Sialoblastoma of the cheek: A case report and review of the literature

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Abstract. Sialoblastoma is a rare salivary gland tumor that recapitulates the primitive salivary gland anlage. The authors herein report a case of sialoblastoma of a minor salivary gland, clinically presenting with progressive enlargement of a mass in the cheek of a 1-year-old female infant. Histopathologically, the mass consisted of tight clusters of basaloid cells and partially formed ductal and pseudo-ductal spaces separated by thin fibrous bands. Immunohistchemical studies demonstrated the presence of cytokeratin AE1/AE3, p63, CD99, α-fetoprotein (AFP) and Hep Par-1 expression in a considerable number of tumor cells. The clinical and pathological characteristics are presented and relevant literature is reviewed. Early complete surgical excision is recommended for the treatment of sialoblastoma. Radiation may be considered in cases with incomplete resection of the tumor. Chemotherapy may play a vital role in extensive, metastatic, or relapsed cases, or in cases with inadequate excision. The follow-up treatment should be frequent and prolonged. To the best of our knowledge, this is the first reported case of sialoblastoma of the cheek with immunoreactivity for AFP and Hep Par-1, which may be associated with the embryonic origin of the tumor. AFP may be a useful marker of tumor response in patient with sialoblastoma.

Introduction

Sialoblastoma is a rare salivary gland tumor that recapitulates the primitive salivary gland anlage. Sialoblastoma was first described in 1966 by Vawter and Tefftas and referred to as embryoma (1). In 1988, Taylor suggested the term 'sialoblastoma', as it describes both the dysontogenic characteristics and the origin of this tumor from the salivary gland (2-4). The various appellations include congenital basal cell adenoma, basal cell adenoma, basaloid adenocarcinoma, congenital hybrid basal cell adenoma-adenoid cystic carcinoma, and embryoma. Sialoblastoma most commonly affects the major salivary glands and is histologically characterized by variably arranged, tight clusters or clumps of basaloid cells and partially formed ductal and pseudo-ductal spaces separated by thin fibrous bands. The overall prognosis of this type of tumor remains controversial. Sialoblastoma has a tendency to progress to local invasion, local recurrence and occasional metastasis. In 1996, according to the third series of the Armed Forces Institute of Pathology (AFIP) classification of salivary gland tumors, sialoblastoma was classified as a benign epithelial neoplasm. However, according to World Health Organization (WHO) classification of head and neck tumor and the fourth series of the AFIP classification of salivary gland tumors, sialoblastoma was reclassified as a malignant epithelial tumor (5). The authors herein report the clinical, histopathological and immunohistochemical characteristics of sialoblastoma.

Case report

Clinical summary. A 1-year-old female infant presented with a palpable mass of the right cheek, which had originally appeared and progressively enlarged since the age of 2 months. The magnetic resonance axial T1-weighted (T1W) images revealed a lobulated soft tissue lesion anterior to the right mandible (Fig. 1A) and the axial contrast-enhanced T1W images showed minimal enhancement (Fig. 1B). An incisional biopsy was performed and histological examination revealed basaloid tumor cells with focal ductal differentiation, suggestive of sialoblastoma. The post-incisional serum α-fetoprotein (AFP) level was 99 ng/ml. Subsequently, complete excision was performed. The final pathological diagnosis was high-grade sialoblastoma with unfavorable histology, T2N0M0. The post-operative course was uneventful. Following complete surgical removal, the serum AFP normalized and radiographic disease disappeared. The patient remains free from recurrence 2 years after complete excision.

Pathological findings. On gross examination, a lobulated soft tissue mass, measuring 3.8x3x2.5 cm and weighing 12 g, was excised (Fig. 2A). The cut sections displayed a homogeneous solid gray-tan surface (Fig. 2B). The microscopic findings

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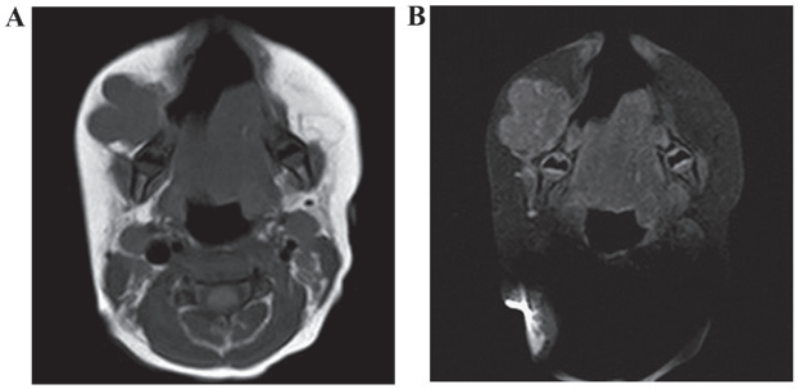

Figure 1. (A) Magnetic resonance imaging (MRI) axial T1-weighted (T1W) image showing a lobulated soft tissue lesion anterior to the right mandible. (B) MRI axial contrast-enhanced T1W image showing minimal enhancement.

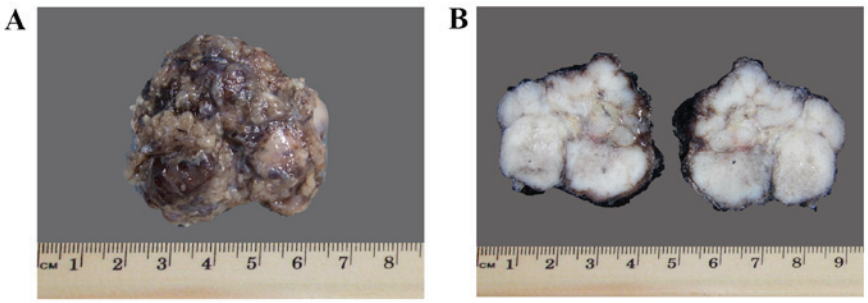

Figure 2. (A) Macroscopically, the excised tumor was a lobulated soft tissue mass. (B) Cut sections of the tumor showing a homogenous solid lobulated gray-tan surface.

included solid nests of basaloid cells and partially formed ductal and pseudo-ductal spaces separated by thin fibrous bands (Fig. 3). The basaloid cells were characterized by high nuclear:cytoplasmic ratio, round to oval nuclei, fine nuclear chromatin, small nucleoli and scant to moderate pale eosinophilic cytoplasm. The number of mitotic figures was 50 per 10 high-power fields (HPFs). Primitive duct formations were observed (Fig. 4). Vascular, perineural and skeletal muscular invasion was also observed, as was 10% tumor cell necrosis. Immunohistochemical staining showed the tumor cells to be positive for cytokeratin AE1/AE3. Some tumor cells were also positive for epithelial membrane antigen, cytokeratin 5/6, smooth muscle actin, p63, CD99, S100 protein, AFP, and Hep Par-1 (Figs. 5 and 6), while immunostaining for cytokeratins 7 and 8/18 was only positive in the ductal structures. Vimentin immunostaining was positive in both tumor cells and fibroblastic stromal cells. Finally, immunostaining was negative for cytokeratin 20, neuron-specific enolase, chromogranin A, synaptophysin, CD56, CD57, CD31, CD34, leukocyte common antigen, placental alkaline phosphatase, human melanoma black 45, Wilms tumor 1, glial fibrillary acidic protein and desmin. The Ki67 proliferative index was 70%. The tumor cells exhibited a negative signal for Epstein-Barr virus-encoded small RNAs on *in situ* hybridization.

Discussion

Primary salivary gland tumors are rare in infancy and childhood (1). The incidence of salivary gland tumors in children aged <5 years is extremely rare (1), particularly during infancy (1). In the first decade of life, the incidence of salivary gland tumors is <0.25% (2). The majority of salivary gland tumors in children are non-epithelial neoplasms (8). Hemangioma is the most common salivary gland tumor during the first year of life (6,7).

Sialoblastoma is a rare epithelial neoplasm of salivary gland origin in children (3), with ~50 cases reported in the English literature (5). This tumor may occur during the congenital, neonatal, or childhood periods (9,10). However, the vast majority of the cases are identified at or shortly after birth (5), with a median age at diagnosis of 9.8 months (9). Sialoblastoma exhibits a male predilection of ~2:1. These tumors are mostly found in the parotid and submandibular glands, although involvement of the minor salivary glands has also been reported. The size of tumor is ranging from 1.5 to 15 cm in greatest dimension (5). The majority of the patients clinically present with a slow-growing, painless, subcutaneous mass (8).

Regarding the macroscopic findings, most tumors are multilobulated, firm, tan-pink to yellow masses (8,10). Microscopically, sialoblastomas exhibit the primitive embryonic histological characteristics of salivary gland tissue, together with basaloid epithelial components and a variable amount of stroma (1,10). This tumor consists of variably arranged, tight clusters or clumps of basaloid-like cells in a background of dispersed epithelial and myoepithelial cells, and partially formed ductal and pseudo-ductal spaces separated by thin fibrous bands (8,11). These microscopic characteristics

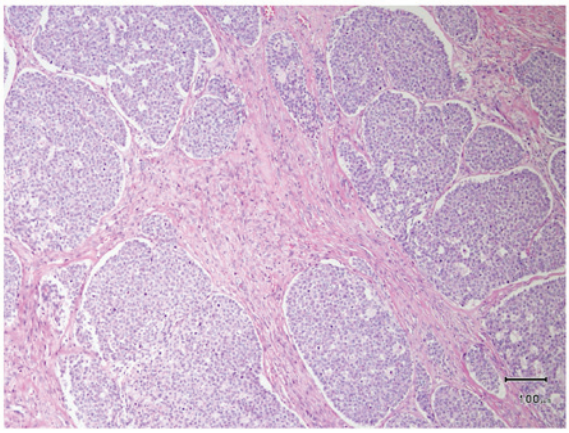

Figure 3. Microscopically, the tumor was composed of solid nests of basaloid cells with thin intervening stroma. The tumor cells exhibited a high nuclear:cytoplasmic ratio, round to oval nuclei, fine nuclear chromatin, small nucleoli and scant to moderate pale eosinophilic cytoplasm (hematoxylin and eosin staining; magnification, x100).

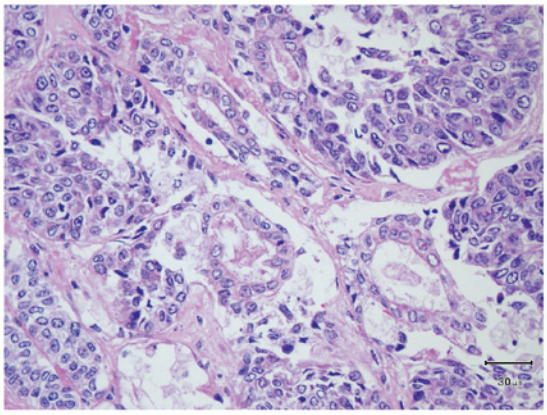

Figure 4. Primitive duct structures were observed on microscopic examination (magnification, x400).

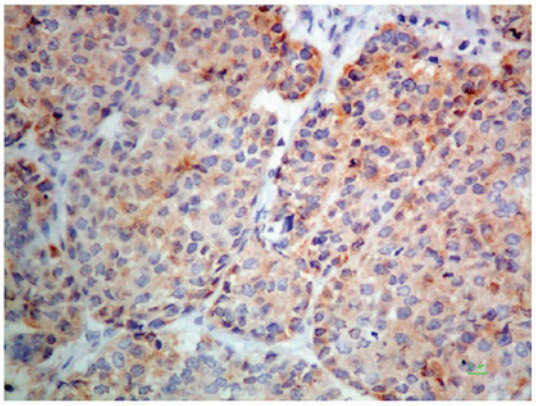

Figure 5. The tumor cells exhibited immunoreactivity for α-fetoprotein (magnification, x400).

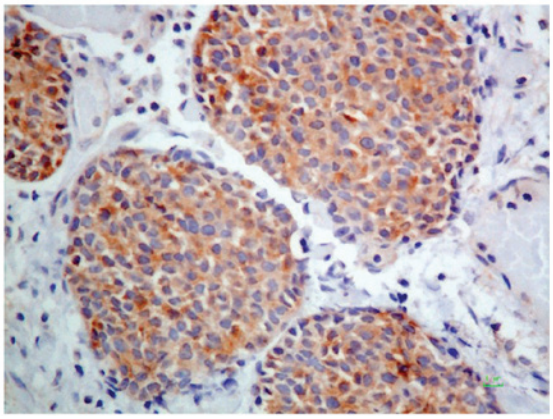

Figure 6. The tumor cells exhibited immunoreactivity for Hep Par-1 (magnification, x400).

reflect the pre-acinar stage of salivary gland morphogenesis, together with primitive cell masses, forming ducts and pseudo-ductular spaces, without acinar differentiation (3,11).

The differential diagnosis includes adenoid cystic carcinoma and basal cell adenoma. One-third of sialoblastomas exhibit a cribriform growth pattern, which is different from adenoid cystic carcinoma regarding various histological characteristics, including prominent, elongated and branching ductal structures within basaloid cells bulbs, thickened tubules with basaloid cells, and larger basaloid cells with more obvious cytoplasm (12). In contrast to basal cell adenoma, sialoblastoma is composed of more primitive cells that exhibit less prominent peripheral palisading of nuclei, significant cytological atypia and higher mitotic activity, and often infiltrate the surrounding tissue, including vascular, perineural and skeletal muscular invasion.

Immunohistochemical studies have reported that sialoblastoma stains positive for cytokeratin in the ductal cells and for vimentin, smooth muscle actin and S100 in the outer ductal parts (5,11). Solid nests of basaloid cells are focally positive for S100 and vimentin (11). The immunohistochemical results in our case were compatible with previous reports. In addition, our case was also immunohistologically and serologically positive for AFP (11,13). Moreover, immunohistochemical investigation demonstrated positivity for Hep Par-1 in a considerable number of tumor cells.

The presence of anaplasia, neurovascular invasion and necrosis were suggested as adverse prognostic factors (2,6). Other adverse histological characteristics include infiltration of the capsule (12). Sialoblastomas may be histomorphologically divided into two groups, namely favorable and unfavorable groups (10). The characteristics of the favorable group include circumscription and infrequent mitoses (<3-4/10 HPFs) (10), whereas the characteristics of the unfavorable group include anaplasia, frequent mitoses (≥4/10 HPFs), apoptosis, necrosis and a high Ki67 index (10). According to this classification, the pathological findings of our patient were those of the unfavorable group, namely frequent mitoses (50/10 HPFs) and high Ki67 proliferation index (70%).

The pathogenesis of sialoblastoma has not been fully elucidated. It has been suggested that sialoblastoma originates from retained blastema cells in the salivary gland, rather than basal reserve cells. Dysembryonic salivary gland changes have been described adjacent to the tumor, with proliferation of the terminal ductal epithelial bulbs. In tumor chromosome study, the cytogenetic karyotype of sialoblastoma was 47,XX,del(3)(q13),inv(9)(p11q12)c,+?r [5]/46,XX,inv(9)(p11q12)c[41] (14).

The aberrations detected in the sialoblastoma (deletion of the long arm of chromosome 3 and ring chromosome formation) are different from those detected in other salivary gland tumors, suggesting that the pathogenetic mechanisms differ between sialoblastoma and other salivary gland neoplasms (14).

A case with a concurrent sialoblastoma associated with hepatoblastoma has been reported (9). Furthermore, there are few reports in the literature documenting the focal expression of AFP in tumor cells. Our patient also demonstrated co-expression of AFP and Hep Par-1 in tumor cells. AFP is an oncofetal antigen that is produced by the fetal liver. These data suggest that there may be an association between hepatic tumorigenesis and the development of sialoblastoma. However, since studies on the association between sialoblastoma and hepatic markers remain scarce, the pathogenesis of sialoblastoma should be further investigated.

The prognosis of sialoblastoma is controversial. Sialoblastoma has a tendency to progress further with local invasion, local recurrence and occasional metastasis (5). In general, in infants and children, sialoblastoma is usually of low-grade malignancy and most cases have a favorable outcome (12). However, although they generally behave benignly, these tumors may be associated with lymphatic metastases (12). Approximately one-third of sialoblastomas develop local recurrence and metastasis (12). Recurrences have been reported as late as 4 years after excision (7) and distant metastases usually involve the lung and lymph nodes (5,12).

Due to the limited number of the cases, definitive treatment guidelines have not yet been established (7,9). Early complete surgical excision remains the cornerstone of the surgical management of sialoblastoma (2,7,9,15), whereas radiotherapy and chemotherapy remain controversial (15). Radiation may play a role in cases with incomplete tumor resection (8). However, since the disease mostly occurs in childhood, the use of radiotherapy may be limited, due to the radiation-related side effects, such as impaired bone growth, abnormal facial structure and mutagenic effects (8,9). Sialoblastoma is likely sensitive to chemotherapy (9), which may be useful in patients with extensive or metastatic tumors, relapsed cases, or inadequate surgical excision of a primary tumor (1,7,9,15). The protocols are usually based on the chemosensitivity, as with other mesenchymal tumors (7). The use of neoadjuvant chemotherapy for locally invasive tumors, rather than extensive, mutilating surgery, has also been suggested (9). The follow-up should be frequent and prolonged. AFP may be a useful marker of tumor response in patients with sialoblastoma.

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