

Pleomorphic Adenoma in the Lower Lip: A Case Report and a Review

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Eur J Dent 2019;13:649–654

Abstract

Pleomorphic adenoma constitutes 50% of salivary gland tumors affecting mostly the parotid gland extraorally, and the palate intraorally. While the upper lip is a common site, it is unusual to encounter this tumor in the lower lip. A 26-year-old man complained of a persistent lump affecting the lower lip. The lesion was excised and was shown on histopathological examination to be a pleomorphic adenoma with squamous metaplasia. At the 18-month review appointment, there was complete healing and no recurrence. Pleomorphic adenoma in the lower lip should be considered among the differential diagnosis of lower labial swellings, especially in young patients. There needs to be reconsideration of the epidemiological and histological characteristics.

Introduction

Pleomorphic adenoma is the most common salivary gland tumor comprising 50% of all salivary gland tumors and 40% of intraoral salivary gland tumors.¹ The name is derived from the varied histopathologic structure of the neoplasm; it consists of an encapsulated proliferation of ductal and myoepithelial cells supported by a stroma that varies from dense hyalinized collagen to loosely arranged ground substance with the possibility of presence of cartilage and bone. The age prevalence of pleomorphic adenoma varies from the second decade onwards with a predilection for females.¹ Parotid is the most common extraoral site, while intraorally, the palate is the most common site followed by the upper lip and the buccal mucosa.¹ Labial pleomorphic adenoma constitutes 20 to 40% of all intraoral pleomorphic adenomas² however, most labial salivary gland tumors arise in the upper lip.¹ The lower lip is considered a rare site of occurrence for this tumor constituting < 3% of all intraoral pleomorphic adenomas.³ The clinical presentation of intraoral pleomorphic adenoma is that of a unilateral, painless, slow-growing submucosal mass covered by intact epithelium, with few cases of ulceration, pain, and bleeding being also reported. Some lesions may consist of a cystic component, develop a bluish appearance, and consequently become clinically indistinguishable from a

deeply seated mucocele or mucoepidermoid carcinoma.² Few cases of lower lip pleomorphic adenoma were reported.^{4–9} Scientific literature written in English reveals a small number of case reports on pleomorphic adenoma of the lower lip; most of them were reported in Asian countries, and Brazil. ►Table 1 describes all cases of labial pleomorphic adenoma that were reported between 2000 and 2019.

Here, we describe a case of pleomorphic adenoma in the lower lip of a 26-year-old man including diagnosis (histological and radiographic findings) and surgical management.

Case Report

A 26-year-old man of Egyptian descent attended for the complaint of a firm lump affecting the lower lip that has been slowly growing since the past 2 years and causing discomfort. There was no pain or infection associated with the lump. The patient was nonsmoker, nondrinker, and he worked as a clerk. The patient also reported no medical history of any significant diseases. Upon examination, there was no submandibular or cervical lymphadenopathy. Intraorally, the patient had generalized periodontitis, carious teeth, and severe gum recession around lower central incisors. The lesion was felt as a firm, nontender submucosal mass of 2.5 × 2.0 cm diameter affecting the lower lip. There was a mild elevation of

Table 1 Cases of pleomorphic adenoma that were reported between 2000 and 2019 affecting the upper lip (UL), and lower lip (LL) in both males (M) and females (F)

Authors (y)	Site	Country/ ethnicity	Gender	Age (y)	Prognosis	Follow-up ^a	Special remarks
Alves et al (2018) ¹⁰	UL	Brazil	M	18	Good	24 mo	
Mair and Aguirre (2016) ¹¹	UL	USA	M	62	Good	24 mo	
Khan et al (2016) ¹²	UL	Pakistan	M	60	NA	NA	
Fatahzadeh (2017) ¹³	UL	USA	M	58	NA	NA	
Ahmedi et al (2017) ¹⁴	UL	Kosova	F	10	Good	12 mo	
Fomete et al (2015) ¹⁵	UL	Nigeria	F	37	NA	NA	
Mariano et al (2013) ¹⁶	UL	Brazil	M	69	Good	30 mo	Carcinoma ex PA
Singh et al (2015) ¹⁷	UL	India	M	55	Good	6 mo	
Mitate et al (2013) ¹⁸	UL	Japan	M	55	Good	6 y	Carcinoma ex PA
Küçük and Tan (2011) ¹⁹	UL	Turkey	M	35	NA	NA	
Taiwo et al (2018) ²⁰	UL	Nigeria	M	33	Good	6 mo	
Stander et al (2013) ²¹	UL	African	F	47	Good	NA	
Tzermpos et al (2014) ²²	UL	Caucasian	F	39	Good	3 y	
Lotufo et al (2008) ²³	UL	Brazil	M	12	Good	1 y	
Asuquo et al (2009) ²⁴	UL	African	F	50	Good	3 mo	
Asuquo et al (2009) ²⁴	UL	African	F	40	Good	26 mo	
Jorge et al (2002) ³	UL	Brazil	F	15	Good	5 y	
Jorge et al (2002) ³	UL	Brazil	F	18	Good	39 y	
Dyalram et al (2012) ²⁵	UL	African American	M	72	Good	8 mo	Carcinoma ex PA
McNamara et al (2009) ²⁶	UL	Australia	F	55	Good	18 mo	Carcinoma ex PA
Kataria et al (2011) ²⁷	UL	India	F	65	Good	1 y	
Ali et al (2011) ²⁸	UL	India	M	33	Good	1 y	
Debnath and Adhyapok (2010) ²⁹	UL	India	F	55	Good	1 y	
Sood et al (2014) ⁵	LL	Asian	M	46	NA	NA	
To et al (2002) ⁶	LL	Hong Kong	M	25	Good	24 mo	
Sengul et al (2011) ³⁰	LL	Turkey	M	49	Good	40 mo	

Abbreviation: PA, pleomorphic adenoma.

^aFollow-up duration is in months (mo), years (y), or not available (NA).

the lower right labial mucosa slightly crossing the midline (**►Fig. 1**). Considering that the lesion was painless, slowly growing, and firm in consistency, an initial diagnosis of mesenchymal tumor (fibroma) was established. Further, a differential diagnosis was considered to include benign tumors arising from labial tissues in general such as pleomorphic adenoma, canalicular adenoma, fibroma/neurofibroma, and granular cell tumor.

Panoramic radiograph showed a calcified mass in the lip and alveolar bone resorption of lower anterior teeth (**►Fig. 2A**). Ultrasound examination revealed a well-defined

submucosal hypoechoic soft tissue mass of approximately $2.3 \times 2.2 \times 1.8$ cm (**►Fig. 2B**).

The lesion showed large areas of calcifications with no evidence of increased abnormal vascularity on color Doppler interrogation. Based on the presence of the calcified mass found in the lesion, sialolithiasis was considered as another differential diagnosis in addition to pleomorphic adenoma containing a cartilaginous/bony component.

It was decided to do an excisional biopsy. The patient was given bilateral mental nerve block using 6 mL of 2% mepivacaine with epinephrine. The mass was 2.0×2.0 cm and it was

completely encapsulated. The lesion was excised (**►Fig. 3**) and sent for histopathology.

Histopathological report revealed that the mass was composed of myxoid spindle-shaped cells intermingled with highly cellular areas formed mainly of myoepithelial cells with glandular and papillary formations. Other areas showed dense stromal fibrosis with solid sheets of myoepithelial cells, and squamous metaplasia (**►Fig. 4**).

Scattered foci of cartilage and bone formation were also seen in between. One month postoperatively the patient showed good healing of the wound. He was reviewed 18 months postoperatively; there was no recurrence, and

there was improvement in the gingival recession associated with the lower incisors (**►Fig. 5**).

Discussion

Salivary gland tumors are considered rare with a prevalence of 2.5 to 3 per 100,000 per year in the Western world, with approximately 80% of these lesions being benign.¹ Among these benign lesions, pleomorphic adenoma is considered a well-described tumor. There is a possibility, however, for confusion in histological interpretation particularly in small incisional biopsies due to the heterogeneity of the morphological patterns.¹ This morphogenic complexity is attributed to differentiation of the tumor cells into fibrous, hyalinized, myxoid, chondroid, and even osseous tissue. In the past two decades, several advanced diagnostic techniques have been developed to examine surgical specimens of salivary



Fig. 1 Swelling of the right lower labial mucosa extending slightly to the left side associated with severe gum recession around lower central incisors.

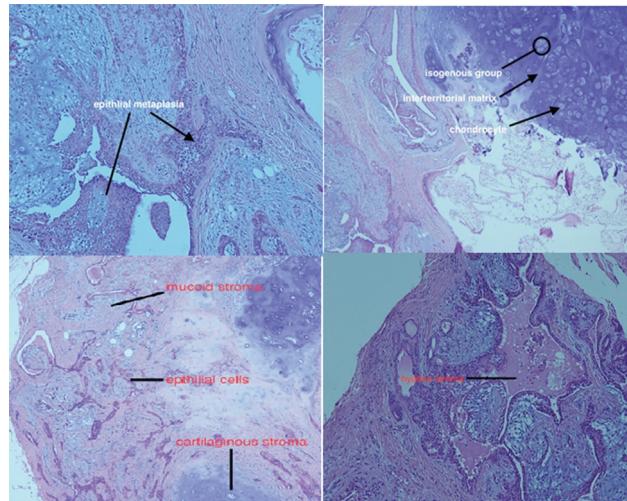


Fig. 4 Histological findings.

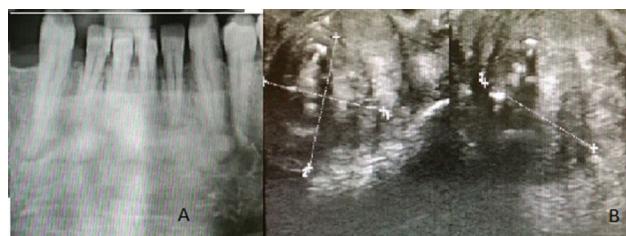


Fig. 2 Panoramic radiograph (A) and ultrasound examination (B) showing multiple calcifications in the lesion.



Fig. 3 Pleomorphic adenoma during (A) and after (B) excision.



Fig. 5 Retracted lower lip to show complete healing and no recurrence after 18 months of surgery. There was an associated scar and improvement of the gingival recession.

gland neoplasms, and they proved to be effective especially in small biopsies or in challenging cases for which histology and immunohistochemistry alone are not sufficient to reach a definite diagnosis.³¹ Such techniques include fluorescence in situ hybridization, polymerase chain reaction, and next-generation sequencing. Several primary antibodies have been developed and utilized to target specific aberrant gene products in pleomorphic adenoma, including PLAG1 and HMGA2.³²

Another important aspect of pleomorphic adenoma is its potential to show cancerous, or metaplastic changes, the latter affecting approximately 25% of pleomorphic adenomas.³³ Carcinoma arising in pleomorphic adenoma is due to transformation of benign lesions into malignancy, and it accounts for approximately 3% of salivary tumors.⁷ Progression to carcinoma is a multistage process that is preprogrammed temporarily in the genome.³⁴ These carcinomas tend to be larger and longer standing than benign lesions,¹ and they tend to affect an older age group with an average age of presentation of 60 years.² Cases reported in the past two decades show that carcinoma ex pleomorphic adenoma affects both males and females above 50 years of age in a ratio of 3:1 (**►Table 1**). A challenging aspect in the management of pleomorphic adenoma arises from the nature of its capsule because it is known to have microscopic pseudopod-like extensions into the surrounding tissues consequently leading to recurrence.³⁵ Pleomorphic adenoma is probably the only benign salivary gland neoplasm that may exhibit such pseudopods or focal infiltration into the adjacent normal salivary gland tissue.³¹ Moreover, recurrent pleomorphic adenoma often presents with numerous miliary nodules in the surgical bed.³¹ However, this could be a problem peculiar to parotid and not labial tumors due to the characteristic anatomical features of the parotid gland.

The differential diagnosis of a persistent slowly growing asymptomatic mass in the lip should include benign lesions³⁶ originating in tissues that form the lip including other minor salivary gland tumors, and mesenchymal lesions such as neurofibroma and schwannoma which usually occurs in adults of a younger age group.³⁷ The calcified mass seen on radiographic examination of the lesion in this case was explained as a sialolith or pleomorphic adenoma. However, sialolithiasis is a rare occurrence in minor salivary glands where the upper lip and buccal mucosa are the most commonly affected areas.³⁸

To et al stated that labial pleomorphic adenoma tends to occur at an earlier age than it does at other sites.⁶ Indeed, in this case report the patient was in the third decade of life similar to other case reports.⁶ Pleomorphic adenomas tend to be soft in consistency; however, in this case, it was firm due to its component of cartilage and bone which could be found in such a tumor.

Prognosis of pleomorphic adenoma is usually good as also reported from literature.^{4,6} Although some believe that salivary tumors of the lower lip tend to be malignant, while those of the upper lip tend to be benign. However, case reports on lower lip pleomorphic adenoma generally

report a good prognosis and no recurrence on follow-up for 2 to 4 years.^{4,6,7}

Squamous metaplasia was observed in this case. This is an incidental finding in some benign and malignant tumors.³⁹ Its origin is not clear, and it has been associated with a traumatic event leading to infarction/ischemia and repair following infarction.⁴⁰ Sharma et al reported that fine needle aspiration of the tumor could be a cause of trauma and development of squamous metaplasia later.³⁹ In our case, there was no history of trauma, as the lesion was excised surgically with no prior traumatic investigations. The transformation of squamous metaplasia into squamous cell carcinoma cannot be excluded and should be considered in determining the prognosis.⁴¹ Close monitoring of the patient and a review conducted at 18 months postoperatively confirmed no recurrence and no development of malignant change. Further, it seems that the persistent pleomorphic adenoma in the patient's lower lip was a major factor contributing to the severe gingival recession around lower central incisors. A careful follow-up of this patient is needed for two main reasons: to monitor the patient for the potential of recurrence for this tumor, and to provide the proper periodontal management.

In conclusion, this report documents peculiar findings in this case of pleomorphic adenoma; occurring in the lower lip, affecting a young male, and characterized by, among common histological features of pleomorphic adenoma, squamous metaplasia. The latter finding confirms that the best therapeutic approach should be to excise the lesion including its capsule and a safety margin. Future research should aim to answer gaps in knowledge concerning this type of tumor such as predisposing factors, histological features, and cancerous transformation particularly that several cases reported neglected to mention prognosis or follow-up data (**►Table 1**).

Ethical Aspects

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from the patient whose case was reported in this study.

Funding

None.

Conflict of Interest

None declared.

Acknowledgments

The authors are grateful to Dr. Hamzah Babcair for his assistance in histopathological interpretation, and Professor Ali Shamaa, College of Dentistry, Taibah University, for his assistance in preparing the photomicrographs. They would also like to thank the staff in Saudi-German Hospital, Al Madinah, for making this study possible.

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