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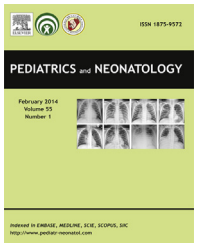

CASE REPORT

Cellular Neurothekeoma of the Upper Lip in an Infant

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Cellular neurothekeoma is an uncommon benign skin neoplasm and also a variant of neurothekeoma. Cellular neurothekeomas usually occur in the skin of the upper trunk, head, or neck of children and young adults; however, they rarely occur in infants or involve the lip. A 6-month-old male infant was incidentally found to have a tumor in the upper lip. The tumor was elastic, nontender, and movable, and the overlying mucosa and skin were normal without discoloration. The tumor was excised from the mucosal side of the upper lip, and a pathological examination revealed cellular neurothekeoma. Cellular neurothekeoma in the lip of an infant without overlying skin discoloration might delay the diagnosis and lead to wrong preoperative diagnosis. No similar case has been reported in the literature.

1. Introduction

Lip tumors in children are uncommon, and most of them are benign.[1,2] The pathology of lip tumors is variable, with hemangioma as the most common one.[1,2] Cellular neurothekeoma is an uncommon benign skin neoplasm and a variant of neurothekeoma.[3] Cellular neurothekeomas usually occur in the skin of the upper trunk, head, or neck of children and young adults; however, they rarely occur in infants or involve the lip.[3—5] We describe a case of cellular neurothekeoma in the upper lip of a 6-month-old male infant. No similar case exists in the literature. The clinical and pathological characteristics of this patient are discussed, and the literature is reviewed.

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2. Case Report

A 6-month-old previously healthy male infant was found incidentally to have a nodular lesion in the upper lip by his mother. On examination, the patient was well except that a nodule was noted in his upper lip. This nodule was elastic, nontender, movable, and measured 1.0 × 0.7 × 0.5 cm. The overlying mucosa and skin were normal without discoloration. No neck lymph node enlargement was found. No other abnormal physical or laboratory findings were present. The patient had no history of trauma, and the family history of neoplasm was negative. Ultrasonogram revealed a well-defined, hypoechoic, heterogeneous mass. The preoperative diagnosis was an epidermoid cyst. An operation was performed under general anesthesia. We approached the tumor from the mucosal side of the upper lip (Figure 1). The tumor was well-defined, elastic, unencapsulated, and extended to the submucosal muscular layer. The tumor was totally excised. The patient stood the operation well, and the postoperative course was uneventful. Histological examination (Figure 2) revealed that the tumor was composed of hypercellular epithelioid cells with diffuse and fascicular growth patterns. Large, hyperchromatic tumor cells and focal mitoses were seen occasionally. Myxomatous change and some trapped nerve bundles were identified. No atypia was found. Immunohistochemically, the tumor was positive for neuron-specific enolase and smooth muscle actin, but negative for S-100 protein, desmin, and glial fibrillary acidic protein. Mild immunoreactivity of CD34 was noted. The immunoreactivity of NKI/C3 was unclear because no such examination was done. Histologically, the tumor was a cellular neurothekeoma. After a 6-month follow-up, the patient was well, and no tumor recurrence was noted.

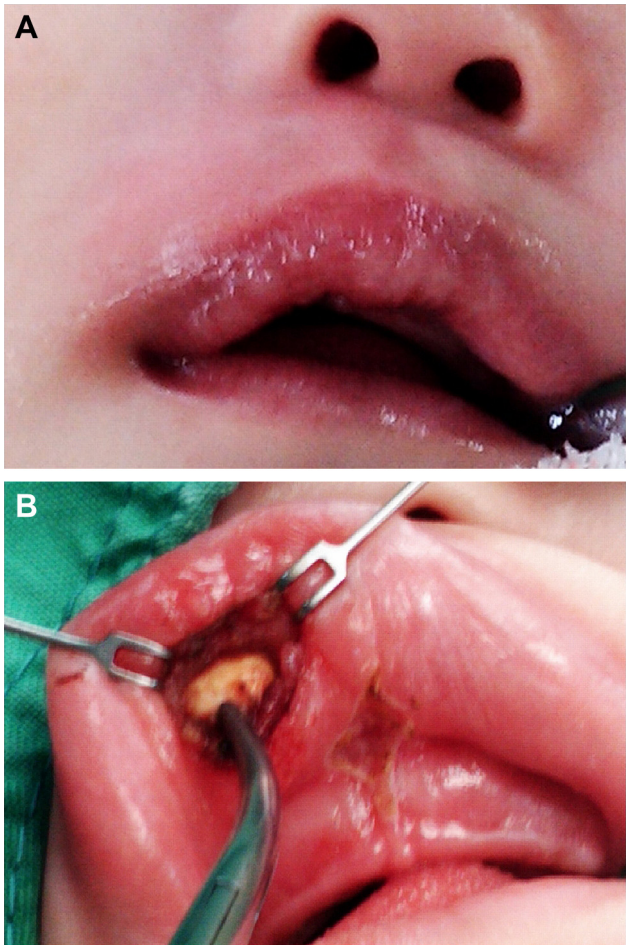

Figure 1 Photographs of the patient. (A) Absence of discoloration of the upper lip. (B) The tumor was excised from the mucosal side of the upper lip.

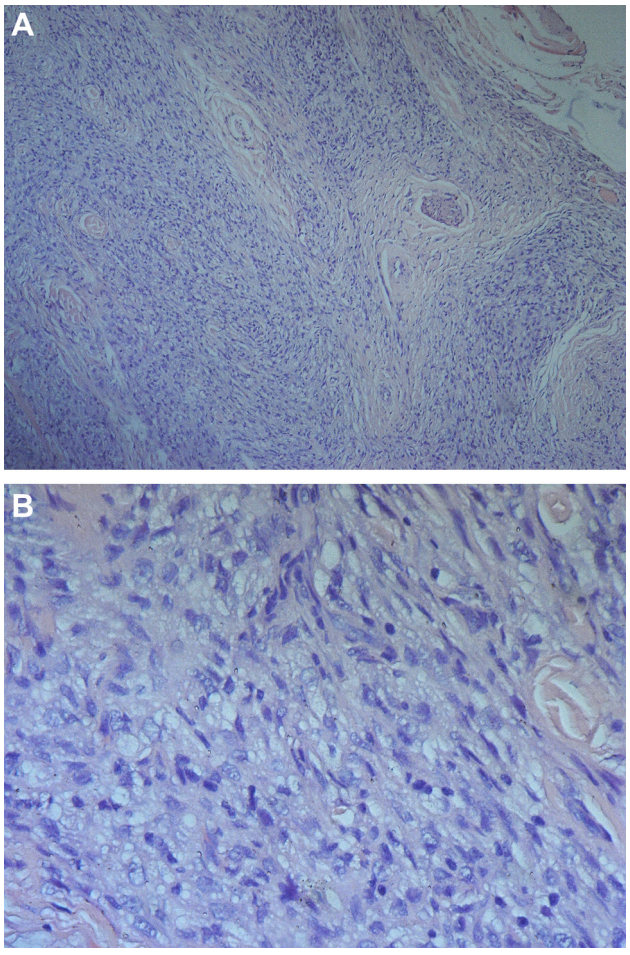

Figure 2 Histopathology of the tumor. The tumor was composed of hypercellular epithelioid cells with diffuse and fascicular growth patterns. [Hematoxylin and eosin staining: (A) 40×; (B) 200×.]

3. Discussion

Soft tissue tumors in children differ from those in adults in frequency, anatomical site, histological types, and prognosis.[6] Tumor occurring in the lip of an infant is extremely rare and difficult to diagnose, especially for a lesion without changes in the overlying skin, as in this case. The pathology of lip tumors includes hemangioma, lymphangioma, hemangiolymphangioma, papilloma, neurofibroma, retention cyst of small salivary glands, venous malformation, eosinophilic granuloma, common

warts, rhabdomyosarcoma, fibrosarcoma, and metastasis of neuroblastoma, with hemangioma as the most common.[1,2] However, our patient's tumor was a cellular neurothekeoma.

Neurothekeoma usually presents a subepithelial Grenz zone, infiltrative growth pattern, mild nuclear atypia, lymphohistiocytic infiltrate, hyalinized collagen, giant cells, and various stroma.[7] Traditionally, neurothekeoma is classified into three types based on cellularity, mucin content, and growth pattern: hypocellular (myxoid) type, cellular type, and mixed type, depending on the amount of myxoid matrix.[4,5] Myxoid neurothekeomas have >50% myxoid matrix, cellular neurothekeomas have ≦10% myxoid matrix, and mixed-type neurothekeomas have >10% and ≦50% myxoid matrix.[4,5] In myxoid neurothekeomas, there are well-circumscribed fascicular masses with a prominent myxoid stroma.[5] This type characteristically produces positive results of stain for S-100, collagen type IV, and nerve growth factor receptor; it does not stain for epithelial membrane antigen or markers of histiocytic differentiation.[5] In contrast, cellular neurothekeomas show no evidence of encapsulation and have a lobular growth pattern; moreover, the cells are epithelioid with eosinophilic cytoplasm.[5] The tumor cells in the cellular neurothekeomas do not stain with antibody to S-100, collagen type IV, or nerve growth factor receptor.[5] The mixed type of neurothekeomas usually shows areas of varied cellularity that contain focal myxoid region and mixed immunohistochemical reactivity.[5]

The origin of cellular neurothekeomas is uncertain because they consist of a mixture of undifferentiated cells with immature features of Schwann cells, fibroblasts, myofibroblasts, perineural cells, smooth muscle cells, and histiocytes.[8] Recent studies have found that the gene expression pattern of neurothekeomas of all subtypes, including cellular neurothekeoma, closely resembles that of cellular fibrous histiocytomas; thus, neurothekeoma is considered a variant of fibrous histiocytoma.[9] However, the origin of cellular neurothekeoma is still debatable, and cellular neurothekeoma is difficult to diagnose because of its morphologic similarity to other dermal tumors.[5,9] Thus, immunohistochemical studies are often performed to establish a diagnosis.[3,4,9] The present case was negative for S-100, desmin, and glial fibrillary acidic protein, and positive for neuron-specific enolase, smooth muscle actin, and mild immunoreactivity for CD34, which is consistent with most cellular neurothekeomas described in the literature.[3,4,9] NKI/C3 has been described as a marker for melanoma, and it has recently been used as a marker to separate cellular neurothekeoma from other dermal tumors.[10] The cellular neurothekeomas frequently have a positive immunoreaction for NKI/C3, whereas myxoid neurothekeomas often show negative NKI/C3 immunoreactivity, which indicates that NKI/C3 immunoreactivity may be of value in distinguishing between cellular and myxoid neurothekeomas.[3,11] However, NKI/C3 stains a broad spectrum of neoplastic tissues including juvenile xanthogranuloma, atypical fibroxanthoma, and cellular fibrous histiocytoma.[10] Thus, this marker seems to lack specificity, and caution should be exercised when diagnosing cellular neurothekeomas based solely on positive staining with NKI/C3.[3]

Neurothekeomas most frequently arise in the dermis or subcutaneous tissue of the face, neck, shoulders, and arms of children or young adults.[5–7] They rarely occur in infants and seldom involve the lips.[3,4] A review of the literature in English reveals only four cases of neurothekeomas in infants, and none is cellular neurothekeoma or involves the lip.[3,12–14] In an infant with a lip tumor that has no skin change and is asymptomatic as in the case with our patient, the tumor might be neglected and is difficult to diagnose. Surgery is another important problem. For lip tumors, complete tumor excision and cosmetics should be considered together. Cellular neurothekeomas may have deep involvement of the subcutis and skeletal muscle when they are located in the face, and such characteristics might contribute to tumor recurrence.[4] Additionally, tumors on the face tend to have enhanced recurrent potential because of a more conservative initial procedure.[4] Therefore, cellular neurothekeomas may recur. Their recurrence rate was estimated to be 7.5%, as 10 of 133 patients with cellular neurothekeomas had tumor recurrence after a mean of 18 months of follow-up, and most recurrent cellular neurothekeomas are located at the face and have been marginally excised or had involved excision margins.[3] In our patient, we approached the tumor from the mucosal side of the upper lip to avoid visible scarring. Although the tumor was totally excised, it extended to the muscular layer; this patient must be followed up regularly to observe whether the tumor recurs.

Although the vast majority of oral lesions in infants and children are benign in character, ranging from 84% to 99% of cases, malignant tumors should be taken into account, and most of them are sarcomas.[2] Clinically, benign tumors are usually slow-growing, mobile, and asymptomatic; furthermore, malignant tumors often present as rapidly enlarging masses and may extend deeply to muscle and fascia.[6] Sometimes it is difficult to differentiate between benign and malignant tumors, and any suspicion of malignancy has to be taken as an indication to perform histopathological examination.[2] In addition, immunohistochemical and ultrastructural studies may be necessary for the differential diagnosis of the oral tumors.[13] Most cellular neurothekeomas present as asymptomatic papules or nodules, with variable consistency, and a mean diameter of 1 cm, but with rapid growth.[7] However, neurothekeomas can occasionally have atypical features, including large tumor size (up to 6 cm), deep penetration (extending into skeletal muscle or subcutaneous fat, or both), diffusely infiltrative bordered, vascular invasion, high mitotic rate, and enlarged cytological pleomorphism.[14,15] These atypical features might suggest the potential for malignant transformation of cellular neurothekeomas.[3,6,14,15] However, cellular neurothekeomas with atypical features do not behave in a low-grade malignant fashion, with rare recurrence and absence of metastasis; thus, such atypical features have been considered to have no clinical significance.[3] Therefore, it is important to differentiate cellular neurothekeomas from malignant lesions because the treatment strategies are different.

In summary, although cellular neurothekeoma rarely occurs in the lip of an infant, it is important to be aware of this rare lesion that often causes diagnostic and/or treatment problems.

Conflicts of Interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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