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Original Research

A comparative study of oral hamartoma and choristoma

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ABSTRACT

Aim: To compare the clinical and microscopic characteristics of hamartoma and choristoma of the oral mucosa and jaws and discuss the challenges in diagnosis. **Materials and Methods:** Analysis of patients diagnosed between 2000 and 2012, and literature review of the same years. A sub-classification into "single tissue" or "mixed-tissue" types was applied for all the diagnoses according to the histopathological description. **Results:** A total of 61 new cases of hamartoma or choristoma were retrieved, the majority were hamartoma. The literature analysis yielded 155 cases, of which 44.5% were choristoma. The majority of hamartoma were mixed. Among these, neurovascular hamartoma was the most prevalent type (36.7%). Of the choristoma, 59.4% were single tissue, with respiratory, gastric and cartilaginous being the most prevalent single tissue types. The tongue was the most frequent location of both groups. **Conclusion:** Differentiating choristoma from hamartoma depends to a great extent on the recognition of the normal tissues expected at every individual location.

KEY WORDS: Choristoma, diagnosis, hamartoma, oral mucosa, tongue

INTRODUCTION

A hamartoma is a disorganized proliferation of mature tissues, composed of elements that are normally found in the specific location in which it develops, often with one predominating element [1]. The borders with the surrounding tissues are typically ill-defined, merging with surrounding tissues [2]. This is in contrast to choristoma that is defined as a histologically normal tissue proliferation or nodule of tissue, of a type not normally found in the anatomic site [1]. Choristoma tends to resemble tumors, as they present a relatively well-organized proliferation [2].

Hamartoma and choristoma of the oral cavity are uncommon and present a wide spectrum of clinical and microscopic features. From a clinical point of view, these lesions are usually exophytic, although other manifestations such as flat pigmented lesions have rarely been described [3]. Traditionally, they are considered developmental anomalies rather than neoplastic and, therefore, thought to be associated with children. However, review of the literature reveals that in fact oral hamartoma and choristoma have been described over a wide age range, from birth to old age [4-8].

From a histopathological point of view, as hamartoma and choristoma may present mixed and overlapping morphological features, the accurate classification may pose a diagnostic challenge. Their relative rarity, the wide variety and combination of structures, may explain why these types of lesions have occasionally been misdiagnosed as benign tumors.

A search of the literature between 2000 and 2012 yielded mostly sporadic case reports and small series, including oral osseous and cartilaginous choristoma, leiomyomatous, and lipomatous hamartoma, glial choristoma, gastric or gastrointestinal choristoma and neurovascular hamartoma (NVH) [9-87].

The objectives of the present study were to compare the clinical and microscopic characteristics of hamartoma and choristoma of the oral mucosa and jaws, in a new and relatively large series of lesions, analyze the recent literature and discuss the challenges in diagnosis.

MATERIALS AND METHODS

The archives of the Institute of Pathology at Rabin Medical Center and of the Tel-Aviv Sourasky Medical Centers have been searched for lesions diagnosed as hamartoma or choristoma of the oral mucosa and jaws, between years 2000 and 2012. Only lesions of the oral mucosa and jaws were included (anterior to the tonsils), while extra-oral cases, including those of the major salivary glands and nasopharynx were excluded. Odontogenic lesions such as odontoma, adenomatoid odontogenic tumor (considered by the some to represent hamartoma), and peripheral hamartomatous lesions with odontogenic or osseous components (which may represent synonyms of peripheral odontogenic or peripheral ossifying fibroma) have been excluded. Clinical and demographic data were retrieved from the files. The microscopic slides have been revised by two oral pathologists (IK, IA) and the diagnoses confirmed. In addition,

a literature search of PubMed and Google Scholar between 2000 and 2012 was performed, using the following keywords: Hamartoma, choristoma, oral, tongue, buccal mucosa, the floor of mouth, gingiva, vestibule, alveolar ridge, jaw, maxilla, and mandible. The 25 cases of NVH previously published by our group were counted only once.

An additional sub-classification into "single- tissue" or "mixed- tissue" types was applied for all cases in the present series, as well as for those from the literature. The study was approved by the IRB of both institutions.

RESULTS

A total of 61 cases of hamartoma and choristoma have been retrieved, 24 male and 37 female patients (1:1.54). The age range was wide, 2 months-85 years, mean 43 years and median 48 years for the entire group. The vast majority of patients were 20 years old or above [Figure 1].

The study group cases comprised 50 (82%) hamartoma and 11 (18%) choristoma cases. All of the hamartoma in the present series were of the "mixed tissue" type, with the majority, 41 (82%) being NVH, and the remaining 9 (18%) presented varying combinations of blood vessels, mucous or serous salivary glands, striated or smooth muscle, nerves and adipose tissue.

Among the 11 choristoma, 6 (54.5%) were single tissue type, predominantly (5 cases) respiratory and one osseous choristoma [Table 1].

All the lesions exhibited a limited growth potential, varied in size between 2 and 20 mm, with a mean and median diameter of 8 mm and 7 mm, respectively.

The three most common locations of hamartoma and choristoma were the tongue 27 (44.3%), lips 14 (23%), and palate 8 (13.1%). There was a single lesion involving the jaws, which occurred in the mandible [Figure 2]. The diversity of histopathological features of both hamartoma and choristoma is demonstrated in Figures 3-6. All the lesions were treated with excisional biopsies and non-recurred after a follow-up of 2-14 years.

Combined Data

In total, 216 cases of hamartoma and choristoma have been included in the analysis, combining the present new case series and the cases from the literature [Table 1]. The hamartoma presented a wide age range, from neonates to 79 years, with the mean age at 29.5 years. The male: female ratio was 1:2.1. Half of the hamartoma cases occurred in the tongue (60), followed in frequency by the labial mucosa, buccal mucosa, and the median maxillary alveolus. The vast majority of the hamartoma (107 cases, 89.2%) consisted of more than one tissue type, hence classified as "mixed." Among these, NVH was the most prevalent, comprising 44 cases (36.7% of

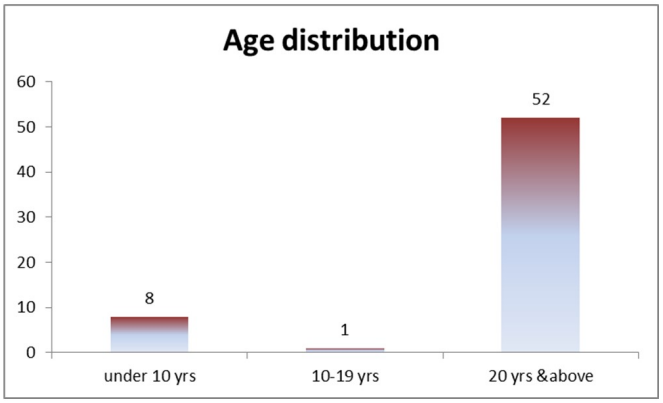

Figure 1: Age distribution in the study group, showing the majority of cases were adults, 20 years or older

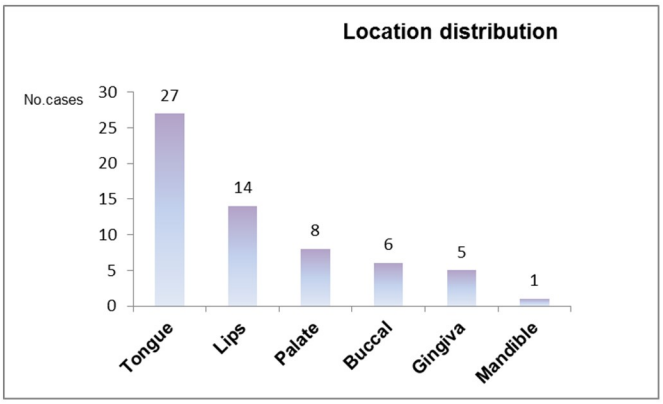

Figure 2: The distribution of the location of the lesions shows that the three most frequent involved areas were the tongue, lips and palate

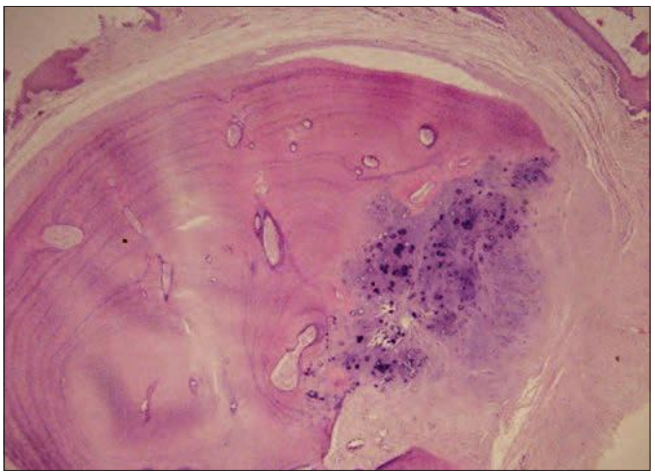

Figure 3: This mixed cartilaginous-osseous choristoma presented as a firm tongue mass in a 44-year-old female (H and E, original magnification ×20)

the hamartoma group). Morphologically, these lesions were composed of small to medium-sized blood vessels, closely packed with small nerve bundles. The loose matrix and lack of clear demarcation between the lesion and the surrounding

Table 1: Characteristics of hamartoma and choristoma of the oral region, combined present series and literature review 2000-2012

Clinical/Pathological parameters	Hamartoma	*n*=120 (55.5%)	Choristoma	*n*=96 (44.5%)
Age (years)	Newborn-79, Mean: 29.5		Newbom-85, Mean: 217	
Gender	M:F=1:2.1		M:F=1.2:1	
Single tissue type	Leiomatous	11 (9.1)	Respiratory	20 (20.8)
	Lipomatous	2 (1.7)	Gastric	17 (17.7)
			Chondroid	13 (13.5)
			Osseous	7 (7.3)
	Total	13 (10.8)	Total	57 (59.4)
Multiple tissues (mixed)	Neurovascular	44 (36.7)	Respiratory-gastric	14 (17.6)
	Other (non-neurovascular)		Epidermal-follicular	8 (8.3)
	Leiomyomatous predom.	22 (18.3)	Neuroglial	7 (7.3)
	Lipomatous predom.	15 (12.5)	Osseous-chondroid	3 (3.1)
	Rhabdomyomatous predom.	6 (5)	Squamous and respiratory epith	2 (2)
	Neuromuscular	5 (4.2)	Gastric and glial	1 (1)
	Pilosebaceous	4 (3.3)	Lipo-mesenchymal	1 (1)
	Salivary glands predom.	2 (1.7)	Fibro-lipomatous	1 (1)
	Lipo-neuro-vascular	2 (1.7)	Lipo-neural-smooth muscle squamous epithelium	1 (1)
	Vascular-smooth muscle	2 (1.7)	Lipo-chondroid	1 (1)
	Vascular, salivary glands, smooth muscle, nerve	4 (3.3)		
	Calcified	1 (0.8)		
	Total	107 (89.2)	Total	39 (40.6)
Location	Tongue	60 (50)	Tongue	51 (53.2)
	Labial	23 (19.2)	Floor of mouth	26 (27)
	Buccal	11 (9.1)	Palate	5 (5.3)
	Median maxillary alveolus	10 (8.3)	Buccal	4 (4.2)
	Palate	9 (7.5)	Gingiva	4 (4.2)
	Gingiva	5 (4.1)	Vestibule	3 (3.1)
	Mandibular ridge	2 (1.7)	Labial	2 (2)
			Mandible	1 (1)

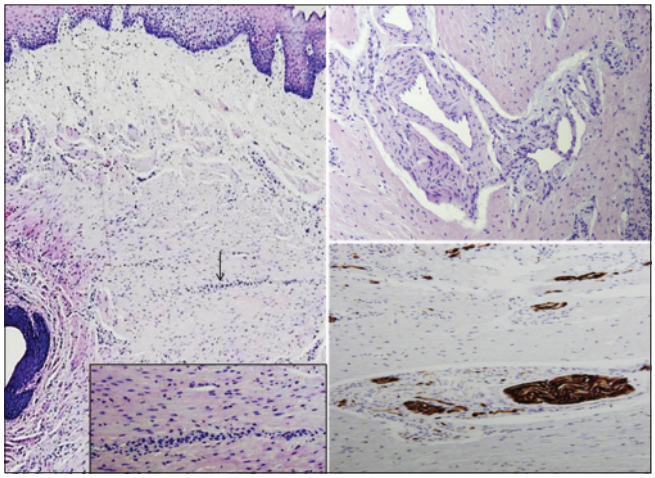

Figure 4: 3-year-old female, with an anterior palatal mass. The mixed hamartoma with ill-defi ned borders is composed of "Indian fi le" strands of epithelium (arrow) shown at higher magnifi cation in the inset (left panel, H and E, original magnifi cation ×40, inset ×100). Other areas show large irregular vessels and nerves (upper right panel (H and E, original magnifi cation ×40)). The irregular neural component is accentuated by S-100 stain, (lower right panel, magnifi cation ×100)

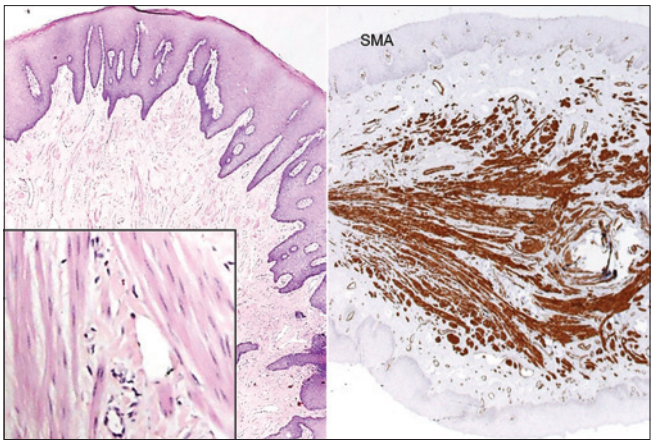

Figure 5: This polypoid mass in the palate of a 5-year-old male was a predominantly leiomyomatous hamartoma, composed of bundles of smooth muscle intermixed with small vessels (left panel, H and E, original magnifi cation ×40, inset ×200, right panel SMA ×40)

tissues were characteristic of these lesions [8]. NVH occurred in various sites within the oral mucosa: tongue, palate, lips, buccal mucosa, and gingiva. Other mixed hamartoma consisted of leiomyomatous or lipomatous predominant types [Table 1].

Only 18.8% (13) of the hamartoma were "single- tissue" type. The majority of these were composed of smooth muscle alone, (leiomyomatous), or adipose tissue (lipomatous) types.

The choristoma group consisted of 96 cases (44.5% of lesions). Ages ranged from newborn to 85 years, mean 21.7. The majority were located in the tongue, 51 (53.2%) and floor of mouth, 26 (27%). They were mostly (59.4%) "single-tissue" type and only 40.6% showed a "mixed- tissue" pattern. Respiratory, gastric, and cartilaginous were the most prevalent single tissue types, while respiratory/gastric and epidermal/follicular were the most prevalent mixed- tissue type choristoma [Table 1].

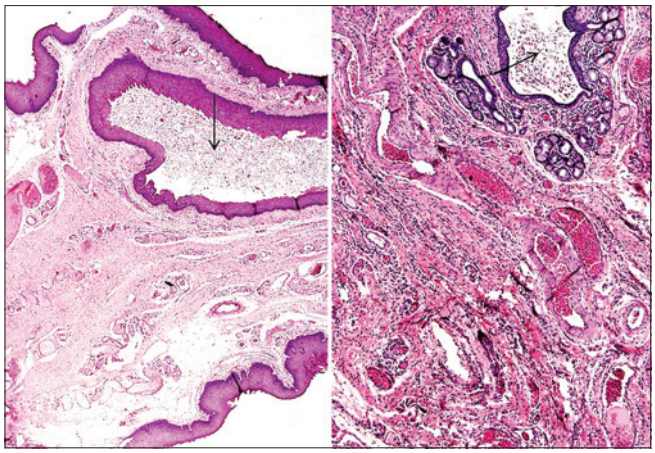

Figure 6: Mixed hamartoma is presenting as a polypoid mass on the uvula of a 6-year-old male. The arrow in the left panel points to a keratin-fi lled cyst resembling epidermoid cyst, in a fi brous and vascular matrix (H and E, original magnifi cation ×20). Other areas exhibit tortuous irregular vessels and mucinous salivary glands with duct ectasia (arrow) (H and E, original magnifi cation ×100)

DISCUSSION

This study aimed at comparing the clinical and microscopic characteristics of hamartoma and choristoma of the oral mucosa and jaws, in a new and relatively large series of lesions, analyze the recent literature and discuss the challenges in diagnosis. Although an analysis of 194 cases of hamartoma has recently been published, it did not include the morphological elements of which the lesions were composed, thus could not be included in the analysis [88].

This study is the first comprehensive analysis combining hamartoma and choristoma and relating to the clinical and histomorphological elements of which the lesions are composed. The study combines data from two central medical centers and a literature analysis of the same 12-year period.

To ensure the cases included in the analysis had been correctly diagnosed, we chose not to include odontogenic lesions such as odontoma, adenomatoid odontogenic tumor (considered by the some authors but not universally accepted, to represent hamartoma), and peripheral hamartomatous lesions with odontogenic or osseous components (which may represent synonyms of peripheral odontogenic or peripheral ossifying fibroma).

A relatively large proportion of the new lesions included in the study were NVH, an entity which had been only recently described in detail [8]. The main focus of the study was to analyze the details of the morphology of these lesions, comparing hamartoma to choristoma, rather than a precise epidemiological prevalence study.

Hamartoma was more common than choristoma. Most of the hamartomas were composed of "mixed tissue" types, of which NVH was the most common combination. On the other hand, choristoma showed an equal distribution between "single" and "mixed tissue" types, with respiratory choristoma being the most common subtype. Both hamartoma and choristoma tended to appear most frequent in the tongue.

In depth evaluation of the literature revealed significant confusion, with some lesions originally diagnosed as hamartoma that should have been diagnosed as choristoma, and vice versa. For example, a tongue lesion reported as "dermoid" was classified by the authors as hamartoma. Since hamartomas should contain elements endogenous to the site of occurrence, it seems that a choristoma would have been a better choice [80]. An opposite example is a periodontal lesion reported as osseous choristoma while in fact hamartoma may have been a better choice since bone is expected to be found in that location [48].

In cases with "single tissue" type lesions, classification as hamartoma or choristoma should be quite simple, and would depend on familiarity with normal anatomy for each particular location. However, in cases in which a mixture of tissue types is observed, the decision is sometimes more complicated, and classification as "endogenous" or "exogenous" may not be straightforward. For example, a lesion composed of smooth muscle, salivary glands and adipose elements: if the location is anterior hard palate, it should be classified as choristoma since fat and salivary glands are not endogenous to anterior hard palate; if the same lesion is located in the soft palate, it would be best classified as a hamartoma because both adipose tissue and salivary glands are native elements in soft palate, and smooth muscle can be found around blood vessels at any site, rendering these elements endogenous to the site of occurrence.

Both hamartoma and choristoma may present mixed tissue types though this feature appears to be more prevalent in hamartoma. What would be the correct terminology in lesions with mixed features, some endogenous and some exogenous to the site of occurrence may be a source of confusion. It seems that by definition, if even one tissue type component is exogenous to the site, the correct classification would be choristoma.

Mixed features in either hamartoma or choristoma, especially in infants, may raise a diagnostic dilemma with teratoma, germ cell tumors derived from pluripotential cells which may be either benign or malignant, and are by definition composed of elements derived from all 3 germinal layers [1]. Head and neck teratoma are very rare, predominantly pediatric cases, and are in the majority of cases benign [1].

An additional potential diagnostic pitfall is the diagnosis of soft tissue osteoma or chondroma versus osseous or cartilaginous choristoma, respectively. Some authors use these diagnoses interchangebly [44,52,71]. While the terms osteoma and chondroma imply true neoplasms (which although slowly growing, theoretically have unlimited growth potential), osseous or cartilaginous choristoma are developmental anomalies, with limited growth potential. The literature is vague on these issues, with no clear sharp criteria suggested. The majority of the lesions analyzed were about 1 cm in largest dimension, with no large lesions retrieved, thus, size may be used as a strong indication that soft-tissue osseous and or cartilaginous masses are in fact

choristoma and not true neoplasia. The terms osteoma and chondroma or osteochondroma of the oral cavity and jaws should, in our opinion, be reserved for lesions involving the jawbones, either as central or peripheral lesions attached to the cortex, but not in relation to lesions involving oral soft tissue alone.

The same confusion may be apparent regarding lipomatous hamartoma or lipomatous choristoma versus true lipoma. Classic lipomas tend to have clear circumscribed borders that can be encapsulated while this is not true in cases of lipomatous hamartoma or choristoma, thus border definition could help in differential diagnosis.

Our results seem to indicate that hamartoma and choristoma may not be genuinely rare, but may be under-reported in recent literature, which tends to put more emphasis on molecular rather than morphologic studies.

CONCLUSION

In conclusion, hamartoma and choristoma of the oral cavity are part of the spectrum of oral lumps. Hamartoma is more common than choristoma and tend to present a mixed morphology as opposed to choristoma, which present single tissue and mixed patterns in almost equal proportions. The tongue is the most common site for both lesions. They tend to affect the oral mucosa rather than jaws and to have limited growth potential. Although traditionally considered a pediatric lesion, they were not restricted to a pediatric population. Histopathologically they may present a wide variety of tissue elements and, therefore, correct classification to hamartoma or choristoma should be derived from clinicopathological correlations, including border definition and tissue composition in comparison to normal anatomy for each particular location.

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