: Neurothekeoma demonstrating whorls and fascicles of spindle-shaped and epithelioid cells with circumscription and intermingled myxoid stroma.

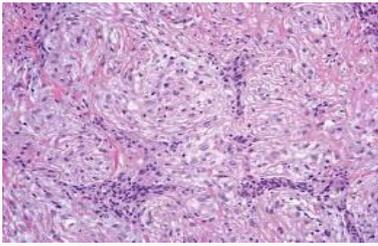


Figure 2: Neurothekeoma with whorls and fascicles of spindle-shaped and epithelioid cells admixed with fibrous tissue and myxoid stroma.

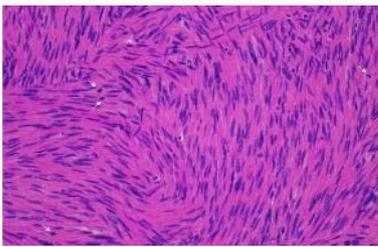


Figure 3: Cellular neurothekeoma with whorls and fascicles of spindle-shaped cells with commingled cellular stroma.

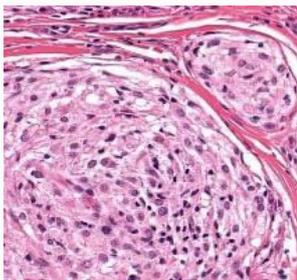


Figure 4: Neurothekeoma with whorls and fascicles of ovoid and epithelioid cells enveloped in a fibrous tissue stroma.

ovoid nuclei and miniature, pinpoint nucleoli [4,5].

Epithelioid to spindle-shaped cells articulate a lobulated, plexiform or focal sheet-like pattern with frequently discerned myxoid metamorphoses. A typical feature such as nuclear atypia, cellular pleomorphism, infiltrative tumour growth, vascular invasion and peri-neural invasion can be discerned although occurrence of atypical histological features lacks pertinent clinical significance [5]. A foresaid neoplastic subtype as cogitated with cellular, myxoid or mixed-type can incriminate the dermis or subcutaneous tissue. Focal fascicular arrangement or whorls of spindle-shaped and epithelioid, mononuclear cells with abundant cytoplasm and an indistinct cell

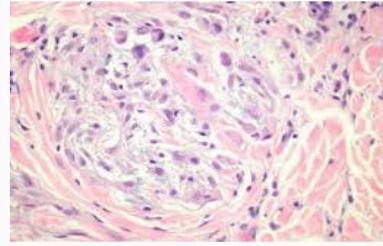


Figure 5: Neurothekeoma with whorls and bundles of epithelioid and elliptical cells surrounded by fibrous tissue aggregates.

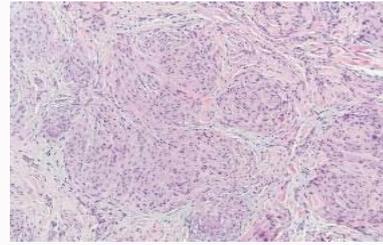


Figure 6: Neurothekeoma with whorls and fascicles of spindly and epithelioid cells intermingled with a cellular stroma.

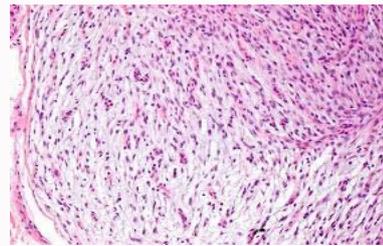


Figure 7: Neurothekeoma with whorls and bundles of elliptical and epithelioid cells admixed with a myxo-cellular stroma.

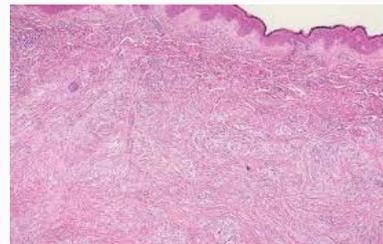


Figure 8: Neurothekeoma with whorls and fascicles of spindle-shaped and epithelioid cells with an admixture of myxo-cellular stroma.

margin are exemplified. Occasional multinucleated giant cells are observed with tumor remnants within surgical resection margin. Nuclear atypia is variable and atypical mitosis can be delineated. Mitotic figures vary from >10 mitosis per 25 high power fields with a median of 4 mitosis/25 high power fields [4,5]. Immune Histochemical Elucidation Cellular variant of neurothekeoma is constituted of bland, epithelioid cell proliferation and demonstrates an intense immune reactivity to vimentin, Microphthalmia Transcription Factor-1 (MITF-1), CD10 or NKI-C3 (CD63). Besides, focal immune reactivity to Smooth Muscle Actin (SMA), Neuron Specific Enolase (NSE) and CD68 is observed. The neoplasm is immune nonreactive to S100 protein, Glial Fibrillary Acidic Protein (GFAP) or Melan-A. Cellular neurothekeoma is comprehensively (~100%) immune

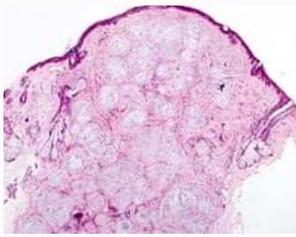


Figure 9: Neurothekeoma demonstrating a well-circumscribed, multinodular tumour and a commingling of myxoid stroma.

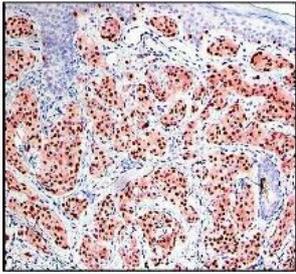


Figure 10: Neurothekeoma demonstrating an immune reactive MITF.

reactive to combined NKI-C3 and CD10 [6,7]. Nerve sheath myxoma is immune reactive to S100 protein although neurothekeoma is immune nonreactive to S100 protein, irrespective of identical and demonstrable histological pattern as myxoid, cellular or mixed-type [6]. Differential Diagnosis Epitheloid cell tumors situated within head and neck region are enunciated as granular cell tumor, cellular neurothekeoma, nerve sheath myxoma, neurofibroma, schwannoma, benign fibrous histiocytoma, infective reactions and melanocytic lesions as Spitz nevus or melanoma. Cogent neoplasia such as neurofibroma, schwannoma, nerve sheath myxoma), fibro-histiocytic lesions as neurothekeoma, fibrous histiocytoma or melanocytic disorders can represent as solitary nodules and appear histologically identical [6,7]. Cellular neurothekeoma can be differentiated from fibrous histiocytoma, dermal nerve sheath myxoma and plexiform fibro histiocytic tumor.

Fibrous histiocytoma lacks foci of tumour cell nesting which are typically enunciated in cellular neurothekeoma [6,7]. Plexiform fibro-histiocytic tumour is distinguished from cellular neurothekeoma on account of presence of tumour nodules constituted by mononuclear histiocytoid cells, osteoclast-like giant cells and fascicles of spindle-shaped myo-fibroblastic cells [6,7]. Distinction of neural and fibro-histiocytic tumors from definitive carcinomas such as malignant melanoma can be challenging on account of variably disseminated epitheloid cells, a “theque-like” cellular arrangement and unusual microscopic features denominated as nuclear atypia, mitosis and tumor extension into circumscribing skeletal muscle or subcutaneous adipose tissue [6,7]. Diverse fibro-histiocytic lesions can be differentiated upon a competent morphological assessment. Focal cellular nests and a clustered tumor pattern is characteristic of conventional cellular neurothekeoma and segregates the neoplasm from superficial angiomyxoma or benign fibrous histiocytoma which are devoid of tumor cell nests. Tumor cell nesting is also cogitated in melanocytic tumors or Spitz nevus. In contrast to true melanocytic neoplasia, neurothekeoma is immune nonreactive to S100 protein

and specific immune markers of melanocytes such as Melan-A and Human Melanoma Black (HMB-45) antigen. Differentiation betwixt neurothekeoma and dermal nerve sheath myxoma can be challenging on account of coincidental clinical and histological representation. Nerve sheath myxoma is immune reactive to S100 protein and immune nonreactive to NKI-C3 (CD63) whereas cellular neurothekeoma demonstrates a contrasting immune reactivity with nonreactive S100 protein and reactive NKI-C3 (CD63) [6,7]. Neural lesions such as schwannoma and neurofibroma can be demarcated upon cogent morphology and immune staining. Schwannoma exhibits a biphasic tumour configuration with immune reactive S100 protein, Glial Fibrillary Acidic Protein (GFAP) and Epithelial Membrane Antigen (EMA). Neurofibroma is immune reactive to S100 protein [8]. Granular cell tumor is typically immune reactive to S100 protein whereas neurothekeoma is immune nonreactive. Infectious aetiologies can be segregated by appropriate evaluation for bacterial or fungal elements on routine or special stains [8]. Therapeutic Options Cogent therapy for managing neurothekeoma is a comprehensive surgical extermination of the neoplasm. Pertinent dimensions necessitated within resected surgical margin remain debatable although a tumor-free, microscopic margin with a few millimeters of grossly normal surgical perimeter is satisfactory. Majority of neurothekeomas are miniature, below <1-cm diameter, demonstrate a predominantly bland histology with minimal to absent cytological atypia along with scanty tumour extension into circumscribing adipose tissue or skeletal muscle [7,8]. Neurothekeoma can enunciate atypical microscopic features indicative of amplified aggressive potential which are designated as clinical dimension exceeding >1-cm, cytological atypia manifesting as pleomorphism, enhanced mitotic activity, infiltration into encompassing skeletal muscle or subcutaneous adipose tissue and vascular invasion. However, irrespective of emerging atypical features, tumor reoccurrence following comprehensive surgical excision is decimated [7,8].

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