CASE REPORT
Volume 15 Issue 1 2020
DOI: 10.21315/aos2020.15.1.424
ARTICLE INFO
Submitted: 15/10/2019
Accepted: 29/06/2020
Online: 15/07/2020

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

Noraida Mamat[a], Nurhayu Ab Rahman[b,c*]

[a]*Paediatric Dentistry Unit, School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia*

[b]*Oral Pathology and Oral Medicine Unit, School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia*

[c]*Hospital Universiti Sains Malaysia, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia*

[*]Corresponding author: nurhayu@usm.my

To cite this article: Mamat N, Ab Rahman N (2020). Pleomorphic adenoma of the upper lip: A rare presentation in a young boy and differential diagnosis. *Arch Orofac Sci*, **15**(1): 81–88. https://doi.org/10.21315/aos2020.15.1.424

To link to this article: https://doi.org/10.21315/aos2020.15.1.424

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.

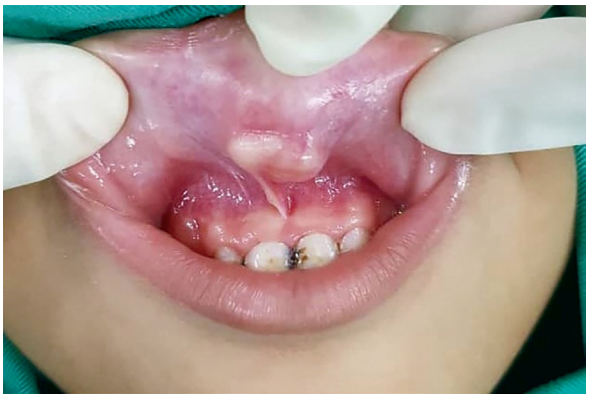

Fig. 1 Intraoral photograph. A firm, solitary lump noted on the upper left lip next to the frenal attachment.

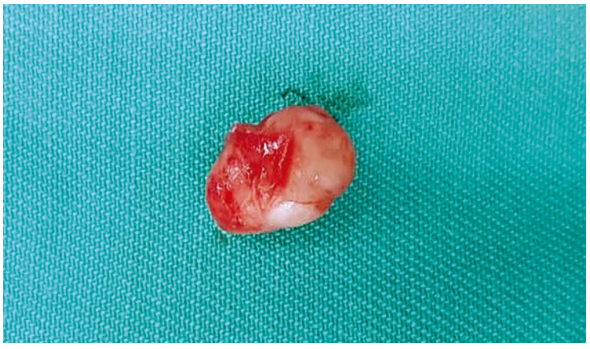

Fig. 2 Gross macroscopy. The lump appeared round to oval, pale-yellowish and slightly lobulated with a smooth surface.

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).

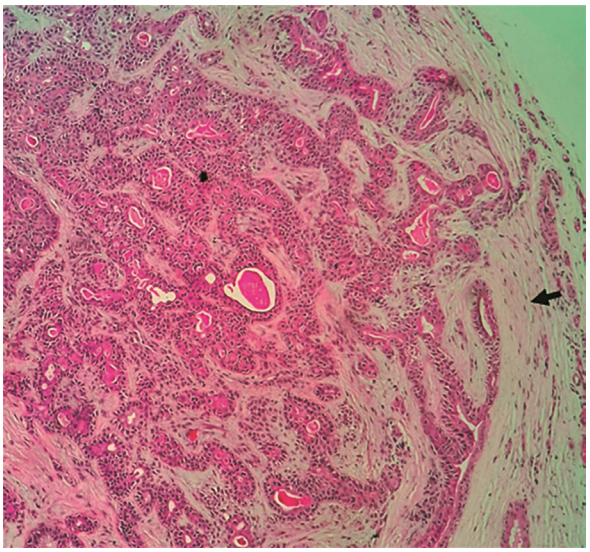

Fig. 3 Photomicrograph of the lesion. Presence of a capsule surrounding the tumour (black arrow). The proliferation of epithelial and myoepithelial cells in tubular/ductal and solid cord/nest arrangement is evident (haematoxylin and eosin, x 100).

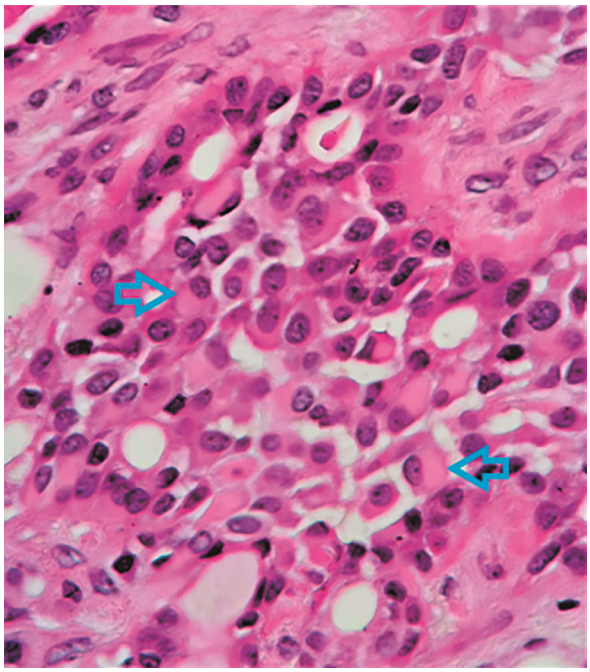

Fig. 4 Photomicrograph of the lesion (higher magnification). A cluster of plasmacytoid myoepithelial cells (blue arrows) (haematoxylin and eosin, x 400).

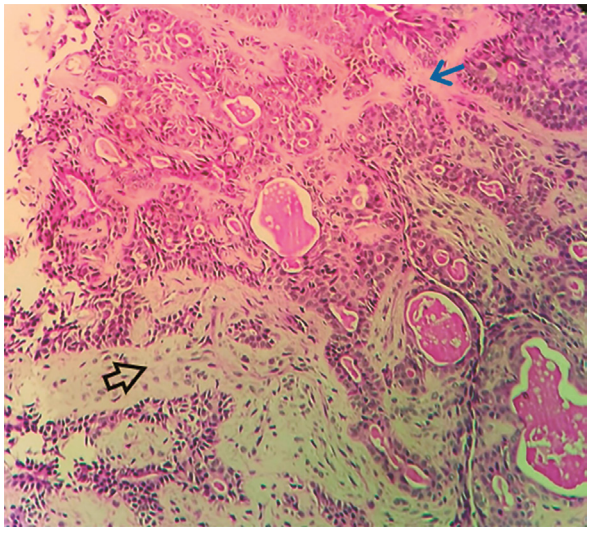

Fig. 5 Photomicrograph of the lesion. Hyalinised (blue arrow) and myxomatous (black arrow) background stroma. The lumen also contains secretory material (haematoxylin and eosin, x 200).

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

buccal mucosa (Furlong *et al.*, 2004; Tettamanti *et al.*, 2014; Punjabi *et al.*, 2017; Dastoor *et al.*, 2018). Common histological presentations are classic lipoma composed of well-encapsulated purely mature adipocytes and fibrolipoma, i.e. a mixture of adipocytes and fibrous connective tissues without the presence of a capsule. Other infrequent histological variants include intramuscular lipoma, minor salivary gland lipoma and spindle cell lipoma (Manor *et al.*, 2011)

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-García and Mosqueda-Taylor, 1999). Nevertheless, given the solitary nature and yellowish colour of the lump in the present case, a differential diagnosis of angiomyolipomatous 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). Nevertheless, 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).

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 *WIF1* 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 predilection (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.

ACKNOWLEDGEMENTS

The authors would like to thank Dr Masitah Hayati Harun and staff of Oral Pathology Laboratory, School of Dental Sciences, Universiti Sains Malaysia for their help in the preparation of materials included in the present case report.

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

Abrahao AC, Almeida P, Júnior VM, da Rocha Curvelo JA, Rumayor-Piña A, Maia De Faria LC *et al.* (2014). Schwannoma of the upper lip in a child. *Oral Surg Oral Med Oral Pathol Oral Radiol*, **117**(2): e189. https://doi.org/10.1016/j.oooo.2013.12.206

Antony J, Gopalan V, Smith RA, Lam AK (2012). Carcinoma ex pleomorphic adenoma: A comprehensive review of clinical, pathological and molecular data. *Head Neck Pathol*, **6**(1): 1–9. https://doi.org/10.1007/s12105-011-0281-z

Bell D, Bullerdiek J, Gnepp DR, Schwartz MR, Stenman G, Triantafyllou A (2017). Pleomorphic adenoma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (eds.), *WHO Classification of the Head and Neck Tumours*, 4th edn. Lyon: International Agency for Research on Cancer (IARC), pp. 185–186.

Brandwein-Gensler M, Bell D, Inagaki H, Katabi N, Leivo I, Seethala R *et al.* (2017). Mucoepidermoid carcinoma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (eds.), *WHO Classification of the Head and Neck Tumours*, 4th edn. Lyon: International Agency for Research on Cancer (IARC), pp. 163–164.

Byrd SA, Spector ME, Carey TE, Bradford CR, McHugh JB (2013). Predictors of recurrence and survival for head and neck mucoepidermoid carcinoma. *Otolaryngol Head Neck Surg*, **149**(3): 402–408. https://doi.org/10.1177/0194599813489659

Callender DL, Frankenthaler RA, Luna MA, Lee SS, Goepfert H (1992). Salivary gland neoplasms in children. *Arch Otolaryngol Head Neck Surg*, **118**(5): 472–476. https://doi.org/10.1001/archotol.1992.01880050018003

Cates JM, Coffin CM (2012). Neurogenic tumors of soft tissue. *Pediatr Dev Pathol*, **15**(1 Suppl): 62–107. https://doi.org/10.2350/11-03-1003-PB.1

Colella G, Cannavale R, Chiodini P (2015). Meta-analysis of surgical approaches to the treatment of parotid pleomorphic adenomas and recurrence rates. *J Craniomaxillofac Surg*, **43**(6): 738–745. https://doi.org/10.1016/j.jcms.2015.03.017

Damm DD, Fantasia JE (2001). Large palatal mass. Carcinoma ex-pleomorphic adenoma. *Gen Dent*, **49**(6): 574–658.

Dastoor PP, Patil RU, Singh Chauhan R, Palaskar SJ, Shah DR (2018). Fibrolipoma on a child's lip: A rare clinical finding. *J Dent Child (Chic)*, **85**(1): 36–39.

de la Rosa-García E, Mosqueda-Taylor A (1999). Leiomyomatous hamartoma of the anterior tongue: Report of a case and review of the literature. *Int J Paediatr Dent*, **9**(2): 129–132. https://doi.org/10.1046/j.1365-263x.1999.00116.x

Desai J (2019). An unexpected and rare outcome of a common nodular mass on upper lip in a pediatric patient with a history of trauma – Schwannoma. *Natl J Maxillofac Surg*, **10**(1): 102–104. https://doi.org/10.4103/njms.NJMS_48_18

Ellis GL, Auclair PL (2008). *Tumors of the Salivary Gland. AFIP Atlas of Tumor Pathology, Series 4, Fascicle 9*. Silver Spring MD: ARP Press, pp. 265–266.

Flucke U, Wenig BM (2017). Schwannoma and neurofibroma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (eds.), *WHO Classification of the Head and Neck Tumours,* 4th edn. Lyon: International Agency for Research on Cancer (IARC), pp. 123–124.

Furlong MA, Fanburg-Smith JC, Childers EL (2004). Lipoma of the oral and maxillofacial region: Site and subclassification of 125 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, **98**(4): 441–450. https://doi.org/10.1016/j.tripleo.2004.02.071

Gnepp DR (1993). Malignant mixed tumors of the salivary glands: A review. *Pathol Annu*, **28** Pt 1: 279–328.

Hemalatha AL, Sanjay M, Anoosha K, Ashok KP, Shantha Kumari BR (2014). Benign triton tumour of upper lip – A rare neoplasm at an extremely uncommon site. *J Clin Diagn Res*, **8**(12): FD03-FD04. https://doi.org/10.7860/JCDR/2014/10289.5295

Jorge J, Pires FR, Alves FA, Perez DEC, Kowalski LP, Lopes MA *et al*. (2002). Juvenile intraoral pleomorphic adenoma: Report of five cases and review of the literature. *Int J Oral Maxillofac Surg*, **31**(3): 273–275.

Kok YO, Yeo MS, Nallathamby V, Lee SJ (2013). Infraorbital nerve schwannoma presenting as an upper lip mass in an adolescent boy. *Ann Plast Surg*, **71**(2): 196–197. https://doi.org/10.1097/SAP.0b013e318248b8a2

Lack EE, Upton MP (1988). Histopathologic review of salivary gland tumours in childhood. *Arch Otolaryngol Head Neck Surg*, **114**(8): 898–906. https://doi.org/10.1001/archotol.1988.01860200082024

Lotufo MA, Júnior CA, Mattos JP, França CM (2008). Pleomorphic adenoma of the upper lip in a child. *J Oral Sci*, **50**(2): 225–228. https://doi.org/10.2334/josnusd.50.225

López-Jornet P, Gomez-Garcia E, Camacho-Alonso F (2010). Solitary oral neurofibroma. *N Y State Dent J*, **76**(5): 54–55.

Manor E, Sion-Vardy N, Joshua BZ, Bodner L (2011). Oral lipoma: Analysis of 58 new cases and review of the literature. *Ann Diagn Pathol*, **15**(4): 257–261. https://doi.org/10.1016/j.anndiagpath.2011.01.003

Mitate E, Kawano S, Kiyoshima T, Kawazu T, Chikui T, Goto Y *et al.* (2013). Carcinoma ex pleomorphic adenoma of the upper lip: A case of an unusual malignant component of squamous cell carcinoma. *World J Surg Oncol*, **11**: 234. https://doi.org/10.1186/1477-7819-11-234

Mitchell A, Scheithauer BW, Ostertag H, Sepehrnia A, Sav A (1995). Neuromuscular choristoma. *Am J Clin Pathol*, **103**(4): 460–465. https://doi.org/10.1093/ajcp/103.4.460

Mulliken JB, Glowacki J (1982). Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. *Plast Reconstr Surg*, **69**(3): 412–422. https://doi.org/10.1097/00006534-198203000-00002

National Cancer Institute (NCI) (2020). Retrieved 13 March 2020, from https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hamartoma.

Ogata H, Ebihara S, Mukai K (1994). Salivary gland neoplasms in children. *Jpn J Clin Oncol*, **24**(2): 88–93. https://doi.org/10.1093/oxfordjournals.jjco.a039689

Olsen KD, Lewis JE (2001). Carcinoma ex pleomorphic adenoma: A clinicopathologic review. *Head Neck*, **23**(9): 705–712.

Pinkston JA, Cole P (1999). Incidence rates of salivary gland tumours: Results from population-based study. *Otolaryngol Head Neck Surg*, **120**(60): 834–840. https://doi.org/10.1016/S0194-5998(99)70323-2

Pires FR, de Almeida OP, de Araújo VC, Kowalski LP (2004). Prognostic factors in head and neck mucoepidermoid carcinoma. *Arch Otolaryngol Head Neck Surg,* **130**(2): 174–180. https://doi.org/10.1001/archotol.130.2.174

Pontes HA, Pontes FS, Cruz e Silva BT, Martel LP, Carneiro JT, Silva BS *et al.* (2011). Angiomyolipomatous hamartoma of the upper lip: A rare case in an 8-month-old child and differential diagnosis. *J Craniomaxillofac Surg*, **39**(2): 102–106. https://doi.org/10.1016/j.jcms.2010.10.006

Punjabi VH, Patel S, Pathak J, Swain N (2017). Fibrolipoma of lip in a young individual: A rare presentation. *J Contemp Dent*, **7**(3): 181–184.

Ritwik P, Cordell KG, Brannon RB (2012). Minor salivary gland mucoepidermoid carcinoma in children and adolescents: A case series and review of literature. *J Med Case Rep*, **6**: 182. https://doi.org/10.1186/1752-1947-6-182

Rodriguez FJ, Folpe AL, Giannini C, Perry A (2012). Pathology of peripheral nerve sheath tumour: Diagnostic overview and update on selected diagnostic problems. *Acta Neuropathol*, **123**(3): 295–319. https://doi.org/10.1007/s00401-012-0954-z

Sedassari BT, da Silva Lascane NA, Tobouti, PL, Pigatti FM, Franco MI, de Sousa SC (2014). Carcinoma ex pleomorphic adenoma of the palate composed of invasive micropapillary salivary duct carcinoma and adenoid cystic carcinoma components. An unusual case with immunohistochemical approach. *Medicine (Baltimore)*, **93**(27): e146. https://doi.org/10.1097/MD.0000000000000146

Tettamanti L, Azzi L, Croveri F, Cimetti L, Farronato D, Bombeccari G *et al.* (2014). Oral lipoma: Many features of a rare oral benign neoplasm. *Head Neck Oncol*, **6**(3): 21.

Thomas DC, Nair VV, Thomas S. (2017). Pleomorphic adenoma: An unusual presentation on upper lip – A case report. *J Indian Acad Oral Med Radiol*, **29**(3): 217–219. https://doi.org/10.4103/jiaomr.JIAOMR_18_17

Yoshihara T, Tanaka M, Itoh M, Ishii T (1995). Carcinoma ex pleomorphic adenoma of the soft palate. *J Laryngol Otol*, **109**(3): 240–243. https://doi.org/10.1017/s0022215100129809