BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

Benign Mixed Tumor of the Upper lip. Report of two cases.

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ABSTRACT

Pleomorphic adenoma, also known as benign mixed tumor, is the most common salivary gland tumor, mostly affecting major salivary glands, but also encountered concerning minor ones. The occurrence of this lesion in the skin, known with the term chondroid syringoma, is unusual and considered to be associated with eccrine or apocrine glands. The two lesions demonstrate almost identical histological features with microscopic characteristics of both epithelial and mesenchymal origin. In this article two cases of benign mixed tumor of the lip are presented and their surgical management and histological features are analyzed. Both cases involved the upper lip, one was located in the subcutaneous tissues and the other in the labial mucosa. The proximity of eccrine sweat gland tumors of the skin with the salivary glands of the oral mucosa makes it often difficult to discern the origin of benign mixed tumor. This report discusses the particular characteristics of each pathological entity, the clinical differential diagnosis and the treatment approach chosen accordingly.

Keywords: benign mixed tumor, pleomorphic adenoma, submucosal swelling

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Received 05 June 2019, Accepted 01 July 2019

Please cite this article as: Danai P *et al.*, Benign Mixed Tumor of the Upper lip. Report of two cases.. British Journal of Medical and Health Research 2019.

INTRODUCTION

Salivary gland tumors are rare lesions consist of 2-6.5% of all head and neck tumors (1). Intraoral minor salivary gland tumors account for 22% of all salivary gland neoplasms. Pleomorphic adenoma (PA), also known as benign mixed tumor, is the most common salivary gland tumor (60-65%), in adult and pediatric population (2, 3, 4, 5, 6). PA is primarily found in the parotid and submandibular glands, as well as in minor salivary glands. The most common intraoral site is the palate, followed by the upper lip and the buccal mucosa, whereas other unusual locations are the retromolar region, the floor of the mouth and the alveolar mucosa (2). According to the latest World Health Organization, pleomorphic adenoma is defined as a neoplasm characterized by the presence of benign epithelial and myoepithelial cells and a mesenchymal component that may contain mucoid, myxoid, cartilaginous, or osseous areas. It may be completely or partially encapsulated and usually presents as a slowly growing painless mass, that may recur after excision or transform to a malignant carcinoma ex pleomorphic adenoma. The lesion is more often encountered in middle-aged patients in the 4th -6th decade of life and presents a prevalence in the female population *(*2, 5).

Mixed tumor of the skin or chondroid syringoma (CS) represent the cutaneous part of "pleomorphic adenoma". This lesion shows strict histological appearance as pleomorphic adenoma of salivary glands (7). In 1892, Nasse reported a primary neoplasm of the skin with microscopic features of both epithelial and mesenchymal origin (8). The term chondroid syringoma was first proposed by Hirsch and Helwig in 1961, who reported a series of 188 cases with an invariable presence of sweat gland-like elements and a cartilage-like material (9). According to their study (9), the upper lip is the most common anatomic location for the development of CS, after the nose and the skin of the cheek. This rare tumor develops from eccrine or apocrine glands and although found mostly on the face it may arise in any location, including pharynx, larynx, esophagus, lacrimal gland, trachea, and mediastinum (10).

Here we present two cases of benign mixed tumor of the upper lip, one of which was located in the skin on the philtrum and the other in the labial mucosa respectively. Their surgical management and histological features are also analyzed.

CASES PRESENTATION

1st case

A 59-year-old man was referred to the Department of Oral and Maxillofacial Surgery for evaluation of an asymptomatic swelling on the upper lip, with a duration of 3 years. The patient's medical history was unremarkable with no known allergies, non-smoker and no history of trauma in the area was reported. The clinical examination revealed a round, elastic

tumor, located on the philtrum. The skin-colored lesion, measuring 1,3x1x1cm, was clearly demarked from the surrounding skin of the lip and was painless on palpation (Figure 1).

Under local infiltration anesthesia (Articamine 4%, 1:200,000 epinephrine) a cutaneous triangular incision was performed. The mass was dissected from the underlying muscles and overlying skin (Figure 2). The architecture of the philtrum and vermillion border was left intact. The oral mucosa was not involved in the lesion. The excisional biopsy produced a soft, elastic, nodular mass, of yellowish hue (Figure 3). The surgical specimen was fixed in 10% neutral formalin and sent for histopathological examination. Microscopically, the lesion was well circumscribed by a pseudocapsule (Figure 4) and consisted of columnar to cuboid cells with round to oval nuclei. The tumor cells arranged in cords, islands or duct-like structures which lined by one or two layers of cells and contained amorphous eosinophilic material (Figures 4, 5). Cystic spaces of varying sizes and keratinous cysts surrounded by flattened cells were also noticed. The stroma was variable in appearance and partly fibrous showing myxochondroid or hyalinized hypocellular areas (Figure 4). The tumor did not demonstrate cytologic atypia, increased mitotic activity, or infiltrative tissue margins. Based on the clinical and histopathological findings, the diagnosis of a benign mixed tumor of the skin (chondroid syringoma) was rendered. The patient had an undisturbed healing and no recurrence has been reported after ten years of follow up.

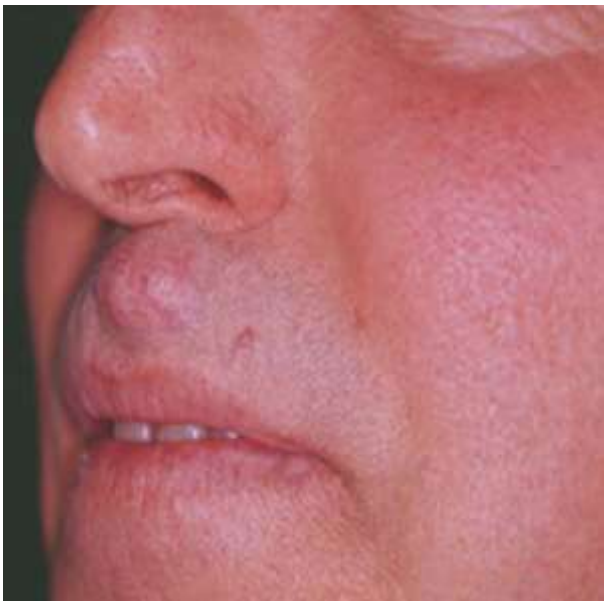

Figure 1: The round, skin-colored, elastic tumor that located on the philtrum was clearly demarked from the surrounding skin of the lip.

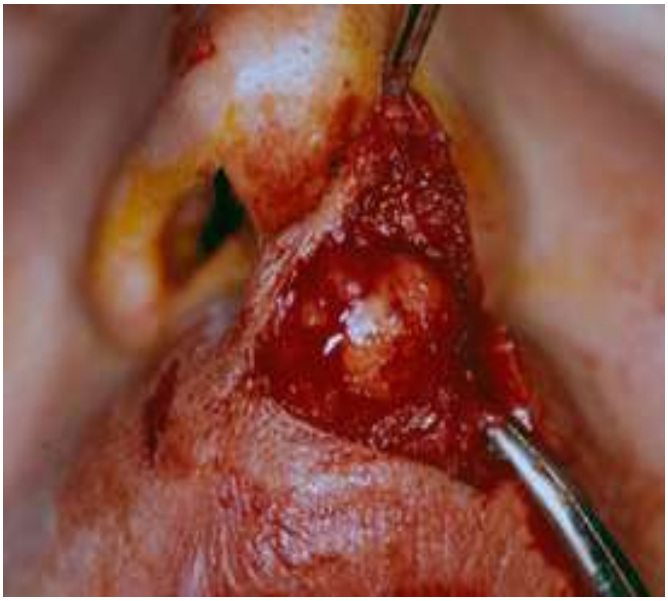

Figure 2: Cutaneous triangular incision through which the mass was dissected from the underlying muscles and overlying skin.

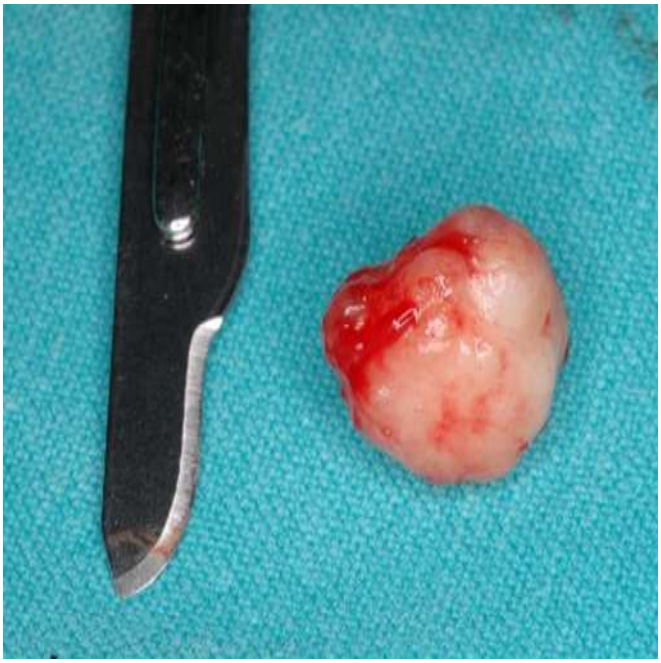

Figure 3: The surgical specimen showing a yellowish nodular mass.

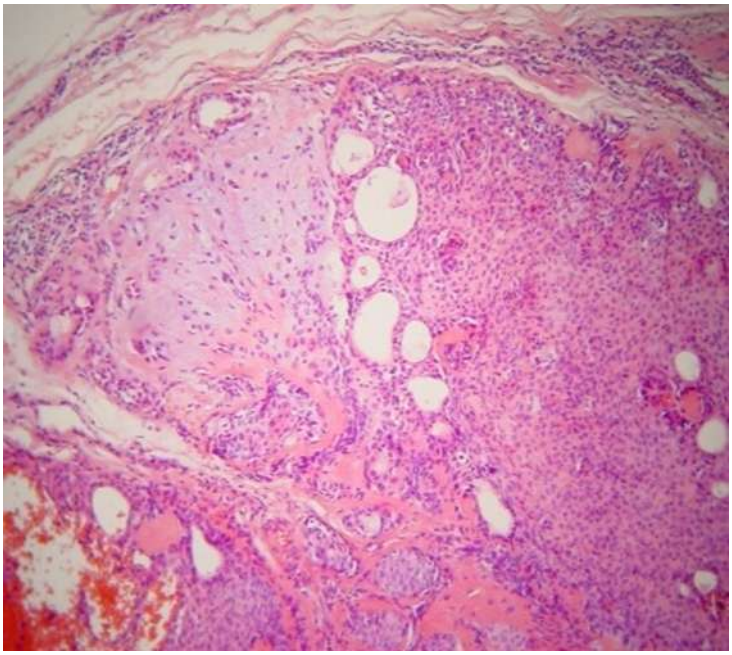

Figure 4: Cords and islands of tumor cells as well as duct-like structures can be seen in a myxochondroid fibrous stroma. The tumor is well circumscribed by a pseudocapsule (H&E X 250).

2nd case

A 30-year-old man was referred to the Department of Oral and Maxillofacial Surgery for evaluation of a raised, dome-shaped, painless, red, submucosal- subdermal nodule on the left side of his upper lip (Figure 6). The lesion was initially noticed three years ago and remained stable up to the last two months, when it slowly started swelling.

The clinical examination revealed a 1 cm in diameter, mobile, well circumscribed, painless mass of firm consistency that was located under the mucosa of the upper lip and caused a swelling (Figure 7) . There was no history of any other disease, no known allergies, no history of smoking. There was also no history of trauma, or prior surgeries in the region. Under local infiltration anaesthesia (Articamine 4%, 1:200,000 epinephrine), a mucosal incision was made and after careful dissection through the orbicularis oris, the encapsulated mass was totally excised (Figure 8). The different surgical approach compared to the first case, was preferred due to the proximity of the lesion to the lip mucosa, as opposed to the upper lip skin. Haemostasis was achieved and the surgical wound was closed in layers. The surgical specimen was fixed in 10% neutral formalin and sent for histopathological examination.

Grossly, the excised surgical specimen was in the form of an ovoid well demarcated, encapsulated, white-brown partly rubbery mass, measuring 1X0.5X 0.5 cm, with solid cut surface (Figure 9). The histopathological analysis revealed a well circumscribed lesion, which consisted of epithelial and stromal component (Figure 10a). The epithelial component was composed of tubular structures, cords or islands of cuboidal and polygonal cells. The stroma

showed mainly myxoid appearance, while aggregates of stromal adipocytes were focally observed as well (Figure 10b,10c) The tubular structures lined by one or two layers of cuboidal cells with hyperchromatic nuclei in the luminal layer and less hyperchromatic at the periphery (10e). These structures contained amorphous eosinophilic material, whereas squamous metaplasia and few scattered keratinous cysts were visible in some areas (Figure 10a, 10d, 10e). Bone formation was seen in direct contact to stromal fibrocytes without intervening cartilage (10f). Nuclear pleomorphism or mitotic figures were not apparent. Based on these histopathologic features and the clinical appearance of the lesion the final diagnosis was intraoral benign mixed tumor or pleomorphic adenoma. The post-operative course was uneventful and there is no recurrence after five years of follow up.

Both patients had provided written informed consent for publication of these cases report and any accompanying images in a scientific journal, after the authors explained the possible benefits to dental science.

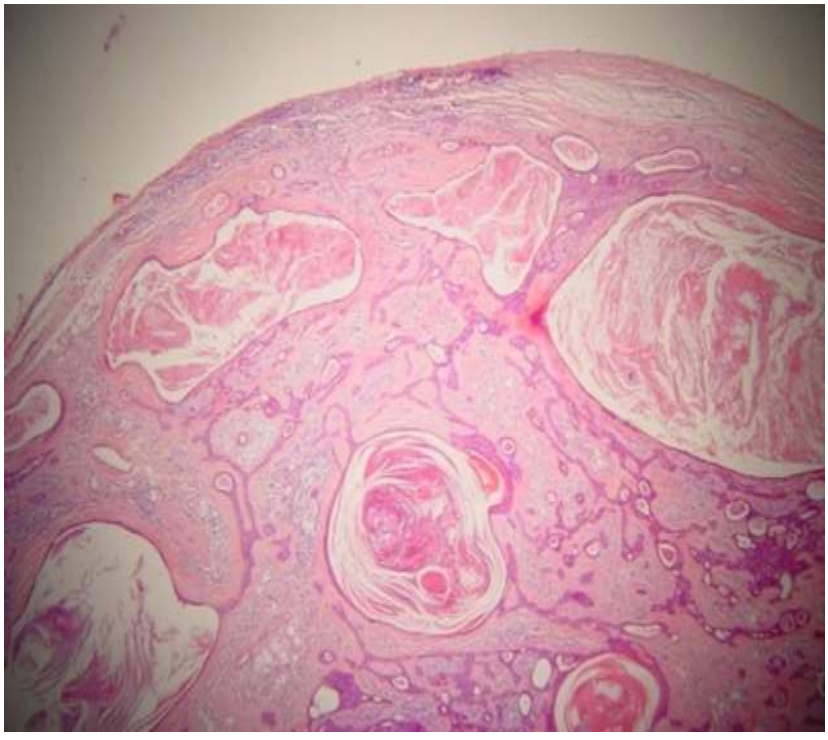

Figure 5: Ductal structures lined by two layers of cells and multiple cystic spaces filled with keratin (H&E X 250)

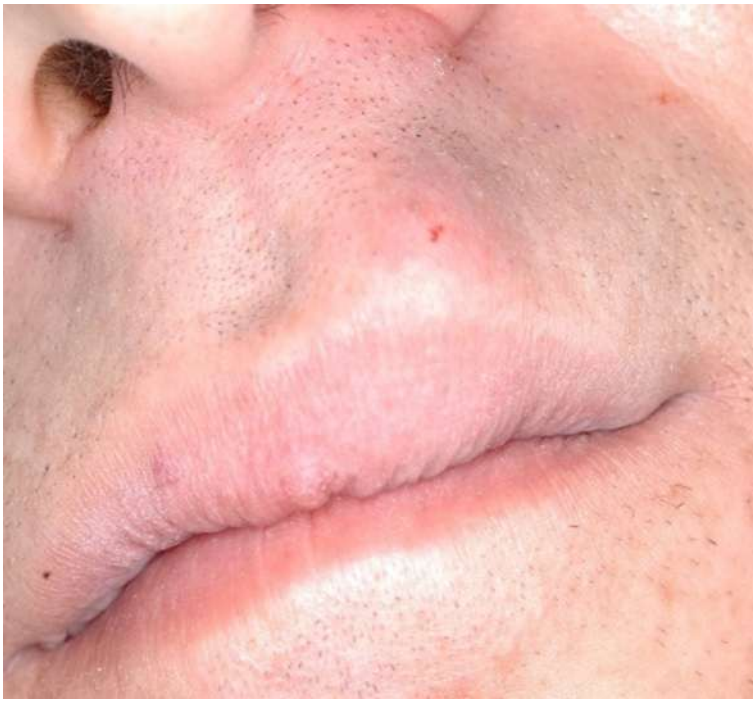

Figure 6: A raised, dome-shaped, red, submucosal- subdermal nodule on the left side of the patient upper lip.

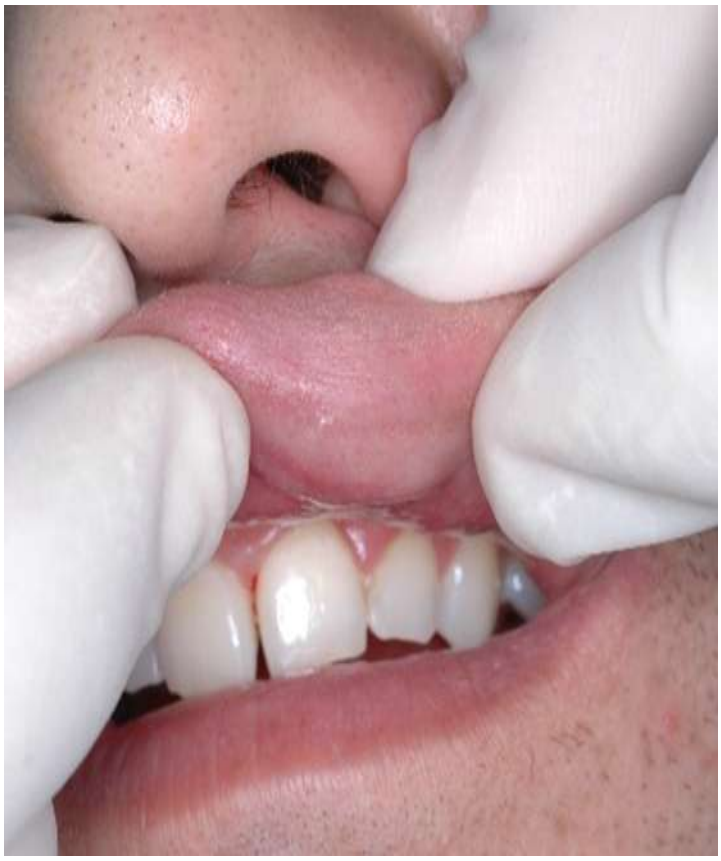

Figure 7: The lesion is prominent through the upper lip mucosa.

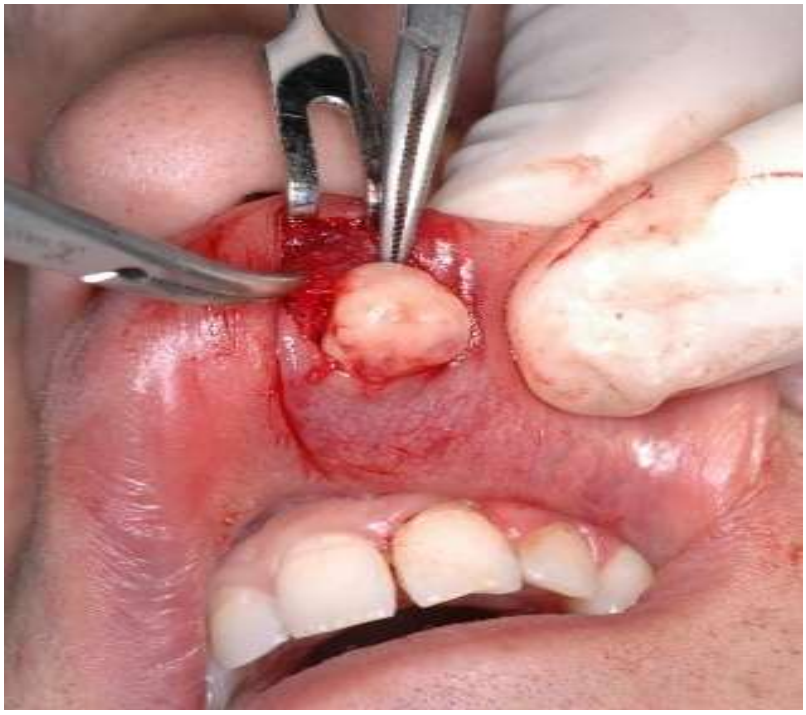

Figure 8: Total excision through a mucosal incision.

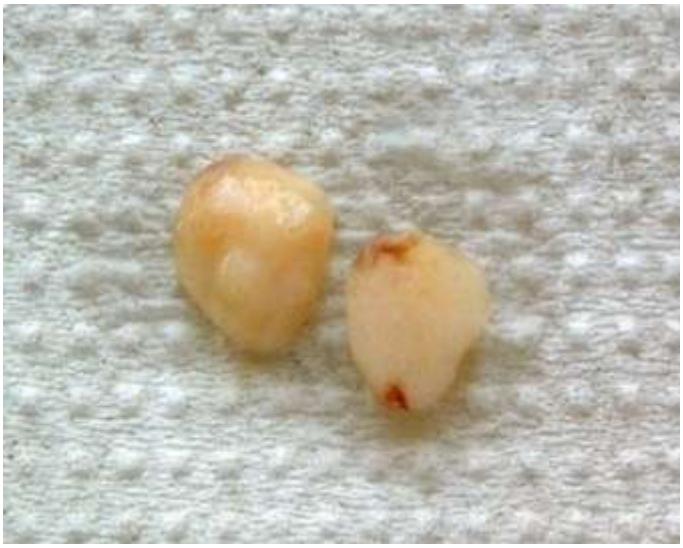

Figure 9: A white encapsulated nodular lesion of firm consistency.

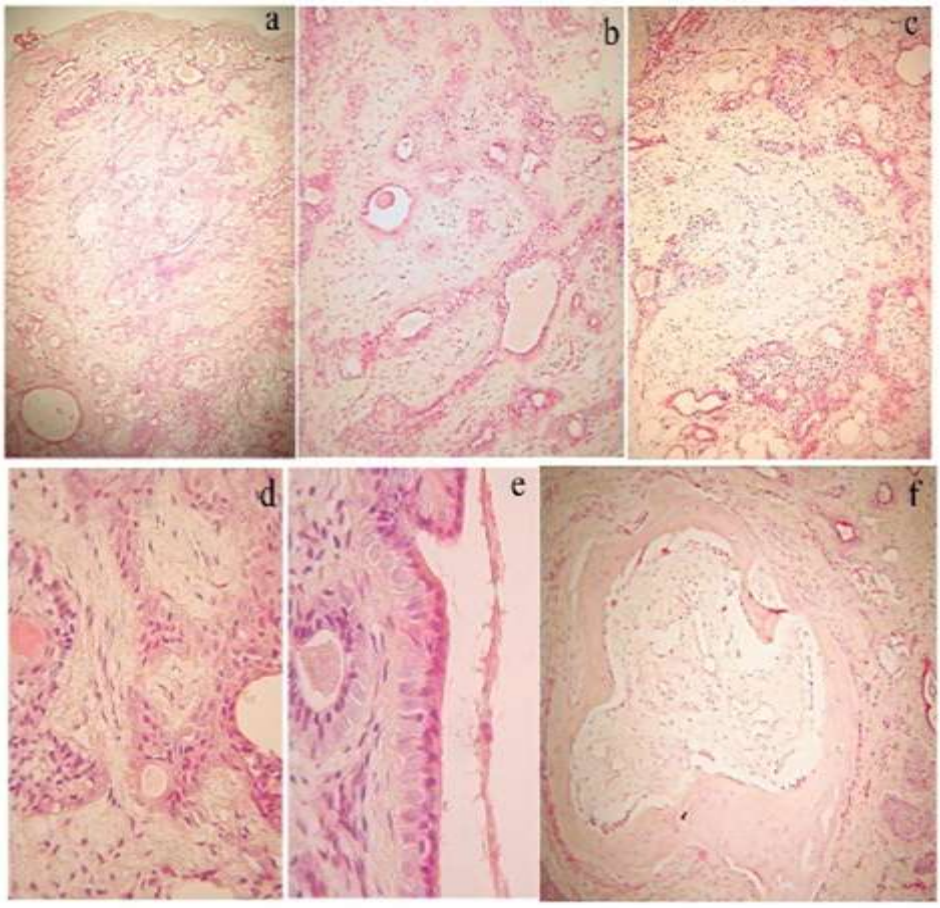

Figure 10 (a): the tumor was encapsulated and demonstrated tubules and cords. Hematoxylin and eosin stain magnification X25 (b): the tubular architecture and the myxoid stroma of the tumor, hematoxylin and eosin stain magnification X200(c): stromal adipocytes can be seen, hematoxylin and eosin stain magnification X100 (d): squamous metaplasia with keratin, hematoxylin and eosin stain magnification X400 (e) tubular structures lined by double epithelium are apparent in this view X400 (f) stromal bone formation without intervening cartilageX100.

DISCUSSION

The differential diagnosis of submucosal or subcutaneous solid, asymptomatic movable nodules in the upper lip comprises a wide range of lesions inflammatory or neoplastic in nature including oral cysts (mucous retention phenomenon, salivary duct cyst, nasolabial cyst), or infection secondary to foreign body's reaction, tumors of minor salivary glands, mesenchymal tumors, such as lipoma, hemangioma, neurofibroma or neurilemoma. Among the aforementioned lesions, the benign mixed tumor of the skin and the labial pleomorphic adenoma are at the top in the differential diagnosis list (10).

The benign mixed tumor of the skin, or CS presents many similarities with the pleomorphic adenoma in what concerns its histopathologic features as well as its location and characteristics in the areas where it is most commonly encountered. The terms pleomorphic and mixed are

used to describe the characteristic diverse microscopic pattern seen in this tumor, which is composed of a mixture of glandular epithelium, myoepithelial cells and connective tissue elements (7,10,11). The proximity of eccrine sweat gland tumours of the skin with the salivary glands of the oral mucosa makes it often difficult to discern the two pathologic entities. For this reason it is important to assess all the evidence, clinical and histological so as to decide the final diagnosis.

The pleomorphic adenoma presents as an asymptomatic firm mass with a long period of slow growth rate, whereas secondary to trauma the clinical features may also include ulceration, pain or bleeding. The second most common location for intraoral pleomorphic adenoma is the upper lip (following the palate), contrary to the lower lip, where it is most rarely found (2,3,12). There is propensity for benign salivary gland tumors to affect the upper lip compared to the lower lip. This site prevalence can be explained due to the embryonic development of the upper lip, which forms with the fusion of three alveolar embryonic processes, thus having a greater possibility of entrapment of embryonic cell nests. This suggestion is further supported by the fact that the lesions on the upper lip are often located along these fusion lines (10,12).

The treatment of pleomorphic adenoma consists of surgical excision. Recurrences are not uncommon and usually concern cases with inadequate surgical removal of the lesion. In the first case presented, the tumor was completely excised and no recurrence has been reported in a 10 year follow-up period. The different approach used in the two cases (cutaneous versus mucosal incision) was selected according to the proximity of each lesion to the lip skin or mucosa respectively so as to avoid extra trauma to the region.

Malignant transformation of pleomorphic adenoma has been reported and accounts for up to 6.2% of all pleomorphic adenomas (13). The greatest risk factor for malignant transformation according to the literature seems to be the amount of time elapsed since the tumor formation. There are three subtypes of malignant PA: carcinoma ex pleomorphic adenoma, carcinosarcoma or true malignant mixed tumour and metastasizing mixed tumour (10). Of these, carcinoma ex pleomorphic adenoma is the most common. In the case of malignant transformation the treatment of choice is surgical excision, including 1-2 cm of healthy tissue borders. In all cases, a follow up of several years is recommended (10).

The CS is an uncommon eccrine sweat gland tumor that may originate from both secretory and ductal elements of the sweat glands (14,15). The tumor is clinically presented as a small, painless, dermal or subcutaneous non-ulcerated, well-demarcated, solitary, firm, multilobulated nodule (16). It has a slow growth for several months or years. The lesion commonly measures 0.5- to 3-cm diameter. The clinical differential diagnosis includes epidermoid or dermoid cyst, sebaceous cyst, compound nevus, clear cell hidradenoma, cystic

basal cell carcinoma, neurofibroma, and histiocytoma (dermatofibroma). CS may also mimic malignant neoplasms such as the nodular basal-cell carcinoma (17).

CSs have been found on most areas of the skin, but the great majority involved the skin of the face and head, including scalp, auricle, forehead, eyebrow, glabella, upper eyelid, lower eyelid, nose, upper lip, lower lip, chin, and neck (18). Of these areas, the nose, upper lip, cheek, and scalp were the areas of predilection. It occurs frequently in male patients and the male: female ratio is calculated 2.17:1. (19, 20)

Malignant chondroid syringomas (MCS) are exceedingly rare and according to the literature only 29 cases have been reported (20). In contrast to their benign counterparts, MCS occur mainly in the extremities (60%). Only 6 cases (20%) occurred on the head or neck with 4 cases on the scalp, 1 on the ear, and 1 on the neck. The median age of MCS patients is 49 years, ranging from 13 to 83. There is a female predilection, with the female: male ratio being 1.7:1. The treatment of choice for such lesions consists of local excision, followed by thorough histological examination, to confirm that complete excision has been accompliced and that the surgical margins are clear. Nevertheless, recurrences may occur, owing to the fact that the tumor is often lobulated, and covered by a pseudocapsule that is usually infiltrated by tumor cells. When complete excision is performed, follow up can be limited to a couple of years.

CONCLUSION

Diagnosis of the intraoral or dermal upper lip neoplasms sometimes is challenging due to the non-pathognomonic clinical appearance and the similarities in histological features. PA and CS are rare pathologic entities derived from different glands (salivary or non-salivary), which are developed within the same anatomic region. They share similar biologic behavior with recurrence potency in cases of incomplete surgical excision. Therefore clinicians, dental practitioners and oral surgeons should be aware concerning the diagnostic procedure and management of lip nodules.

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