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Case Report

Lingual alveolar soft part sarcoma in a pediatric patient: Case report and literature review

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ABSTRACT

Alveolar soft part sarcoma (ASPS) is a rare soft tissue sarcoma that presents most commonly in the extremities of adolescents and young adults. Involvement of the head and neck is more common in younger patients. A 2-year-old found to have localized lingual ASPS and was treated successfully with partial glossectomy. We describe this rare form of sarcoma, discuss management options, review updated literature and present our patient's outcome after 5 years of close follow-up.

1. Introduction

Alveolar soft part sarcoma (ASPS) is a rare soft tissue sarcoma with a predilection for adolescents and young adults that tends to occur in the extremities. In younger patients, the head and neck are more likely to be involved, with the orbit and tongue most commonly affected [1]. The lesion is typically slow growing, and when present in the tongue, patients may have dysphagia, dysarthria, and discomfort [2]. ASPS is often initially misdiagnosed and the proper diagnosis is not made until final surgical pathology. Delay in diagnosis can be devastating as the disease becomes challenging to treat once it metastasizes, although hematogenous spread to areas such as the brain and lungs is uncommon [1].

We present a case of lingual alveolar soft part sarcoma in a toddler, discuss surgical treatment, and report on over 5 years of follow-up. We also provide an updated review of the literature, which includes reports of potential new treatment options for ASPS.

2. Case report

A 12-month-old male was incidentally noted to have a "thickened tongue" at his 12-month well visit to his primary pediatrician. The patient was asymptomatic, without feeding problems or failure to gain weight. A mucocele was suspected, and given his lack of clinical symptoms, observation was advised. Over time, however, a more well-defined lesion developed and with further growth there was some associated retrodisplacement of the tongue. At this time, the patient, now 23-months-old, was referred to Pediatric Otolaryngology, and examination revealed an approximately 2-cm cystic appearing, bluish lesion involving primarily the right ventral tongue and floor of mouth. The findings were most consistent with a mucocele, and therefore imaging was not felt to be necessary. Surgical excision was recommended on a non-urgent basis.

The surgical date was ultimately moved up after the patient became symptomatic with drooling and discomfort. At the time of surgery, the lesion was noticed to be more consistent with a soft tissue mass than a cystic mass (Fig. 1), and therefore intra-operative frozen section was obtained. Pathology reported plump cells with small nuclei forming gland-like structures, reminiscent of acinic cell carcinoma. Given the high suspicion for malignancy in frozen section, the patient underwent partial glossectomy for definitive

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surgical management. Microscopic sections of the tumor showed alveolar (nested) and solid arrangement of the neoplastic cells (Fig. 2) with a rich vascular network. The neoplastic cells had moderate to abundant eosinophilic cytoplasm and nuclei with prominent nucleoli (Fig. 2B). At the periphery of the tumor there was conspicuous vascular space invasion (Fig. 2C). Immunohistochemical staining with the antibody to translocation factor E3 (*TFE3*) demonstrated diffuse strong nuclear staining (Fig. 2D). Both periodic acid-Schiff with diastase treatment (PAS-D) stain and electron microscopy failed to demonstrate the characteristic intracellular crystalline material. However, the characteristic histologic findings and *TFE3* positive staining were sufficient for rendering a diagnosis of ASPS. Subsequently, fluorescent in-situ hybridization (FISH) performed at a reference center was positive for *TFE3* rearrangement confirming the diagnosis.

Given the rarity of the malignancy, there is no protocol to guide workup, management, and post-treatment surveillance for this disease. Following his operation, the patient was evaluated by the Pediatric Oncology service. Post-operative workup to assess sites of reported metastases in this disease was performed, including CT chest, MRI of the head and neck, and a bone scan. The patient had no definitive evidence for metastatic disease in the lungs, brain, or bone. The consensus of the multidisciplinary Pediatric Tumor Board was to observe the patient and monitor with serial imaging studies with specific focus on a 2 mm subpleural pulmonary nodule not thought to represent disease. The patient was followed closely in Pediatric Otolaryngology clinic and Pediatric Oncology clinic. He initially underwent thorough examination under anesthesia every 3–4 months while he was sedated for imaging studies, but was later able to cooperate for examination and imaging without sedation. One year after diagnosis, he continued to have MRIs as well as surveillance imaging of the chest consisting of CT alternating with x-ray every 6 months due to the presence of the identified pulmonary nodule. Bone scan and focused brain imaging were not pursued serially in the absence of clinical symptoms and the rarity of metastases to such sites. The patient has been followed for 5 years with no evidence of recurrence or spread of disease, including the unchanged pulmonary nodule.

3. Discussion

ASPS was first described by Christopherson et al., in 1952 [3] in a retrospective study of twelve similar cases seen at Memorial Sloan Kettering Cancer Center. Since then the literature has primarily consisted of case reports of ASPS in both adults and children.

Histologically, individual tumor cells in ASPS are large and round or polygonal with eosinophilic, finely granular cytoplasm. Nuclear atypia and mitoses are uncommon. An organoid or nesting pattern of cells is characteristic, with these areas being separated by delicate webs of connective tissue containing vascular channels lined by flattened endothelium. Solid areas are also identified, a pattern especially seen tumors identified in infants and children [4]. Intracytoplasmic crystals are found in 80% of cases with PAS-D [5]. Multiple attempts to determine the differentiation of the tumor have resulted in disparate findings, with some investigators suggesting similar cellular origin to myoblastoma or paraganglioma, and others suggesting similar origin to rhabdomyosarcoma [6,7]. The inability to reach consensus resulted in the World Health Organization classifying this as a tumor of uncertain differentiation.

ASPS represents less than 1% of all soft tissue sarcomas. Traditionally, the tumor occurs in adolescents and young adults, 15–35 years of age, with a slight female preponderance. When considering all patients with ASPS, the tumor involves the extremities in 44% of cases, and occurs in the head and neck in up to 27% of cases. In children, however, the head and neck region is more common, with particular involvement of the orbit and tongue. One of the largest case series of ASPS revealed lingual ASPS present in 5% of cases [4]. Approximately 70% of cases of non-lingual ASPS occur in patients older than 20 years, whereas lingual ASPS has a median age of 5 years. The lesion is typically slow growing, although is considered incurable if metastasized. On the tongue, it is brought to the attention of the patient by localized symptoms such as dysphagia, dysphonia, and discomfort [2].

Due to its vascularity, the lesion resembles a benign vascular tumor on imaging, similar to hemangioma or venous malformation. However, low attenuation on CT images as well as high signal intensity with flow voids on T2-weighed images can be used to distinguish ASPS from other more benign diagnoses in the tongue [8].

Previously, basic immunohistochemistry was of limited diagnostic value in these tumors: the tumor is generally negative for epithelial markers as well as neuroendocrine markers. Pathologic evaluation of these cases was revolutionized with the identification of chromosome 17q25 involvement by multiple investigators and the subsequent description of the gene deletion 17q25 by Heimann [9] with fluorescence in situ hybridization (FISH) in 1998. Landmark

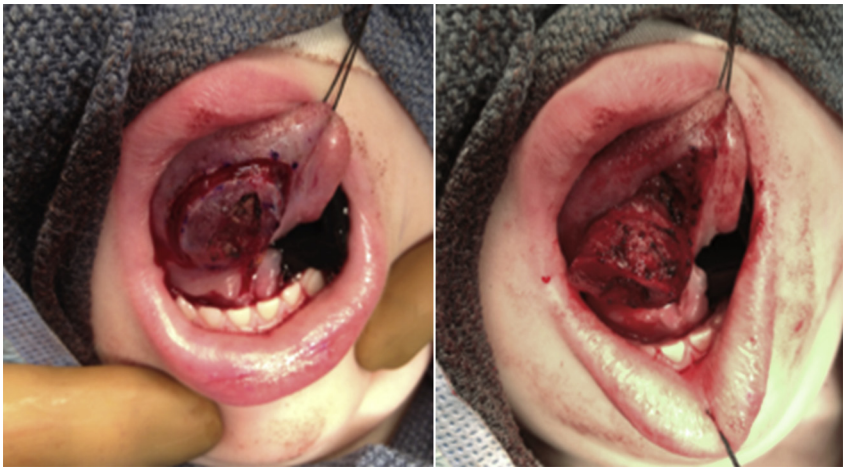

Fig. 1. Left: Intra-operative photograph demonstrating the incision around the margins of the ventral tongue lesion. Right: Intra-operative photograph depicting dissection of the lesion from the tongue musculature; the solid nature of the lesion raised concern for malignancy.