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Case Report

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Oral Leiomyomatous Hamartoma of the Midline Maxillary Gingiva: A Case Report and Review of the Literature

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Abstract

Oral leiomyomatous hamartoma (OLH) is a rare lesion characterized by abnormal growth, with smooth muscle tissue as the predominant component. It mainly presents on the midline region of both the dorsal tongue and the maxillary alveolar ridge. This article reported a case of OLH in a 7-year-old Thai girl. The lesion presented as a pedunculated, normal-colored, soft tissue nodule located on the palatal gingiva at the midline between the maxillary deciduous central incisors. Panoramic radiograph showed no bony changes associated with the lesion. The clinical differential diagnoses included irritation fibroma, congenital epulis and non-angiomatous hamartoma. Complete excision was performed under local anesthesia. Microscopically, it revealed soft tissue mass surfaced by parakeratinized stratified squamous epithelium with mild acanthosis. Proliferative smooth-muscle fascicles were dispersed in the loose fibrous connective tissue stroma. The diagnosis of OLH was supported by positive immunohistochemical reactivity of smooth-muscle actin and desmin with no reactivity for S-100 protein. Postoperative wound healing was uneventful, and no recurrence was found during the 10 months follow-up period.

The focus on OLH in the anterior maxilla, epidemiological data, pathogenesis, clinical and histopathological features, and differential diagnosis are discussed herein.

Keywords: anterior maxilla, differential diagnosis, midline, midline maxillary gingiva, oral leiomyomatous hamartoma

Introduction

Hamartoma derives from the Greek word "hamartanein" which means "to fail". Hamartoma is a benign tumor-like malformation manifested as a mass of an abnormal mixture of tissues indigenous to the site involved.[1] By definition, there is usually a relative overgrowth of one element of the tissue, but without the tendency towards progressive growth found in benign neoplasm.[2] A hamartoma is histopathologically classified by its main composite elements. In oral regions, lymphangiomas and hemangiomas are hamartomas of a vascular origin, which are commonly found.[2] However, oral hamartoma of other tissues is rare.[3] Oral leiomyomatous hamartoma (OLH) corresponds to a disorganized, abnormal mass with a predominance of smooth muscle tissue first reported by Stamm and Tauber in 1945.[4] It typically presents early in life as a soft tissue nodule on the anterior maxillary alveolar tissues or the tongue. Due to its nonspecific symptoms, diagnosis remains a challenge.[5] Thus far, only 28 cases of OLH of the anterior maxilla region have been reported in the English-language literature.

This case report described a case of OLH occurring in a healthy 7-year-old Thai girl treated successfully by excision under local anesthesia. Clinical, histological and immunohistochemical features are presented, along with a review of the literature.

Case Report

A healthy 7-year-old Thai girl was referred to the Oral Surgery Clinic, Dental Devision, Phramongkutklao Hospital for evaluation of a painless nodular soft tissue mass on the palatal gingiva at the midline between maxillary deciduous central incisors. The patient complained of a slow-growing mass that had been present for three years, with the lower anterior teeth occluding on it. The right maxillary deciduous central incisor had exfoliated the previous week. Her medical history was non-contributory, and no family history of any importance pertaining to the lesion was reported.

Intraoral examination revealed a pedunculated soft tissue mass measuring 15 mm x 12 mm x 5 mm, with a smooth, normal-colored, and intact mucosal surface (Figure 1). The lesion was firm in consistency. Panoramic radiograph revealed no calcifications within the soft tissue nodule and no bony changes associated with the lesion (Figure 2). Based on the clinical presentation, a provisional diagnoses of irritation fibroma, congenital epulis and non-angiomatous hamartomas were made.

An excisional biopsy was performed under local anesthesia. Microscopically, the specimen was a mucosal mass of fibrovascular fibrous tissue intermixed with numerous randomly oriented fascicles of smooth muscle cells (Figure 3). The lesional tissue was unencapsulated and covered by intact parakeratinized stratified squamous epithelium with mild acanthosis. Immunohistochemical staining revealed that the spindle cells were positive for smooth muscle actin (SMA) and desmin, but negative for S-100 protein, confirming their muscular differentiation (Figure 4). Based on the clinical histopathological findings, a final diagnosis of OLH was established. The postoperative wound healing was uneventful. No recurrence was found during the 10-month follow-up period.

Discussion

Leiomyomatous hamartoma is defined as a hamartoma composed primarily of smooth muscles. Leiomyomatous hamartomas are commonly found in the lungs, liver, spleen, or kidneys but are rarely found in the oral

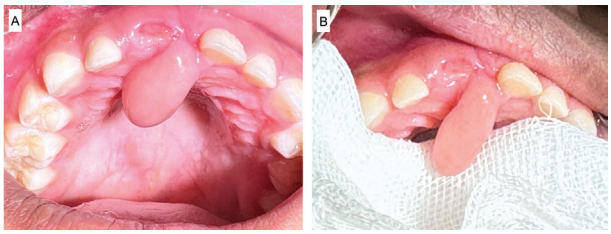

Figure 1: (A and B): Clinical presentation of the lesion showing a pedunculated, soft tissue mass covered by smooth, normal-colored mucosa located at the midline of the maxillary alveolar ridge. Note the recent exfoliation of the right maxillary deciduous central incisor.

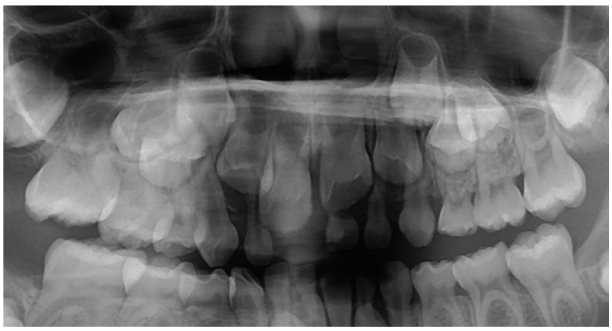

Figure 2: Cropped panoramic radiograph revealing no bony changes associated with the lesion.

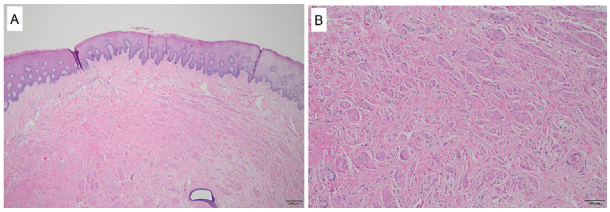

Figure 3: Histopathological features of oral leiomyomatous hamartoma. (A) The lesion composed of a subepithelial non-encapsulated proliferation of eosinophilic smooth muscle tissues fascicles intermixed with small blood vessels (H&E, 40x magnification); (B) Proliferation of delicate smooth muscle fascicles arranged in an irregular pattern with occasional blood vessels (H&E, 100x magnification).

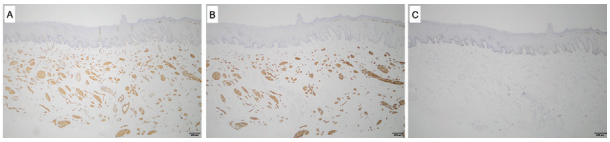

Figure 4: Immunohistochemical features of oral leiomyomatous hamartoma. (A, B) Smooth muscle bundles showed strong positivity for smooth muscle actin (SMA) and desmin, respectively (40x magnification); (C) The lesion exhibited negative immunoreactivity for S-100 protein (40x magnification)

cavity.[6] Systematic review of Alarcón-Sánchez *et al*.,[7] reported 66 OLH cases, with a mean age at presentation of 6 years and no sex predilection. Most lesions presented normal-colored color (24.24%), pedunculated base (31.81%), and firm consistency (22.72%), with an average size of 1.20 cm. The most commonly found location was the tongue (49.98%), followed by the anterior maxillary alveolar ridge (37.87%).

OLHs are frequently located in the midline region of both the dorsal tongue and the maxillary alveolar ridge. In the anterior maxilla region, especially at the midline, their occurrence could result from embryogenic errors during the fusion of processes and prominences in the developing embryo. The primary palate and palatine crests meet to form the nasopalatine foramen where nerves and blood vessels emerge. These developmental processes are complex and susceptible to errors. Dysgenic events of smooth muscle cell differentiation around the arteries could lead to the formation of leiomyomatous hamartoma.[8]

Thus far, only 28 OLH cases of the anterior maxilla region have been reported in the English-language literature. The clinical features of OLH at the anterior maxilla from the previous case reports and case series, including the present case are summarized and illustrated in Table 1.[2,3,6,8-29] The mean age of patients in this current review is 44.79 months (3.74 years), ranging from 1 month to 20 years, with female predominance (60.71%). Most patients are Japanese. The majority of lesions present with normal-colored (68.41%), smooth surface (100.00%), pedunculated base (76.47%) and firm consistency (100.00%). The average size is 8.97 mm, ranging from 3 mm to 2.5 cm. A unilobed nodular mass is observed in 93.10% of cases. Most OLH (93.10%) manifest as a single lesion; however, two Japanese patients presented with multiple OLHs with no associated syndrome. One was a 2 years 7-month-old boy who had three lesions at the incisive papilla and two isolated lesions on the dorsal tongue.[6] The other was a 3-year-old boy with two lesions on the tongue and the midline of the upper gingiva.[12] No OLH cases have been associated with any syndromes and they occurred in otherwise healthy individuals.[6] Nevertheless, Falci *et al*.,[22] showed an incipient lip cleft corresponding to an OLH in the anterior maxilla. Although hamartomas are congenital lesions, they may only be detected at later developmental stages. Their growth is slow and self-limited. In addition, these lesions are asymptomatic and may develop over several years.[7,8]

This present case is the first case report of OLH found in a Thai patient. This soft tissue mass at midline maxillary gingiva has occurred since she was 4 years old. The lesion's size is slowly increasing until she came for a treatment 3 years later. The maxilla generally completes its growth by the age of 14 years in female.[30] Therefore, this present lesion may be associated with proliferation of smooth muscle cells' remnants from this region during the incomplete maxilla growth period. In addition, this mass was 15 mm in maximum dimension which is relatively larger than overall OLH (12 mm in average) and OLH case of anterior maxilla region (8.97 mm in average). This may be associated with a history of slow and prolonged lesion growth.

According to the clinical characteristics of the present case, including its appearance, anterior location, absence of pain, long duration and slow growth, the clinical differential diagnoses include benign lesions such as irritation fibroma, congenital epulis, and non-angiomatous hamartoma. First, irritation fibroma (traumatic fibroma or focal fibrous hyperplasia) is commonly detected among pediatric reactive lesions and associated

with fibrous tumor-like growths caused by trauma or local irritation.[31] Lesions in the anterior region may have the same clinical appearance and can be triggered by chronic irritation such as digit sucking or bottle feeding.[6] However, the patient reported no history of exposure to irritant factors. Second, congenital epulis, also called granular cells congenital epulis, is a benign lesion frequently found on the anterior alveolar ridge of the maxilla and is among the most common congenital oral lesions.[18,31] Histologically, the lesion is characterized by sheets or nests of polygonal cells with eosinophilic granular cytoplasm.[32] Lastly, oral hamartomas are more frequently detected in children and young adults. Typically, non-angiomatous hamartomas show normal-colored, slow-growing soft tissue masses without bleeding and or pulsatile.[33] Therefore, non-angiomatous hamartoma must be considered in the differential diagnosis.

Microscopically, OLH is characterized by a soft tissue mass containing a diffuse proliferation of fascicles and bundles of eosinophilic spindle cells of varying size, oriented in longitudinal and/or transverse patterns. These fascicles are composed of spindle cells compatible with mature smooth muscle cells, exhibiting indistinct borders, elongated blunt-ended (cigar-shaped) nuclei. The presence of a fibrous capsule is unclear.[1-3,5-8,14-29] In addition, some authors described a non-inflammatory Grenz zone.[3] These fascicles are irregularly scattered and mixed up with various sizes other tissue elements, such as lymphatic vessels, blood vessels, and nerve fibers. The presence and distribution of multiple tissues types are characteristics of hamartomatous lesions. In contrast, in OLH, the predominant element is the smooth muscle tissue.[7] Occasionally, adipose tissues and minor salivary glands may be seen in the OLH.[6]

Although histopathological entities consisting of fusiform cells vary widely,[34] OLH should be differentiated histopathologically from oral spindle cell neoplasms including solid leiomyoma, benign mesenchymoma, irritation fibroma and other benign neural tumors. First, solid leiomyoma is primarily diagnosed in middle-aged adults although it can be found at any age.[14,35] Histologically, it is well-circumscribed with or without capsulation and comprised intertwining bundles of spindle-shaped or smooth-muscle cells with elongated, blunt-ended, and pale-staining nuclei.[36] In some areas, the neoplastic smooth muscle tissue may be poorly demarcated and embedded in scarce fibrous tissue.[6,35] If diagnostic uncertainty remains, additional serial sections may be helpful. Second, benign mesenchymoma is an unencapsulated soft tissue tumor consisting of fibrous tissue stroma and the at least two or more benign mesenchymal components not typically associated with each other.[37] Notably no single mesenchymal tissue should predominate in benign mesenchymoma.[37] On the other hand, OLH is characterized by the predominance of smooth muscle tissue and lacks infiltration or invasion to surrounding tissue. Third, irritation fibromas infrequently contain dense collagenous tissues with occasional spindle cells which may mimic smooth muscle tissue.[24] Last, various types of benign neural tumors demonstrate spindle cells with wavy nuclei, which may be similar to smooth muscle cells.[38] The pattern of spindle-cell proliferation and immunohistochemical staining can be useful for accurate diagnosis. Summary of histopathologic differential diagnosis of OLH and immunohistochemical staining is presented in Table 2.[1-8,14-29,34-38]

Immunohistochemical staining is highly beneficial for confirming a diagnosis of OLH. SMA, desmin, muscle-specific actin, caldesmon, CD34, collagen IV and calpontin are among common markers showing positive reactivity for smooth muscle spindle cells.[1,7,14,16-29] In contrast, markers such as Neuron-specific enolase, laminin, melanosome, S-100 protein and CD31 are typically negative for this cell type.[3,7,16] Notably, Zaitoun and Triantfyllou[3] discovered positive expression of Collagen IV in the basement membrane of smooth-muscle cells and CD34+ in the interstitial cells surrounding smooth-muscle bundles. The existence of these cells could be an intrinsic component of OLH or merely represent tissue remnants from the incisive papilla region.[3,8] These findings support the theory of underlying dysgenic events affecting blood vessel formation in the anterior midline region of the maxilla, leading to the development of OLH.[21] In the present case, the lesional cells exhibit strong positivity for SMA and desmin, confirming their smooth-muscle origin and supporting the diagnosis of OLH. According to the majority of published reports, SMA and desmin are the reliable markers for confirming the smooth muscle cells of the OLH.[9-29]

The recommended treatment modality for OLH is surgical excision which has an excellent prognosis. Across reported cases with follow-up period ranging from

Table 1: Summary of clinical features of oral leiomyomatous hamartoma at the anterior maxilla.[2,3,6,8-29]

Parameter	Number of cases (n=29)	%
Sex		
Male	11	39.29
Female	17	60.71
Not reported	1	
Age (month)		
Mean ± SD	44.79+10.51	
Range	1 to 240	
Country		
Japan	10	34.48
USA	6	20.70
India	3	10.34
Brazil	3	10.34
United Kingdom	2	6.90
Others (Malaysia, Mexico, Saudi Arabia, Peru, Thai)	5	17.24
Size (mm)		
Mean±SD	8.97+2.13	
Range	3 to 25	
Color		
Normal-colored	13	68.41
Pink	4	21.06
Red	2	10.53
Not reported	10	
Surface		
Smooth	18	100.00
Not reported	11	
Base		
Pedunculated	13	76.47
Sessile	4	23.53
Not reported	12	
Consistency		
Firm	15	100.00
Not reported	14	
Uni/bi/multi-lobed nodule		
Unilobed nodule	27	93.10
Bilobed nodule	1	3.45
Multilobulated nodule	1	3.45
Single/multiple lesion(s)		
Single	27	93.10
Multiple	2	6.90

Table 2: Summary of histopathologic differential diagnosis of oral leiomyomatous hamartoma and immunohistochemical staining.[1-8,14-29,34-38]

	Well-circumscribed lesion	Fibrous capsule	Lesional cells and pattern	Infiltrative border	Positive markers
Leiomyomatous hamartoma	No	Unclear/no	Predominant element of mature smooth muscle cells with varying size and irregularly arranged fascicles	No	SMA, desmin, muscle-specific actin, caldesmon, calponin, smooth muscle myosin heavy chain
Solid leiomyoma	Yes	Yes/No	Dense intertwining bundles or whorled pattern of cellular smooth muscle cells	No	SMA, desmin, muscle-specific actin, caldesmon, calponin, smooth muscle myosin heavy chain
Benign mesenchymoma	No	No	Fibrous connective tissue interspersed with at least two other mature mesenchymal tissues with no single dominant element	Yes	Depending on type of mesenchyme
Irritation fibroma	Yes/No	No	Dense fibrous connective tissues with collagen bundles and some blood vessels	No	Not applicable
Traumatic neuroma	Yes/No	No	Haphazard proliferation of nerve bundles within fibrous connective tissue stroma	No	S-100 protein, neurofilament
Solitary circumscribed neuroma	Yes	Yes/No	Moderately cellular interlacing fascicles of spindle neural tissues	No	S-100 protein, neurofilament
Neurofibroma	Yes	No	Interlacing bundles of neural tissues mixed with delicate collagen bundles and scattered mast cells	No	S-100 protein, CD34
Neurilemoma (Schwannoma)	Yes	Yes	Biphasic spindle cell tumor composing of Antoni A tissue (compact hypercellular areas with nuclear-palisadind) and Antoni B tissue (less cellular and less organized areas)	No	S-100 protein, CD56, calretinin, neurofilament

6 months to 5 years, no recurrence or malignant transformation have been reported.[7,8]

Conclusion

OLH is an uncommon and diagnostically challenging lesion. However, when a soft tissue mass is in the anterior midline of the maxilla in children, OLH should be considered among the differential diagnoses. Its histopathological features are relatively distinctive, typically consisting of small fascicles of fusiform or spindle shaped cells, irregularly distributed in the subepithelial connective tissue. The lesion is characteristically unencapsulated. A definitive diagnosis of OLH requires histopathological evaluation supported by immunohistochemical staining such as SMA, desmin.

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Conflict of Interest

The authors declared that they have no conflict of interest.

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