Hamartomas of the oral cavity

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Abstract

The majority of oral diseases present as growths and masses of varied cellular origin. Such masses may include simple hyperplasia, hamartoma, choristoma, teratoma, benign or malignant neoplasms. The distinguishing features of hamartomatous lesions are not certain, and often these non-neoplastic masses are indiscreetly denoted as neoplasms without weighing their pathology or biological behaviour. Essentially, understanding the dynamics of each of these disease processes forms an integral part of the appropriate treatment planning.

Key words: Developmental disorders, hamartoma, oral cavity, syndrome, tumour

INTRODUCTION

The term hamartoma is derived from the Greek word “hamartia” referring to a defect or an error. It was originally coined by Albrecht in 1904 to denote developmental tumour-like malformations. It can be defined as a non-neoplastic, unifocal/multifocal, developmental malformation, comprising a mixture of cytologically normal mature cells and tissues which are indigenous to the anatomic location, showing disorganized architectural pattern with predominance of one of its components. The occurrence of multiple hamartomas in the same patient is often referred as hamartomatosis or pleiotropic hamartoma.

Hamartomas are commonly observed in lung, pancreas, spleen, liver and kidney. They are rare in the head and neck region. Within the oral cavity, indigenous tissues that might result in hamartomatous growths include odontogenic and non-odontogenic epithelial derivatives, smooth and skeletal muscle, bone, vasculature, nerve and fat. Few hallmarks of a hamartoma based on literature include:

- Developmental malformation may be present at birth, but manifests later
- Self-limited growth, co-ordinated with that of the surrounding tissues
- Can present as solitary or multiple masses
- May regress spontaneously
- Usually not encapsulated with ill-defined margins
- Not a true neoplasm, but a true neoplasm may develop in a hamartoma
- Microscopically, it consists of cytologically normal mature cells, native to the anatomic location
- Association with chromosomal abnormalities and syndromes.

Nevertheless, not all the lesions stated as hamartomas in the literature justify completely the above features. According to the data tabulated in Table 1, the most important features perceived are its limited growth potential after adolescence, microscopic appearance of...
### Table 1: Summary of characteristic features of oral hamartomas

| Hamartomas (possible hamartomatous lesions) | Congenital origin | Limited growth potential after adolescence | Unencapsulated | Cytologically normal cells & tissues, native to location | Associated chromosomal abnormalities | Malignant transformation | Spontaneous regression | Recurrence |
|---------------------------------------------|-------------------|------------------------------------------|----------------|----------------------------------------------------------|-------------------------------------|------------------------|------------------------|-------------|
| Dens invaginatus                            | +                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Dens evaginatus                             | +                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Enamel pearl                                | +                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Odontoma                                    | –                 | +                                       | –             | +                                                        | +                                   | -                      | -                      | -           |
| Oral and labial melanotic macule            | –                 | +                                       | +             | +                                                        | +                                   | -                      | -                      | -           |
| Oral melanotic nevi                         | +/-               | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Hemangiomas                                 | +/-               | +                                       | +             | +                                                        | +                                   | -                      | +                      | -           |
| Vascular malformations                      | +/-               | +                                       | +             | +                                                        | +                                   | -                      | -                      | *           |
| Glomuvenous malformations                   | –                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Exostoses                                   | –                 | –                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Rhabdomyomatous hamartoma                   | +                 | +                                       | +             | +                                                        | +                                   | -                      | -                      | -           |
| Leiomymatous hamartoma                      | +                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Neurofibroma                                | –                 | +                                       | +             | +                                                        | +                                   | *                      | -                      | -           |
| Fibrolipomatous hamartoma of nerve           | +                 | +                                       | +             | +                                                        | +                                   | *                      | -                      | -           |
| Oral neurovascular hamartoma                | –                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Oral neuromuscular hamartoma                | –                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Adenomatoid odontogenic tumour               | –                 | ?                                       | –             | +                                                        | -                                   | -                      | -                      | -           |
| AF, AFD and AFO                            | –                 | ?                                       | –             | +                                                        | -                                   | -                      | -                      | -           |
| Hyperplastic dental follicle                | +                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Adenomatoid hyperplasia of minor SG         | –                 | –                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Fibrous dysplasia                           | +                 | +                                       | +             | +                                                        | +                                   | *                      | -                      | -           |
| Familial gigantiform cementoma              | +/-               | –                                       | +             | +                                                        | -                                   | -                      | +                      | -           |
| Mucosal neuroma                              | –                 | +                                       | +             | +                                                        | -                                   | -                      | -                      | -           |
| Congenital granular cell tumour                | +                 | +                                       | +             | +                                                        | -                                   | -                      | +                      | -           |

+ (yes); – (no); ? (not determined); * (occasional). AF=Ameloblastic fibroma, AFD=Ameloblastic fibro-dentinoma, AFO=Ameloblastic fibro-odontoma, SG=Salivary gland
unencapsulated admixture of mature cells native to the anatomic location and association with chromosomal aberrations.

The pathogenesis of hamartomas still remains speculative.[1] They are derived from any one of the embryonic lineages, most commonly the mesoderm. This is almost never in the case of neoplasm, where the neoplastic cells are clonally derived.[9]

Clinically, majority are asymptomatic and rarely pose any complications except when situated at the base of tongue. Given the non-neoplastic nature of hamartomas, conservative surgical excision is the treatment of choice. The prognosis is excellent, with nil or minute chances of recurrence.[3]

HAMARTOMATOUS GROWTH OF ODONTOGENIC APPARATUS

Dens invaginatus

Dens invaginatus is a developmental anomaly resulting in invagination of the enamel organ into the dental papilla before the mineralization of the dental tissues begin. The prevalence is 0.3–10%. Associated syndromes include William’s syndrome, Nance-Huron syndrome, cranial suture syndromes and Ekman-Westborg–Julin syndrome.[10,11]

Dens evaginatus

Dens evaginatus (DE) represents an accessory cusp and is predominantly seen in people of Asian descent with a varying incidence of 0.5–4.3%. Clinically, DE may cause malocclusion resulting in abnormal wear or fracture and is treated accordingly.[12]

Enamel pearl/Enameloma

They represent deposits of enamel located at the cemento-enamel junction or at the furcation area. Its prevalence varies between 1.1 and 9.7%. Rarely, it may be detected within the dentin, when it is known as internal enamel pearl. Clinical significance varies depending upon its topographic relation with the furcation area.[13,14]

Odontoma

According to Reichart and Philipsen and the World Health Organization (WHO) 2005, compound and complex odontomas are hamartomatous lesions.[15,16] They have a relative frequency of 4.2–73.8% and 5–30%, respectively.[15] Associated syndromes include Gardner’s and Hermann’s syndromes.[17]

HAMARTOMATOUS GROWTH OF EPITHELIAL DERIVATIVES

Oral and labial melanotic macule

They represent a well-circumscribed flat area of brown to black mucosal pigmentation. There is an increase in melanin production by normal mature melanocytes (without increase in their number).[18] It is associated with Peutz-Jeghers syndrome and Addison’s disease.[19]

Oral melanocytic nevi

Nevi or mole represents collection of nevus cells which are derivatives of melanocytes or their precursor neural crest cells. Oral nevi are usually small and show regular symmetrical outline with no change in colour, shade or texture over time. Static nevi do not require excision and may be followed up.[19]

HAMARTOMATOUS GROWTH OF MESENCHYMAL DERIVATIVES

Congenital and infantile haemangioma

Congenital haemangioma (CH) and infantile haemangioma (IH) are present at birth or develop in the infancy period.[20,21] Majority of them involute spontaneously or gradually over the years. Microscopically, the proliferative phase of IH and CH comprises complex cellular mixtures, chiefly the endothelial cells.[20,22] Associated syndromes include PHACES and LUMBAR syndrome.[20]

Vascular malformations

Vascular malformation (VM) refers to congenital morphogenic anomalies of the various vessels.[20] Histologically, they comprise of normal vascular components.[20,22] VM may occur as primary or in association with regional or diffuse syndromes such as Sturge-Weber, Klippel-Trénaunay, proteus syndrome, Bannayan–Riley–Ruvalcaba syndrome, and Osler–Weber–Rendu, to mention a few.[20]

Glomuvenous malformations

Glomuvenous malformation (GVM) occurs more often in children.[23] Clinically, it appears as red-to-blue nodules or multifocal plaque-like lesions. Microscopically, GVM is composed of varying
proportion of blood vessels and glomus cells. The familial cases have been linked to mutations in the glomulin gene located in chromosome 1p21-22.[22,24]

**Exostoses**

They are described as peripheral localized overgrowth of the bone. Based on the anatomic location in the jaws, they are termed as buccal bone exostoses, torus palatinus, and torus mandibularis.[25] Surgical intervention is required only in case of tissue trauma, periodontal or prosthodontic impediment.[26]

**Rhabdomyomatous mesenchymal hamartoma**

It is an exceptionally rare congenital lesion of the oral cavity. It chiefly comprises of striated muscle tissue.[27] It is associated with Delleman, amniotic band and Goldenhar syndromes.[28]

**Leiomyomatous hamartoma**

Leiomyomatous hamartoma is another rare entity which commonly involves the midline of palate and tongue. Microscopically, it consists of an unencapsulated mass of smooth muscle.[29,30]

**Neurofibroma**

As the name indicates, it is an admixture of perineural fibroblasts and Schwann cells. It is associated with von Recklinghausen’s neurofibromatosis syndrome. Approximately 12% of cases are associated with the syndrome tend to develop malignancy.[6]

**Fibrolipomatous hamartoma of nerve**

Neural fibrolipoma or fibrolipomatous hamartoma of nerve (FLHN) is a tumour-like lipomatous process. FLHN was reported in the pharyngeal mucosa by Kumar et al.[31] Some lesions may represent carpal tunnel syndrome as a late complication.[23]

**Oral neurovascular hamartoma**

The hamartomatous nature of oral neurovascular hamartoma can be supported by the characteristics such as limited growth potential, ill-defined borders and histologically consisting of closely packed groups of well-formed nerve bundles and vessels.[5]

**Oral neuromuscular hamartoma**

Oral neuromuscular hamartomas or triton tumours are reported to occur in the trigeminal nerve and tongue. Histologically, they show presence of mature neural and striated muscle tissue.[32,33]

**SYNDROMIC HAMARTOMAS**

**Tuberous sclerosis**

Tuberous sclerosis (TS) is a rare syndrome characterized by the classic triad of seizures, mental deficiency and angiofibromas, affecting about 1 in 6000 people.[34] Oral hamartomas in TS were reported by Celenk et al. (2005) and Amin and O’Callaghan (2012).[34,35]

**Cowden syndrome/multiple hamartoma syndrome**

Cowden syndrome represents the principal PTEN (phosphatase and tensin homolog) gene-related disorder which occurs in 1 in 200,000 people.[34] The oral manifestations include multiple papules involving the gingivae, buccal mucosa and dorsum of tongue.

**Proteus syndrome**

Proteus syndrome is a rare congenital hamartomatous condition with an incidence of less than 1 in a population of 1 million.[34] Reported associated oral hamartomas include exostoses of facial bones and lymphangiomas.[36]

**Oral-facial-digital syndrome**

Oral-facial-digital syndrome (OFDS) comprises a group of heterogeneous disorders with an incidence of 1 in 50,000–250,000 newborns.[34] The oral hamartomatous findings include lingual hamartomas (in 70% cases of OFDS I). Microscopically, they are composed of muscles, adipose tissues and salivary glands.[37]

**CONTROVERSIAL ORAL HAMARTOMATOUS LESIONS**

**Adenomatoid odontogenic tumour**

The hamartomatous nature of adenomatoid odontogenic tumour is supported by its limited growth potential and lack of recurrence.[38] Nevertheless, its biological behaviour has been a topic of long debate and the related research is depicted in Table 2.

**Ameloblastic fibroma, ameloblastic fibro-dentinoma and fibro-odontoma**

Reichert and Philipsen proposed a neoplastic and hamartomatous line of development for the mixed odontogenic tumours. But currently, there is no substantial evidence to prove either of the above hypothesis.[15]
Hyperplastic dental follicle

It has been referred as an odontogenic hamartomatous lesion associated with single/multiple unerupted teeth. It commonly involves permanent first and second molars. Microscopically, it comprises of odontogenic epithelium and calcifications.[33,34]

Adenomatoid hyperplasia of minor salivary gland

It is a rare lesion of the minor salivary glands. Clinically it presents as a solitary, painless mass or nodule.[6] Microscopically, it comprises of lobular aggregates of normal mucus acini.[6,25] Recurrence and malignancy are not reported.[6]

Fibrous dysplasia

Fibrous dysplasia is a developmental tumour-like condition that becomes relatively static after skeletal maturation.[6,28] It is associated with Jaffe–Lichtenstein syndrome, McCune Albright syndrome, and Mazabraud’s syndrome.[25] Malignant transformation is reported in 0.5% (1 in 200) of cases.[6]

Familial gigantiform cementoma

It is an extremely rare cemento-osseous disease restricted to the jaws.[55,56] Its growing potential can be correlated with skeletal growth and maturation.[55] If left untreated, the enlargement eventually ceases during the fifth decade.[25]

Mucosal neuroma

It is commonly associated with multiple endocrine neoplasia (MEN) IIB syndrome. Clinically, it occurs in multiple small masses. Microscopically, it is partially encapsulated and contains aggregation or proliferation of histologically normal nerves.[6]

Congenital granular cell tumour

Congenital granular cell tumour is thought to be a variant of granular cell tumour, but the exact nature of the lesion is unclear. It exclusively occurs in infants or immediately after birth. Most of the lesions cease to grow or regress spontaneously without intervention.[19,23]

CONCLUSION

Oral hamartomas are unique presentations of the head and neck region. Nevertheless, the criteria to delineate hamartomas from other similar masses are ambiguous. To conclude, hamartomas should promptly be included in the differential diagnosis of the tumours of oral cavity, essentially the paediatric tumours, to avoid aggressive treatment and morbidity.

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Conflicts of interest

There are no conflicts of interest.

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