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Pleomorphic Adenoma of the Upper Lip: A Rare Presentation in a Young Boy and Differential Diagnosis

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ABSTRACT

A healthy 4-year-old boy presented with a painless lump on his upper lip for three years duration with no significant changes in size. Clinical examination revealed the presence of firm and mobile lump on the labial mucosa measuring approximately 15 mm × 10 mm, slightly pale yellowish compared to the surrounding tissues. The covering mucosa was intact and was non-tender upon palpation. Excisional biopsy was performed under general anaesthesia and the histopathological results revealed the presence of a partially encapsulated pleomorphic adenoma with variable epithelial and stromal components.

Keywords: Pleomorphic adenoma; lip; boy; plasmacytoid; painless lump

INTRODUCTION

Pleomorphic adenoma is the most common benign salivary gland tumours affecting the parotid glands of the adult population. It has significant female gender predilection (F:M = 2:1) of the 20–60 years age groups and commonly presented as a painless unilateral slow-growing swelling over the pre-auricular area (Bell et al., 2017). Clinically, the eversion of the earlobe on the affected sides, when examined from behind, was one of the key clinical signs elicited, as the tumour mostly arises from the superficial lobe of the parotid glands. The occurrence of this neoplasm arising from a minor salivary gland on the upper lip of a male child under five years old is very uncommon (Ogata et al., 1994). Only a handful of cases reported in individuals less than 20 years old with the common intraoral site at the palate, cheek, upper and lower lips (Callender et al., 1992; Jorge et al., 2002; Lotufo et al., 2008).

CASE PRESENTATION

A healthy 4-year-old boy was brought to the dental clinic of Hospital Universiti Sains Malaysia by his mother with a complaint of a painless lump on his upper lip. The lump was first noticed back in 2016,
with no noticeable size change. Clinical examination revealed the presence of firm and mobile lump on the labial mucosa measuring approximately 15 mm × 10 mm with a slightly yellowish colour compared to surrounding tissues. The covering mucosa was intact and was non-tender upon palpation (Fig. 1). No other lump noted intraorally, and his oral hygiene was fair. An excisional biopsy was carried out under general anaesthesia and, a well-circumscribed, slightly yellowish nodule was found (Fig. 2). The histopathological findings showed a partially encapsulated well-circumscribed tumour composed of variable epithelial and stromal components. The epithelial and myoepithelial cells were arranged mainly in duct/tubules admixed with clusters formation and the lumen contained secretory material (Fig. 3). The inner epithelial cells appeared as columnar, cuboidal or flat surrounded by an outer layer of myoepithelial cells in variable thickness. Its cytological appearances ranged from cuboidal, spindled, stellate, epithelioid, clear or plasmacytoid (Fig. 4). The backgrounds stroma appears partly hyalinised, exhibiting collagenous fibrillar structures, and partly myxomatous (Fig. 5). The central areas of proliferating epithelial sheets also showed squamous differentiation, as evidenced by keratin pearls formation. No cellular atypia was noted, and the histological picture depicted a localised benign appearance. Subsequently, the biopsy site healed uneventfully after one-week follow-up and at one- and six-month follow-up review, no sign of recurrences was noted.

**DISCUSSION**

An asymptomatic solitary lump on the upper lip of children less than five years old is uncommon and, the differential diagnosis includes benign mesenchymal tumours, developmental hamartomas and minor salivary gland neoplasms (Lotufo *et al.*, 2008; Thomas *et al.*, 2017).
Benign Mesenchymal Tumours

Neurofibroma and schwannoma (neurilemmoma) are two common soft tissue neoplasms that usually presented as slow-growing submucosal mass within the oral region (Flucke and Wenig, 2017). Both arise from the peripheral nerve sheath and, the common intraoral sites include the tongue, palate, buccal mucosa and floor of the mouth (Cates and Coffin, 2012). The occurrences of these tumours on the upper lip were previously reported (López-Jornet et al., 2010; Desai, 2019). Generally, benign peripheral nerve sheath tumours are rare in children less than five years old (< 1%) but it does constitute approximately 5% of benign tumours in children between 6 and 15 years of age (Cates and Coffin, 2012). These neoplasms are important entities in children as they are encountered as part of the manifestation of various genetic disorders. Nevertheless, in most cases, these lesions in the oral region occur sporadically (Cates and Coffin, 2012).

Neurofibromas are the most common peripheral nerve sheath affecting children and adolescent (Cates and Coffin, 2012) while schwannoma, also known as neurilemmoma, usually occurs in an adult. However, few cases were reported occurring in the upper lips of children (Kok et al., 2013; Abrahao et al., 2014). Histopathologically, neurofibroma composed of an admixture of cell types, i.e. Schwann cells, fibroblast, perineurial-like cells and axons, whereby schwannoma is composed of spindle cell proliferation of Schwann cells with alternating cellular Antoni A and hypocellular Antoni B areas (Rodriguez et al., 2012).

Another benign mesenchymal tumour that includes in the differential diagnosis is lipoma. It is the most common benign mesenchymal tumours and is composed of normal adipose tissues giving rise to a soft, movable, painless lump with a yellowish colour. In the oral cavity, the lip is the second most common site after
it is more common in adults, with the usual presenting age of approximately 45 years (Pinkston and Cole, 1999). It is typically presented as a single, firm, mobile, well-circumscribed mass. There is a higher female predilection compared to men with 2:1 ratio (Bell et al., 2017).

The term ‘pleomorphic’ refers to the variability of its histological tissue architecture as it is composed of active proliferation of epithelial (spindled, oval, epithelioid and plasmacytoid) and stromal components (myxoid, lipomatous, chondroid and osseous) rather than atypical cytological features (Bell et al., 2017). The treatment of choice is surgical excision with normal margins, and the recurrence rates are reportedly low (Colella et al., 2015). Most recurrences are associated with female gender, tumour cell disruption and spillage into surrounding tissues after capsule rupture, and conservative enucleation resulting in incomplete excision (Bell et al., 2017, Thomas et al., 2017). Approximately 6.2% of long-standing untreated pleomorphic adenoma (PA) may develop carcinomatous changes, i.e. carcinoma ex-PA (Gnepp, 1993; Antony et al., 2012). This subset of tumour mainly arises from major salivary glands, mostly parotid, followed by submandibular glands (Antony et al., 2012). Nevertheless, these occurrences of malignant transformation were reported in PA arising from minor salivary glands mostly on the hard and soft palate (Yoshihara et al., 1995; Damm and Fantasia, 2001) and around 10.5% affects the upper lip (Ellis and Auclair, 2008; Mitate et al., 2013; Sedassari et al., 2014). Due to the long-standing nature of the transformation, it is rarely encountered in children (Lack and Upton, 1988) and more commonly seen in patients in the sixth and seventh decade of life (Olsen and Lewis, 2001). Nonetheless, young age at presentation and the male gender, as seen in this case, has been considered as a risk factor for malignant changes (Bell et al., 2017).

Developmental Hamartomas

Hamartoma is a benign, non-cancerous growth made up of an abnormal mixture of cells and tissues normally found at the site of the lesion (NCI, 2020). In the head and neck, common forms of hamartoma composed of blood vessels (haemangioma) and lymphatics (lymphangioma) or a mixture of both (Mulliken and Glowacki, 1982). Other mixture of tissues derived from neural, skeletal muscles and lipomatous origin are considered rare (de la Rosa-Garcia and Mosqueda-Taylor, 1999). Nevertheless, given the solitary nature and yellowish colour of the lump in the present case, a differential diagnosis of angiomylipomatous hamartoma is possible, and the occurrence of the upper lip of a child has been reported (Pontes et al., 2011).

Another rare hamartoma of neuromuscular origin, i.e. benign triton tumour was previously reported occurring in the upper lip of young children (Hemalatha et al., 2014). Histopathologically, this tumour exhibits peripheral nerve proliferation with focal skeletal muscle differentiation in an organised architecture (Mitchell et al., 1995). The word ‘triton’ was coined from Triton salamander, an amphibian with the neural ability to induced skeletal muscle regeneration.

Minor Salivary Glands Neoplasms

Epidemiologically, the most common salivary gland tumour affecting children is pleomorphic adenoma (PA). It is more common in adults, with the usual presenting age of approximately 45 years (Pinkston and Cole, 1999). It is typically presented as a single, firm, mobile, well-circumscribed mass. There is a higher female predilection compared to men with 2:1 ratio (Bell et al., 2017).

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Histologically, the carcinomatous component constitutes up to 33%–84% of these neoplasms apart from the original PA lesions. It expresses both epithelial and myoepithelial differentiation when arising from minor salivary glands as opposed to expression of mostly epithelial differentiation seen in carcinoma ex-PA of its major counterparts (Antony et al., 2012). Frequent malignant changes reported were adenocarcinoma and salivary duct carcinoma (Olsen and Lewis, 2001). Additionally, a case of squamous cell carcinoma ex-PA on the upper lip was previously reported (Mitate et al., 2013). At the molecular level, a subset of this tumours was found to demonstrate the expression of PLAG1, HMGA2 fusions and downregulation of WIFI which implicates malignant transformation. The mainstay treatment is surgical disregard of the location. Generally, carcinoma ex-PA arising from minor salivary glands is smaller (less than 5 mm) and has a better prognosis compared to the lesions arising from the major glands (Olsen and Lewis, 2001).

Among other entities of salivary gland neoplasms, mucoepidermoid carcinoma (MEC) is regarded as the most common salivary gland malignancy affecting children and young adults (Ritwik et al., 2012). Most of the cases involved parotid gland, followed by palatal minor salivary glands (Byrd et al., 2013). Generally, MEC contributes to 12–40% of malignant salivary gland tumours and slight male gender predominance was observed when all head and neck site is considered (Pires et al., 2004; Byrd et al., 2013). Additionally, around 20 cases of intraoral MEC were reported with the mean age of 13.5 years and a slight female predominance (2.3:1). Five per cent of these cases affected the upper lip (Lack and Upton, 1988; Ritwik et al., 2012). The clinical presentation on the upper lip may mimic a benign lesion, ranging from a soft lump with cystic and smooth shiny surfaces resembling mucocele to a palpable firm, circumscribed nodule (Brandwein-Gensler et al., 2017).

A biopsy usually revealed cystic areas with low-grade tumour composed of predominantly mucous cells and minimal proliferation of solid sheets of epidermoid and intermediate cells whereby the presence of less mucous and more epidermoid component indicates higher grade lesions (Brandwein-Gensler et al., 2017). Most of the intraoral MEC in children and adolescents were of low to intermediate histological grades and wide local excision with tumour-free surgical margins generally suffice. The recurrence rate was less than 10%, and bone removal only indicated in cases where there is clear evidence of gross periosteal involvement (Ritwik et al., 2012).

CONCLUSION
This case highlights the necessity of further investigation of a clinically benign lump on the upper lip of young children to rule out a possible risk of malignancy despite more reported incidences of benign developmental and neoplastic lesions.

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CONFLICTS OF INTEREST
The authors declare that there is no conflict of interest regarding the publication of this article.

ETHICAL CONSIDERATION
The present case report was prepared in agreement with the guidelines of the Helsinki Declaration as revised in 1975.
CONSENT

Informed consent was obtained from the patient’s legal guardian before the preparation of the case report and the authors endeavoured to ensure anonymity.

REFERENCES


