Pathological Features of Atypical Cellular Neurothekeoma of the Nasal Ala

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Abstract: Atypical cellular neurothekeoma (NTK) is a rare soft tissue tumor primarily arising in the skin. This study aimed to investigate its clinicopathological features, immunophenotype, differential diagnosis, and prognosis. We analyzed the clinical and pathological data of a 6-year-old boy who presented with a painless, red, round lesion measuring approximately 0.5 cm on the right nasal ala for two years. The lesion was moderately soft with rich surface vascularization and no ulceration. Histologically, the tumor was located in the dermis without connection to the epidermis and composed of epithelioid, mononuclear, and short spindle-shaped cells arranged in cord-like or small nodular structures separated by extensively hyalinized collagen fibers. Tumor cells exhibited mild atypia, eosinophilic cytoplasm, round and vacuolated nuclei with prominent nucleoli, and visible mitotic figures, with occasional eccentric nuclei and scattered multinucleated giant cells. Focal infiltration into deep striated muscle and perineural invasion was observed. Immunohistochemistry revealed strong positivity for PGP9.5 and CD10, focal positivity for CD99, scattered positivity for CD68, and negativity for S-100, SMA, Desmin, MyoD1, MelanA, ALK (1A4), and PCK. The Ki-67 proliferation index was 3%. Following complete surgical excision, the patient remained free of recurrence or metastasis over a 7-year follow-up period. The diagnosis of atypical cellular NTK relies on a combination of characteristic histological morphology and immunophenotypic profile.

Keywords: Neurothekeoma; Fibrohistiocytic Tumor; CD10

1. Introduction

Neurothekeoma (NTK) is a rare fibrohistiocytic tumor of the skin. Some tumors exhibit local aggressiveness but can be cured by complete surgical excision. Here, we report one case of atypical cellular NTK of the nasal region, analyzing its morphological and immunohistochemical features to improve recognition and avoid misdiagnosis.

2. Materials and Methods

2.1 Materials

Clinical and pathological data of one case of atypical cellular NTK diagnosed by the Department of Pathology, Yichang Central People's Hospital in June 2018 were collected and followed up via telephone for 7 years.

2.2 Methods

The skin tumor resection specimen was fixed in 10% neutral formalin, routinely dehydrated, paraffin-embedded, sectioned at 4 μm thickness, and stained with HE and immunohistochemistry using the EnVision method. Primary antibodies included PGP9.5, CD10, CD99, CD68, S-100, SMA, Desmin, MyoD1, MelanA, ALK (1A4), PCK, and Ki-67. All antibodies were monoclonal antibodies purchased from Maixin Biotechnology Company. PBS was used in place of primary antibodies as a negative control, and known positive tissue served as the positive control. Experimental procedures were strictly carried out according to the reagent instructions.

3.Results

3.1 Clinical Data

The patient was a 6-year-old boy admitted for "a painless red papule on the right nasal ala for 2 years with progressive enlargement." Specialist examination revealed a red, round-shaped mass of 0.5 cm in diameter on the right nasal ala (Figure 1A), moderately soft in texture, with a richly vascularized surface and no ulceration or bleeding. No other notable findings were observed. The preliminary clinical diagnosis was hemangioma. Skin tumor resection and nasolabial flap repair were

performed. No recurrence or metastasis was noted during 7 years of follow-up.

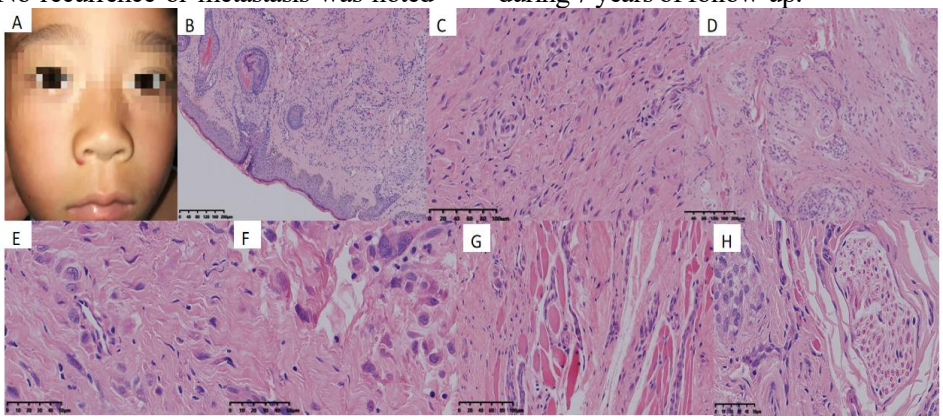

Figure 1. Appearance of the Tumor and HE Staining

A. A painless red papule on the right nasal ala.
B. The tumor is located in the dermis and not connected to the epidermis.
C. The tumor is separated by hyalinized collagen fibers into cord-like structures.
D. Some tumor cells are arranged in small nodular structures.
E. Observable mitotic figures.
F. Scattered multinucleated giant cells.
G. Tumor cells infiltrating deep into the skeletal muscle tissue.
H. Tumor cells involving a nerve.

3.2 Pathological Examination

Microscopically, the tumor was located in the dermis and not connected to the epidermis (Figure 1B). Tumor cells appeared epithelioid, mononuclear, and short spindle-shaped, separated by extensively hyalinized collagen fibers into cord-like (Figure 1C) or small nodular structures (Figure 1D). The stroma within the nodules showed mild myxoid degeneration. Tumor cells showed mild atypia, eosinophilic cytoplasm, round vacuolated nuclei, prominent nucleoli, and observable mitotic figures (Figure 1E). Some nuclei were eccentrically located. Scattered multinucleated giant cells were seen (Figure 1F). Focal areas showed tumor cells infiltrating into deep skeletal muscle tissue (Figure 1G) and involving individual nerves (Figure 1H). Immunohistochemically, tumor cells showed strong positivity for PGP9.5 and CD10, focal positivity for CD99, scattered positivity for CD68 (Figure 2), and negativity for S-100, SMA, Desmin, MyoD1, MelanA, ALK (clone 1A4), and PCK. The Ki-67 proliferation index was 3%.

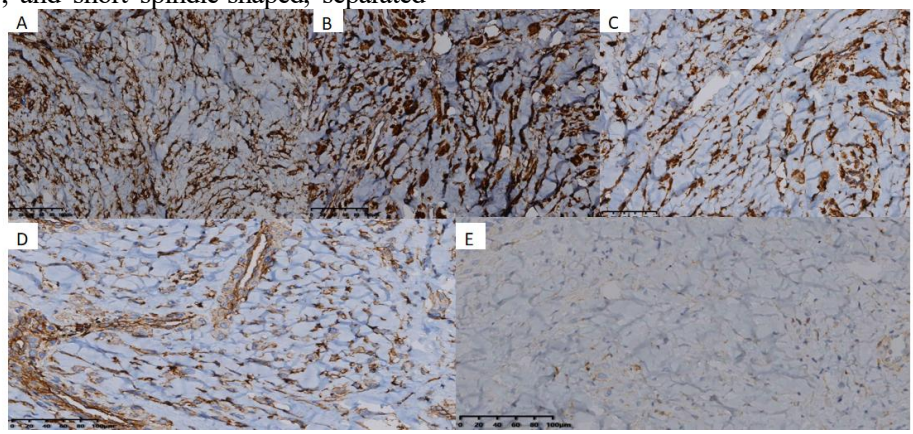

Figure 2. Immunohistochemical Stainin

A. Diffuse positivity for CD10.
B. Diffuse strong positivity for PGP9.5.
C. Scattered positivity for CD68.
D. Focal positivity for CD99.
E. Negative staining for S-100.

3.3 Pathological Diagnosis

Atypical cellular neurothekeoma.

4. Discussion

NTK is a rare soft tissue tumor. It was first reported by Harkin and Reed and diagnosed as a myxoid nerve sheath tumor [1]. In 1980, Helwing and Gallager proposed that it is a benign neural tumor of Schwann cell origin and officially named it neurothekeoma [2]. In recent years, gene expression

profiling studies have revealed its fibrohistiocytic origin, reclassifying it as part of the fibrohistiocytic tumor family [3].

4.1 Clinical Features

This tumor most commonly occurs in young women and children, with about 25% of patients being under 10 years of age. It typically presents as a slow-growing, red papule that is dome-shaped or hemispherical, slightly firm on palpation, and generally painless. It most often appears on the head, neck, or trunk. It is frequently misdiagnosed as various superficial skin or adnexal cysts, hemangiomas, pyogenic granulomas, basal cell carcinomas, or melanocytic nevi [4-6]. Histopathological diagnosis is usually made after surgical excision.

4.2 Pathological Features

NTK is often located in the dermis or subcutis, usually measuring less than 1 cm. The cut surface is gray-white, solid, and firm. Under low-power magnification, the tumor exhibits a cord-like, whorled, lobular, or nodular arrangement, separated by hyalinized fibrous connective tissue; mild myxoid degeneration may be present within the lobules or nodules. High-power magnification reveals epithelioid, mononuclear, or spindle-shaped tumor cells with eosinophilic cytoplasm, round or oval nuclei, vacuolated chromatin, and prominent nucleoli. Multinucleated giant cells may also be present [4,6,7].

Histologically, NTK can be divided into three subtypes based on the proportion of myxoid stroma:Cellular type (myxoid stroma <10%), Mixed type (myxoid stroma 10–50%), Myxoid type (myxoid stroma >50%) [8].

Features suggestive of atypical NTK include: Tumor diameter >6 cm, Infiltrative growth involving subcutaneous fat or skeletal muscle, Poorly defined tumor margins, Cytologic atypia, Increased mitotic activity, including atypical mitoses, Vascular or neural involvement [4.7].

In our case, the tumor showed minimal myxoid stroma, poorly defined borders, mild atypia, infiltration into skeletal muscle, visible mitoses, and focal nerve involvement—meeting five of the six criteria for atypical NTK.

Immunophenotypically, NTK cells commonly express NKI/C3 (CD63), CD10, and MiTF; partially express CD68, CD99, PGP9.5, SMA, and muscle-specific actin; and are negative for S-100, GFAP, Melan-A, and CD34 [4-7]. In this case, tumor cells were strongly positive for CD10 and PGP9.5, focally positive for CD99, and scattered positive for CD68, while negative for all other markers, consistent with previous reports.

4.3 Differential Diagnosis

4.3.1 *Dermal myxoid nerve sheath tumor:* Clinically appears as a slow-growing, painless nodule. Microscopically composed of lobules of varying sizes with scant cellularity and a loose, myxoid stroma. Immunohistochemically positive for S-100, GFAP, and S100a6, negative for PRAME.

4.3.2 *Melanocytic tumors (e.g., melanoma, epithelioid blue nevus, Spitz nevus):* These skin tumors share spindle and epithelioid morphology and contain intracytoplasmic pigment. Immunohistochemically positive for S-100, Melan-A, and HMB-45, which are negative in NTK.

4.3.3 *Cutaneous neurofibroma:* Typically a solitary, flesh-colored papule. Histologically small and localized in the dermis, composed of wavy spindle cells embedded in collagen. Immunohistochemically positive for S-100.

4.3.4 *Epithelioid fibrous histiocytoma:* Clinically appears as a dome-shaped nodule. Microscopically located in the dermis with clear borders, composed of eosinophilic epithelioid cells in a whorled or mosaic pattern. Immunohistochemically positive for ALK.

5. Treatment and Prognosis

Clinically, complete surgical excision is the most common treatment for this tumor. However, due to the rarity of NTK, there is still no consensus on the appropriate surgical margin. At present, the common standard is that the tumor is considered adequately excised if no residual tumor is observed at the surgical margins under a microscope.Given the potential for local invasion in atypical NTK, some scholars recommend wide excision to prevent recurrence. Nevertheless, to date, there have been no reported cases of metastasis or recurrence following complete excision of this tumor[9-11].Although the present case showed histological features of atypia, the lesion was completely excised, and no recurrence or metastasis was observed during a 7-year follow-up.

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