Hamartoma of the Oral Cavity with Ectopic Meningothelial Elements in Infants: A Rare Entity with Report of Two Cases

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Abstract

Choristomas and hamartomas within the oral cavity are relatively uncommon lesions and may present with diverse clinical and histopathological appearances. In this report, we describe two infant patients with hamartoma with ectopic meningothelial elements involving tongue and maxillary alveolar ridge. To the best of our knowledge, these are the first two cases in which a meningothelial proliferation has been identified in the oral cavity. Hamartoma with ectopic meningothelial elements is a rare condition that has been classically described occurring in the scalp. These lesions are characterized by bland round to spindle-shape cells that interdigitate through collagen bundles and express progesterone receptor and epithelial membrane antigen by immunohistochemistry supporting a meningothelial origin.

Keywords Meningothelial · Hamartoma · Choristoma · Hemangioma

Introduction

The term hamartoma denotes a growth or mass of disordered normal tissues indigenous to the location, while choristomas refers to growth of disordered tissue not indigenous to the location [1]. Within the oral cavity, several types of disordered growths, both hamartomas and choristomas have been described, including neurovascular [2], cystic and glial [3], rhabdomyomatous [4], leiomyomatous [5, 6], intramuscular capillary [7], angiomyolipomatous [8] and ganglioneuromatous hamartoma [9]. The majority of these types of lesions in the oral cavity are located in the tongue and present in individuals less than 2 years old [10].

A benign growth in the head and neck with ectopic meningothelial elements is a rare condition. Five such cases

were described as “hamartoma of the scalp with ectopic meningothelial elements” and involved scalp of young children [11]. The histology shows meningothelial elements in intimate association with vessels, adipose tissue and other connective tissue elements. It was proposed that the meningothelial proliferation arises from ectopic meningothelial rests which are abnormally displaced during cranial development. Similar cases, probably best considered choristomas, in skin have been reported under different names, such as ‘rudimentary meningocele’ [12], ‘cutaneous heterotopic meningeal nodules’, ‘cutaneous meningioma’ and ‘meningothelial hamartoma’ [13]. Ectopic meningothelial elements can also be seen in teratomas [14, 15], an axillary lymph node of a patient with Cowden Syndrome [16] and oropharyngeal hairy polyp [17].

We report two cases diagnosed as hamartoma with ectopic meningothelial elements in tongue and maxillary alveolar ridge.

Case 1

A 14-month-old boy presented with a 0.5 cm tongue mass. Histologic findings are illustrated in Fig. 1.

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Fig. 1 **a** A slightly polypoid well-circumscribed submucosal mass without ulceration (HE, $\times 40$). **b** Overlying squamous epithelium without atypia and bland submucosal proliferation surrounding arte-

rioles (HE, $\times 100$). **c** Irregular interconnecting spaces are lined by flattened bland cells without nuclear pleomorphism (HE, $\times 200$). **d** Nuclear expression for progesterone receptor (PR, $\times 200$)

Case 2

A 22-month-old boy presented with a 0.8 cm in great dimension nodular mass on the maxillary alveolar ridge with intact overlying mucosa. The lesion was present at birth by report, was asymptomatic, and demonstrated minimal growth. There was a previous incisional biopsy one year ago diagnosed as “features are compatible with hemangioma”. However, the parents remained concerned about the mass and the patient was referred to an oral-maxillofacial surgeon who removed the mass in its entirety. No detectable alveolar bone extension was noted intraoperatively. Histologic findings are illustrated in Fig. 2.

Both cases shared similar histopathologic features (Figs. 1, 2). The overlying epithelium demonstrated mild parakeratosis and atrophy of the rete ridges. Under the surface epithelium, bland round to spindle-shape cells infiltrate haphazardly through connective tissue. Anastomosing slit-like channels were mostly devoid of red blood cells and lined by flat to cuboidal cells. Immunohistochemical endothelial markers CD34, CD31, ERG, and Glut-1

were negative. The cells composing the slit-like channels expressed progesterone receptor (PR) and epithelial membrane antigen (EMA) by immunohistochemistry supporting a meningotheelial origin. S100 protein stain highlighted small nerve twigs and occasional dendritic cells. Cytokeratin and desmin stains were negative.

Discussion

The designation of these lesions as hamartomas or choristomas is somewhat controversial, arbitrary, and is mostly of academic interest. Some might designate these as choristomas citing that meningotheelial elements are not seen within the normal histological spectrum of oral soft tissue. However, during embryogenesis, neural crest is an important contributor to the connective tissue of the craniofacial region, in addition to giving rise to meninges in central nervous system development. Embryonic connective tissue in the head is known as ‘ectomesenchyme’, reflecting its origin from neuroectoderm. The proper migration of neural crest cells is essential for the development of the teeth and the face.

Fig. 2 **a** A polypoid mass covered by squamous oral epithelium and poorly circumscribed mass in the connective tissue (HE, $\times 100$). **b** and **c** The meningeothelial elements intermingling haphazardly within

the collagen (HE, $\times 200$ and $\times 400$ respectively). **d** Expression of lesional cells for epithelial membrane antigen (EMA, $\times 400$)

All supporting apparatus of the tooth are also derived from neural crest cells [18] and therefore ectopic meningeothelial elements might be plausible in this location. We prefer to accept this proliferation as ‘hamartoma with ectopic meningeothelial elements’ rather than choristoma because of this plausible embryogenesis.

The entity “hamartoma with ectopic meningeothelial elements” is a rare condition most commonly seen in the scalp in the pediatric population. To the best of our knowledge, no reported cases of hamartoma with meningeothelial elements have been described occurring in the oral cavity or tongue. However the histopathological features and immunohistochemical profile in our cases were quite similar with those described in the scalp lesions. However, none of the oral cases presented here had certain characteristic histological features seen in scalp lesions (i.e. psammomatous calcifications or pigmented dendritic cells).

The clinical presentation of our cases was not specific and the clinical differential diagnoses include vascular lesions, non-specific reactive gingival nodular lesions and hamartomas. The histopathological differential diagnoses includes perineurioma, angiomyoma, muscular/neuromuscular

choristoma, ectopic meningioma, rhabdomyomatous hamartoma, rhabdomyoma or ganglioneuromatous hamartoma, and hemangioma. The lack of nuclear atypia or increased mitotic activity excludes malignancy. Vascular markers such as CD31 and CD34 are negative which excludes vascular tumors. Lack of desmin expression and ganglion cells excludes hamartomas with rhabdomyomatous differentiation and ganglioneuromatous lesions. Perineurioma can have morphological and immunophenotypic overlap with the entity described here and other markers may be helpful in this important distinction. Epithelial membrane antigen expression is ubiquitous in both entities, and does not distinguish between them. SSTR2 and claudin-1 are additional markers that are highly expressed in meningiomas and perineuriomas respectively [19]. Their utility in these hamartomatous entities (scalp, oral cavity) has not been verified. They may be helpful in distinguishing between the two entities, particularly in cases of meningioma occurring at unusual (extracranial) sites.

Ectopic meningiomas are also reported in oral cavity [20, 21]. Despite the similarity of histopathologic and immunohistochemical features to the hamartoma, the hamartomas

distinguish themselves by limited growth potential, poorly defined borders, and the meningotheial elements intermingled haphazardly within the collagen.

Oral hamartomas have also been described in some syndromes. The oral lesions vary in severity from patient to patient and usually affect the gingivae, dorsal tongue, and buccal mucosa. Syndromic associations include Cowden Syndrome (Multiple Hamartoma Syndrome) which has multiple papules/papillomas, representing fibroepithelial hyperplasia, Proteus-like syndrome (PTEN mutations with oral hamartomas, exostoses of facial bones, lymphangiomas), and oral-facial-digital syndrome type-I (hamartomas composed of cartilaginous tissue, minor salivary glands, and smooth muscle) [1, 22]. None of our cases was associated with one of these disorders.

In summary, hamartomas of the oral cavity exclusively composed of meningotheial cells are rare and can be challenging to recognize and diagnose. Vascular, leiomyomatous and rhabdomyomatous proliferations, and perineurioma should be excluded. EMA, progesterone receptor, CD31, smooth muscle actin, desmin, and claudin-1 and SSTR2 may be helpful markers in arriving at the proper diagnosis.

Compliance with Ethical Standards

Conflict of interest The authors declare that there is no conflict of interest.

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