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*Case Report*

# Cellular Neurothekeoma
# A Case Report with an Immunohistochemical Study

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**Cellular neurothekeoma preferentially affects women and has a predilection for the head, neck and arms of children and young adults. Cellular neurothekeoma is a well-circumscribed tumor involving the reticular dermis and consisting of fascicles of polygonal or spindle cells with eosinophilic cytoplasma and neuroid characteristics. We describe an additional case of cellular neurothekeoma on the upper lip. Microscopically, the neoplasm had a multinodular or lobulated architecture that were partially or completely invested by a dense band of collagen and was composed of plump, spindled, and epithelioid cells arranged in solid, infiltrating nests and fascicles. Cytologically, the neoplastic cells were relatively large and contained lightly eosinophilic, finely vacuolated cytoplasm. The nuclei were round to oval with vesicular chromatin, with no atypical mitotic figures identified. Immunohistochemical examinatioa showed that the neoplastic cells were diffusely positive for vimentin and positive for NSE, but were negative for S-100 protein. Our case was a representative example of a typical cellular neurothekeoma.**

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**Key Words:** neurothekeoma, cellular neurothekeoma, Vimentin, S-100 protein

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## Introduction

Neurothekeomas are benign neoplasms with probable neural differentiation. They were described originally in 1969 by Harkin and Reed[1] who used the name nerve sheath myxoma. The term neurothekeoma was coined by Gallager and Helwig[2] in 1980 based on their 53 patients. Names including pacinian neurofibroma, bizarre cutaneous neurofibroma, cutaneous lobular neuromyxoma, and perineurial myxoma have been used by other authors[3, 4, 5, 6]. A similar lesion consisting predominantly of epithelioid cells with minimal mucin was termed cellular neurothekeoma by Rosati et al.[7] in 1986. Several years later, Barnhill and Mihm[8] described five additional cases of cellular neurothekeoma. In this report, we describe an additional case of cellular neurothekeoma on the upper lip.

## Case report

The patient was a 59-year-old woman presenting with an asymptomatic nodule on the upper lip, which had been present for several years. The tumor had been gradually increasing in size. Clinically, the lesion was firm in consistency, measuring 0.7x0.7 cm in diameter, and was covered by normal-appearing skin. The clinical diagnosis considered was histocytoma. The lesion was completely removed and submitted for microscopic examination

The specimens were fixed in 10% buffered formalin and embedded in paraffin. Sections of 4 $\mu$ m thick were stained with hematoxylin and eosin, and alcian blue stain. Immunohistochemical staining was

performed using the avidin-biotin-peroxidase complex (ABC) method and antibodies for vimentin, neuron-specific enolase (NSE), S-100 protein, glial fibrillary acidic protein (GFAP), Leu 7 (CD57), neurofilament protein, epithelial membrane antigen (EMA), cytokeratin, smooth muscle actin (SM-actin), and desmin.

The excisional specimen revealed a rather well circumscribed tumor in the dermis. The cut surface was nodular, yellowish white. Microscopically, the neoplasm had a multinodular or lobulated architecture that were partially or completely invested by a dense band of collagen and was composed of plump, spindled, and epithelioid cells arranged in solid, infiltrating nests and fascicles (Fig 1). Cytologically, the neoplastic cells were relatively large and contained lightly eosinophilic, finely vacuolated cytoplasm. The nuclei were round to oval with vesicular chromatin, with no atypical mitotic figures identified (Fig 2). The stroma consisted of wispy collagen fibers that tended to condense in the more epithelioid areas, scattered capillary-sized vessels, and stromal mucosubstance. Focal myxomatous change, demonstrated by alcian blue staining, was present.

Immunohistochemical examination showed that the neoplastic cells were diffusely positive for vimentin (Fig 3) and positive for NSE (Fig 4), but were negative for S-100 protein. The immunohistochemical results for this case are given in Table 1.

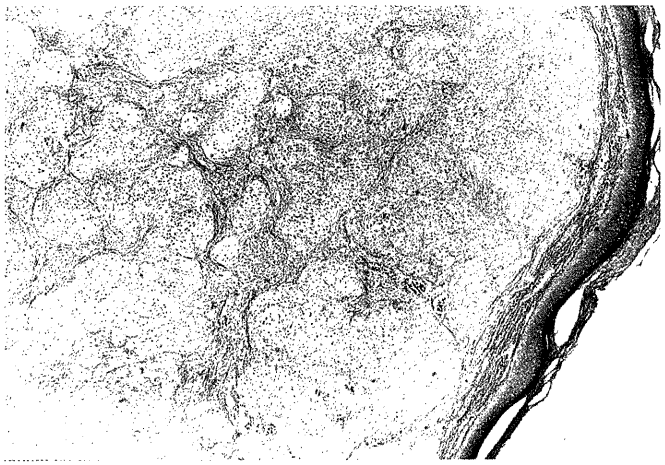

**Figure 1.** Microscopically, the neoplasm had a multinodular or lobulated architecture that were partially or completely invested by a dense band of collagen and was composed of plump, spindled, and epithelioid cells arranged in solid, infiltrating nests and fascicles. Hematoxylin & eosin, x40

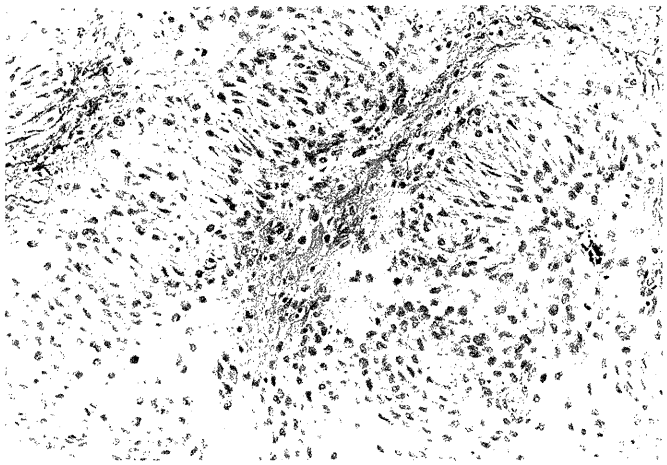

**Figure 2.** Cytologically, the neoplastic cells were relatively large and contained lightly eosinophilic, finely vacuolated cytoplasm. The nuclei were round to oval with vesicular chromatin, with no atypical mitotic figures identified. Hematoxylin & eosin, x200

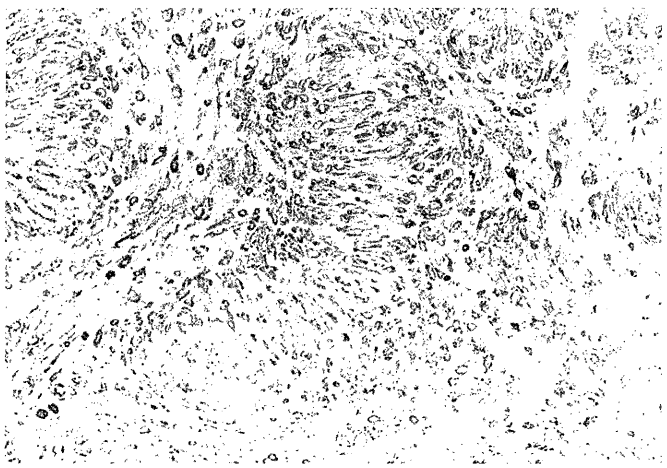

**Figure 3.** Immunohistochemical examination showed that the neoplastic cells were diffusely positive for vimentin. Vimentin, x200

**Figure 4.** Immunohistochemical examination showed that the neoplastic cells were positive for NSE, NSE, x200

**Table 1.** Results of the immunohistochemical studies

| | |
|---|---|
| Vimentin | ++ |
| NSE | + |
| S-100 | - |
| GFAP | - |
| Leu 7 | - |
| Neurofilament protein | - |
| EMA | - |
| Cytokeratin | - |
| SM-acti | - |
| Desmin | - |

++: diffusely positive, +: positive, -: negative

## Discussion

Neurothekeoma occurs most commonly as a cutaneous neoplasm in young women. Histologically, the classic or myxoid type of neurothekeoma is characterized by a lobulated, well-circumscribed proliferation of spindle and epithelioid cells in varying proportions embedded in an abundant myxoid stroma intervened with scant collagen fibers. The tumor commonly shows immunoreactivity to S-100 protein and vimentin, but is generally negative for other neural markers including Leu 7 (CD57), synaptophysin, glial fibrillary acidic protein, NSE, and other markers including EMA, cytokeratin, carcinoembryonic antigen, desmin, factor VIII-related antigen, HMB-45, $\alpha$-1-antichymotrysin, and $\alpha$-1-antitrypsin[8, 9, 10]. Tumor differentiation is assumed to be Schwannian based on ultrastructural and immunohistochemical studies[6, 11].

The concept of a histologic spectrum of neurothekeoma from myxoid to intermediate to cellular types was introduced by Barnhill and Mihm[8] in 1990 and by Husain et al.[10] in 1994. The classic myxoid type is characterized by hypocellular spindle cells with abundant mucin content whereas the cellular type is characterized by hypercellular epithelioid cells and minimal mucin content. Tumors with features of both cellular and myxoid types are classified as the intermediate type.

Cellular neurothekeoma preferentially affects women and has a predilection for the head, neck and arms of children and young adults. There has been only one reported case of cellular neurothekeoma on the lip[12]. Cellular neurothekeoma is a well-circumscribed tumor involving the reticular dermis and consisting of fascicles of polygonal or spindle cells with eosinophilic cytoplasma and neuroid characteristics.

A previous immunohistochemical study demonstrated that tumor cells of cellular neurothekeoma were positive for vimentin and negative for S-100 protein[13], while the myxoid type of neurothekeoma shows consistent S-100 protein immunoreactivity[10], supporting a Schwannian differentiation. The cell of origin of the cellular type of neurothekeoma is less clear due to the lack of S-100 protein immunoreactivity. Our findings support the observation that cellular neurothekeoma differs from the myxoid type of neurothekeoma.

In a study of cellular neurothekeoma, Zelger et al[14] noted additional similarities between cellular neurothekeoma and fibrous histiocytoma, including immunohistochemical expression of SM-actin. In our case, however, SM-actin and CD68 were not expressed. Although Laskin et al[15] reported that cellular and mixed neurothekeoma variants lack neurosustentacular differentiation and may be potentially related to tumors included in the fibrohistiocytic category, their true origin is unclear.

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