S-100 negative myxoid neurothekeoma: a new type of neurothekeoma?*

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Dear Editor,

Neurothekeomas are rare benign dermal tumors, which originate from the peripheral nerve sheath. They are divided into myxoid, intermediate, and cellular types, based on the amount of myxoid matrix and on the immunohistochemical study. We report an unusual S-100 negative case of myxoid neurothekeoma, which is currently described in the literature as a new type of neurothekeoma. A 73-year old male patient presented with an asymptomatic erythematous nodule (0.8 x 0.6 x 0.5 cm in size) in the right inframandibular region for about a year (Figure 1). Diagnostic hypothesis were adenoid basal cell carcinoma, neurofibroma, and others skin adnexal neoplasms. After surgical excision with 3-mm margins, pathological studies showed multiple nodules of varying sizes, containing abundant mucin and sparse stellate cells in the dermis, consistent with myxoid neurothekeoma (Figure 2). Immunohistochemistry was focally positive for CD-68 and diffusely positive for vimentin, but negative for S-100, CD-10, CD-57, EMA, and GFAP (Figure 3). Histopathological and immunohistochemical findings corroborated the diagnosis of S-100 negative myxoid neurothekeoma, also described as myxoid neurothekeoma cell. The term neurothekeoma was coined in 1980 by Gallagher and Helwig to describe a skin tumor of neural origin. This neoplasm that originates from the sheath of peripheral nerves mainly affects the face and upper limbs of women between the second and third decades of life. It manifests as a solitary and asymptomatic papule or nodule with indolent growth.[1] Local trauma and high levels of estrogen have been linked to triggering factors.[2] Differential diagnoses include dermal nerve sheath myxoma, superficial angiomyxoma, melanocytic neoplasms, reticulohistiocytoma and plexiform fibrohistiocytic tumor. Since its initial description, there remains inconsistency

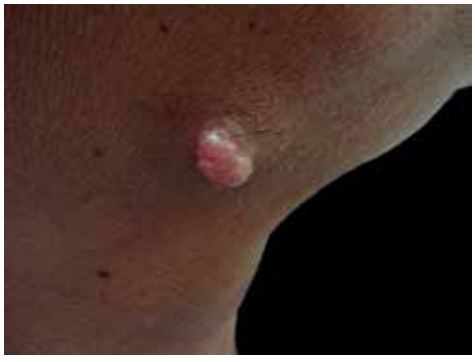

Figure 1: Erythematous nodule in the right inframandibular region

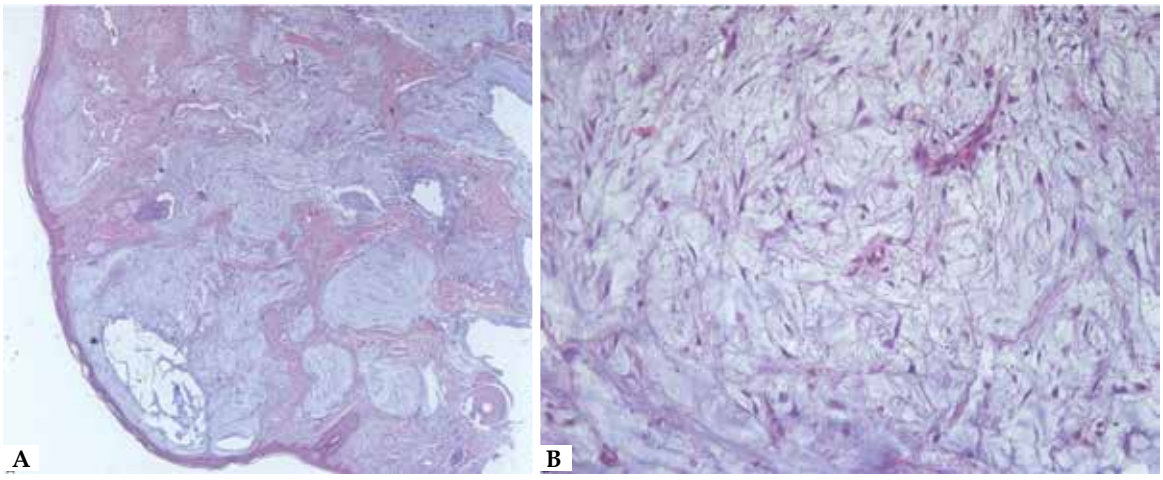

Figure 2: **A)** nodules of varying sizes with large amounts of mucin and stellate cells (Hematoxylin & eosin x20); **B**) detail of stellate cells (Hematoxylin & eosin x200)

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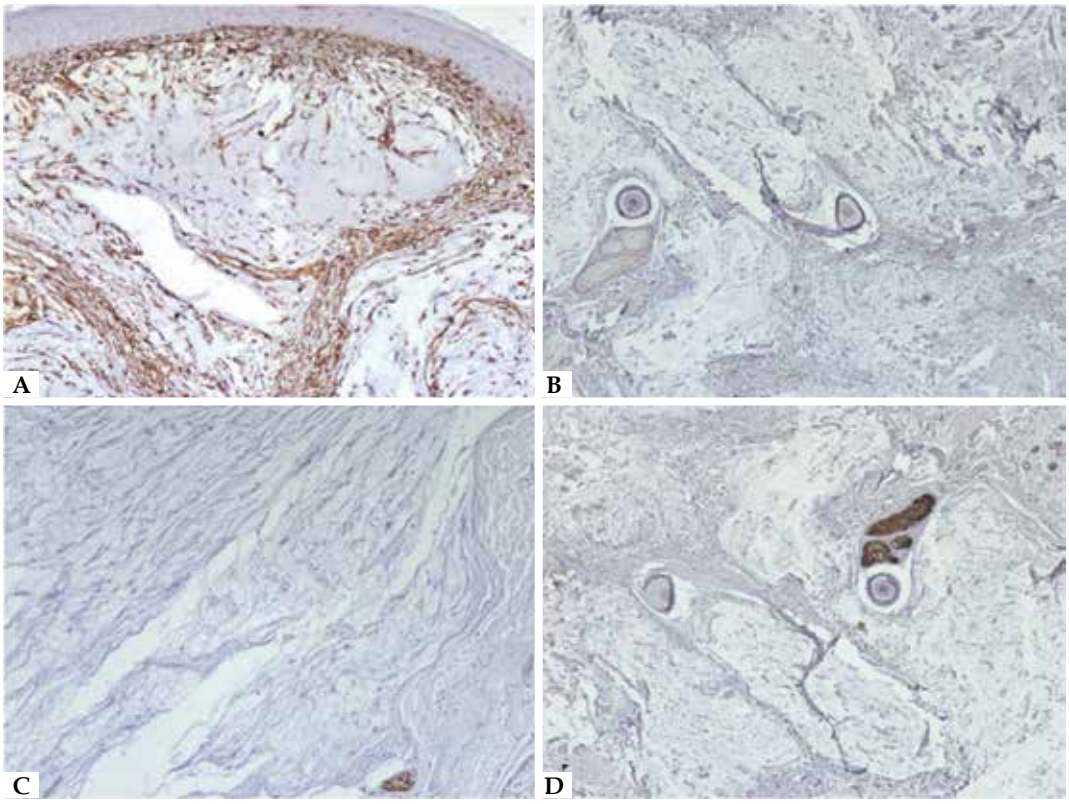

Figure 3: Immunohistochemistry: **A)** positivity for vimentin (Hematoxylin & eosin x200); **B)** positivity for CD-68 (Hematoxylin & eosin x40); **C)** negativity for S-100 in tumor cells and positivity in the nerve (Hematoxylin & eosin x100); **D)** negativity for EMA (Hematoxylin & eosin x20)

regarding the relationship of the tumor with the dermal myxoma of the nerve sheaths. Studies of large case series have shown that they are two distinct entities.[3] Myxoma also affects men and women, preferably on hands, with higher recurrence rates. Histologically, it appears as superficial multilobular masses, rich in myxoid material, with well-defined fibrous edges and stellate cells, spindle cells, and epithelioid Schwann cells. It demonstrates positivity for S-100 and GFAP.[1] The myxoid, intermediate, and cellular neurothekeoma subtypes depend on the amount of myxoid matrix and immunohistochemical profile observed. Tumors with 10% or less of myxoid matrix are classified as cellular neurothekeomas; those with more than 50% are considered myxoid neurothekeomas; values in between are considered intermediate neurothekeomas.[1,2,4] The three different variants share some histopathologic features: presence of epithelioid and spindle cells with granular eosinophilic cytoplasm; tendency to form multiple small nodules with spiral or fascicular arrangement; association with variable amount of sclerotic collagen; and occasional presence of giant osteoclast-like cells. They may exhibit increased mitotic figures and nuclear atypia.[1] Myxoid neurothekeoma is typically positive for markers of neural origin – such as S-100 protein, GFAP, and NGFR – and negative for macrophage markers – such as Ki-M1P and CD-68. The cellular variant is negative for S-100 and positive for NKI/C3, Ki-M1P, and CD-68. Immunohistochemistry suggests that neurothekeomas show differences in their origins: myxoid neurothekeomas would display neural differentiation; the cellular subtype, fibrohistiocytic differentiation.[5] Neuroectodermal antigens – such as NKI/C3, PGP9.5, and Leu-7 – and fibrohistiocytic antigens – including XIIIa factor, vimentin, EMA, or SMA – have limited diagnostic value in differentiating the subtypes.[4] S-100 negative myxoid neurothekeoma is rare, with a few cases reported in literature.[4] Some authors consider that the immunohistochemical profile is more important than histopathology to establish the subtype of the tumor. There are some similar cases reporting cellular myxoid neurothekeoma.[4] Some authors characterize this variant as a new entity, which features histopathology results typical of neurothekeomas, negative immunohistochemical markers for neural differentiation, and positive results for other markers (such as CD-68).[4] Neurothekeoma treatment consists of the complete excision of the tumors with low recurrence rates.[4]❑

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