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Pleomorphic Adenoma in Lower Lip- A Rare Case Report with Literature Review

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Abstract

Pleomorphic adenoma is most common benign salivary gland tumor, but it is unusual to encounter this tumor on lower lip. In this case report we have discussed a case of 50yr old female presented with a painless persistent lump affecting the lower lip for 5 years. The lesion was excised and histopathologic examination revealed to be a pleomorphic adenoma. This case highlights the importance of diagnosing and treating the painless masses as this tumor is small in size and is prone to long term neglect and has potential for recurrence and malignant transformation. Therefore, it becomes necessary to excise these lesions and careful post-operative monitoring should be continued.

Keywords: Pleomorphic adenoma, Nodule, Lower lip, Salivary gland tumor

Introduction

Pleomorphic adenoma is benign epithelial derived tumor consisting of cells exhibiting ability for epithelial (ductal and non-ductal) and mesenchymal (myxoid, hyaline,

chondroid, osseous) differentiation. In major salivary gland they are typically encapsulated but in minor salivary gland they are not. Many other names like mixed tumor, enclavoma, branchioma, endothelioma, endochondroma have been given but the term 'pleomorphic adenoma' suggested by Willis characterizes the unusual histologic pattern of this tumor. Mixed tumor is misnomer as it is not a mixed tumor in sense of being teratomatous or being derived from one or more than one primary tissue. [2,3]

Epidemiology and Clinical features

The annual incidence of salivary gland tumors is 1.0 to 6.5 cases per 100000 people worldwide.[1] Pleomorphic adenoma represents 45-74% of all salivary gland tumors, it comprises of one third of all benign and malignant salivary gland tumors and about 35% of all parotid neoplasm. It constitutes of 66% of benign salivary gland tumors comprising 67% of benign major salivary gland tumors and 63% of benign minor salivary gland tumors.[3]

The palate is the most common intra oral site for minor salivary gland tumor with 42% to 54% of all cases. Most of which occurs in hard palate as compared to soft palate probably because greater number of glands aggregation.[2]The lips are the second most common site (21%-24% cases) followed by buccal mucosa (12%-15% cases). Labial tumors are significantly more common on upper lip (74%-87%) of all lip tumors.[2]

Similarly for pleomorphic adenoma palate is the most common intraoral site followed by upper lip and buccal mucosa. They rarely involve lower lip and tongue.[3] The lower lip constitutes <3% of all intraoral pleomorphic adenomas. The clinical presentation of intraoral pleomorphic adenoma is a solitary, painless, slow-growing (many months or years), submucosal firm 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. [4]Most commonly females are affected within age range of fourth to sixth decade but they are also relatively common in young adults.[2]

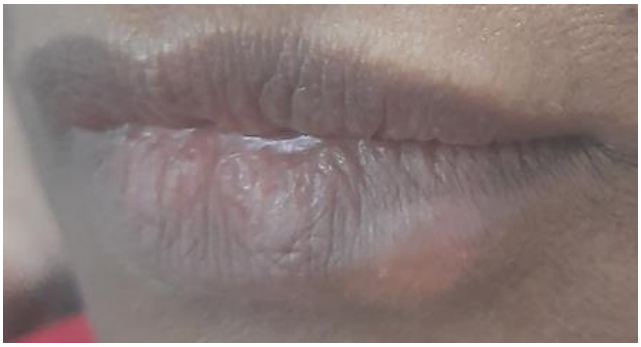
Case Report

A 50-year-old female patient reported to the department with painless lump on lower lip which was present for last 5years. The patient's medical, dental and family history were non-significant, no history of trauma, paraesthesia and discharge from the lesion was reported. On extra oral examination a solitary, non-tender, well defined, firm nodule of 1.0x1.0cm in greatest dimension of roughly ovoid in shape with smooth surface and same colour as mucosa was appreciated causing slight elevation of the vermillion border of left side of lower lip.(Fig-1) No lymph nodes were palpable. On intraoral examination no significant findings were seen and lesion was not assessed. Considering that the lesion was slow growing, painless, smooth firm mass of <3cm size provisional diagnosis of benign mesenchymal tumor (Lipoma) was considered as it constitutes about 13% of head and neck tumors and differential diagnosis included lesions occurring in lips : Cyst (epidermoid cyst, mucocele), benign mesenchymal tumor (fibroma, neurofibroma) and benign salivary gland tumor (pleomorphic adenoma, canalicular adenoma, myoepithelioma, basal cell adenoma).

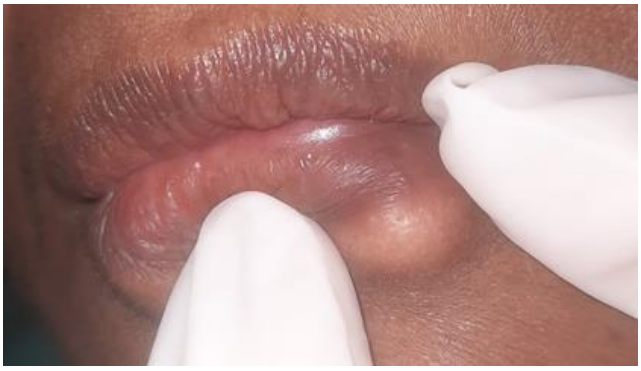
An excisional biopsy was performed. On gross examination the tissue revealed a well encapsulated ovoid mass with homogenous, white and slippery cut surface with firm consistency and smooth surface texture. The histopathological examination (Fig-2)revealed partially capsulated lesion showing proliferation of glandular epithelium in the form of

numerous duct like structure, islands, groups and anastomosing cords. The glandular epithelial cells were composed of cuboidal hyperchromatic ductal cells and angular to ovoid appearing myoepithelial cells. Few foci of keratinization were also evident within ductal proliferations. The mesenchymal background showed fibrous areas, basophilic appearing myxoid areas, eosinophilic amorphous hyalinised and basophilic chondroid areas. Based on these histopathological features, diagnosis of pleomorphic adenoma was established.

A



B



C

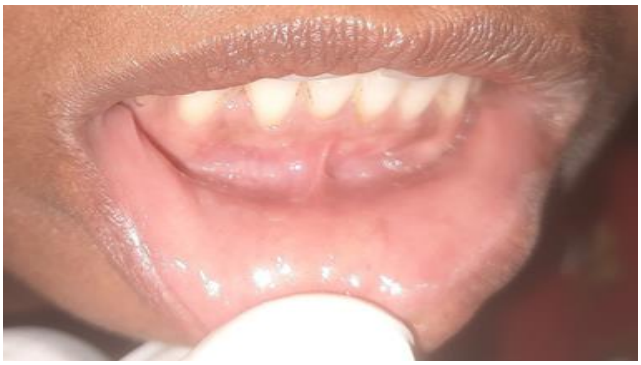


Figure 1: Clinical examination: A& B- shows endophytic firm well defined nodule in lower lip on extraoral examination. C- shows no significant intraoral findings.

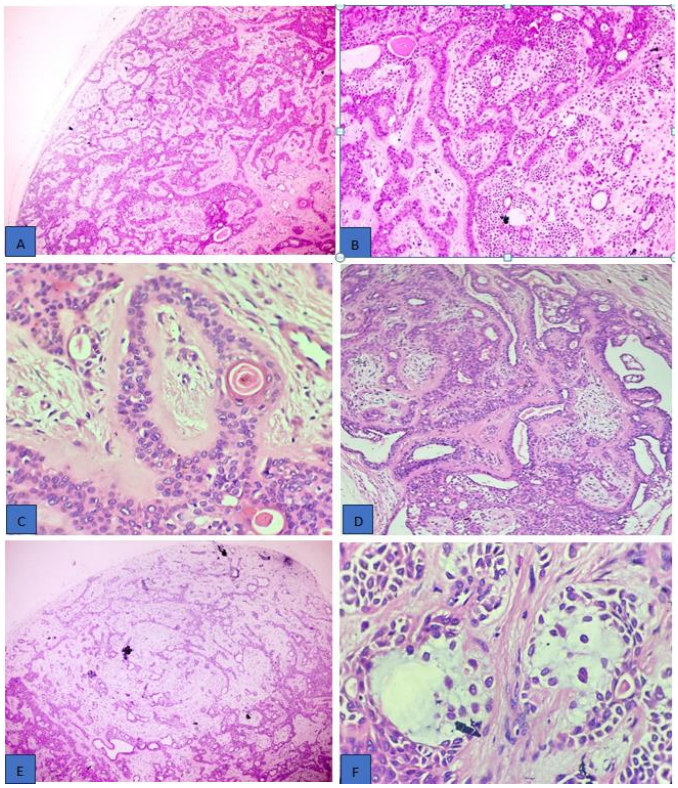


Figure 2: Histopathological examination (10x):

A&B: partially encapsulated lesion with proliferation of ductal and myoepithelial cells.

C: foci of keratinistaion within ductal proliferation. D: eosinophilic amorphous hyalinized areas.

E: slightly basophilic myxoid area.

F: chondroid areas showing binucleated cells.

Discussion

Caretonuto reported a mixed tumor of the upper lip in 1961. To best of our knowledge, after twelve years, Krolls firstly described it on the lower lip in 1973. After one year, Kerr detected a pleomorphic adenoma of the lower lip. Then two authors from Japan pointed out two cases of pleomorphic adenoma of the lower lip in 1985 and 2002, separately. Cwalina et al studied 16 cases of pleomorphic adenoma of minor salivary glands. They

found that, 8 were originated from oral cavity, 6 from palate, one from lower lip and one from cheek. Two oral adenomas were malignant. Out of 16 cases only one was located on the lower lip. Then, Yih et al analyzed 213 cases of intraoral minor salivary gland neoplasms retrospectively and determined 56 % of the cases as malignant and 44 % of them as benign. Additionally, the palate was indicated as the most common site for the neoplasms of the minor glands in that study, from U.S.A. The benign labial salivary gland neoplasms were more common in the upper lip, whereas the malignant ones were seen mostly in the lower lip. That may indicate that the region of the lower lip may be more critical for the malignancy as well as it is a rare site of occurrence for pleomorphic adenoma.[5]

We conducted a search of the literature on labial pleomorphic adenomas (in worldwide) and to the best of our knowledge we found 39 cases reported between 2000 and 2014 (Table 1)[4,6]

Out of 39 past cases, 34 cases were seen on upper lip (U) and only 5 cases were reported in lower lip (L).

Krolls and Hicks suggested that the difference in the frequency of occurrence of pleomorphic adenoma between the upper and lower lip is due to the fact that, from an embryological point of view, the upper lip is formed by the fusion of three protuberances, whereas the lower lip is formed by the fusion of two protuberances, and hence the embryonic cells are more likely to stay in the upper lip than the lower lip. Another potential reason is the difference in the number and distribution of labial glands between the upper and lower lip. Specifically, the upper labial glands are densely located between and scattered outside the corners of the mouth, whereas the lower labial glands are scattered between and densely located outside the corners of the mouth. The upper lip thus has a large number of well-developed labial glands and the lower lip has only a few small labial glands, which may also contribute to the difference in the frequency of upper- versus lower-lip Pleomorphic adenomas.[6]

Pleomorphic adenoma is the most common benign neoplasm consisting of cells exhibiting the ability to differentiate into epithelial (ductal and non-ductal) cells and mesenchymal(chondroid, myxoid and osseous) cells. Its morphological complexity is the result of differentiation of tumor cells and the fibrous, hyalinized, myxoid, chondroid and osseous areas are the result of metaplasia or are actually products of tumor cells per se. The myoepithelial cells and reserve cells in intercalated duct have been implicated for histogenesis. Hubner postulated that the myoepithelial cell is responsible for the morphologic diversity of tumor including production of the fibrous, mucinous, chondroid and osseous areas. Cytogenetic abnormalities involving chromosomal region 12q13-15, mutation in PLAG1 mapped on chromosome 8q12 have been implicated in its pathogenesis but the studies have not yet established the role in diagnosis of pleomorphic adenoma.[1,2]

The clinical differential diagnosis of swelling of the lip that can be easily confused with pleomorphic adenoma includes cystic lesions (e.g., mucocele, dermoid cyst, epidermoid cyst), benign tumors (e.g., fibroma, hemangioma, lipoma, schwannoma), other benign salivary gland tumors (canalicular adenoma, basal cell adenoma, myoepithelioma) and malignant salivary gland tumors (e.g., mucoepidermoid carcinoma, adenoid cystic carcinoma).[6]Mucoceles, which commonly arise from the rupture or blockage of salivary glands, often due to trauma, present as soft dome shaped, fluctuant swellings, usually with a bluish tinge. They are typically smaller and more superficial than pleomorphic adenomas. The simple benign tumors such as lipomas, fibromas,

sebaceous cysts, present with a variety of characteristics. Lipomas are generally soft, movable, shows positive slip sign clinically. Fibromas are firmer and may be pedunculated and sebaceous cysts tend to be cystic, freely movable with a central punctum.[7]

These tumors are often smaller and vary in consistency compared to pleomorphic adenomas, and their histopathological features are distinctly different from those of pleomorphic adenomas. As on histological picture both epithelial and myoepithelial cells are seen, which rules out mucoepidermoid carcinoma. The absence of perineuralinvasion and mitotic figures obscure the chances of polymorphic low-grade adenocarcinoma.[7] Canalicular adenoma lacks chondroid or myxoid matrix, distinguishing it from PA. When diagnosing these conditions, clinical features like the growth rate, consistency and are crucial considerations. The imaging studies and histopathological examination through biopsy are necessary to confirm the diagnosis and effectively differentiate these lesions from each other.[6,8]

The microscopic features of pleomorphic adenoma is characterised by variable, diverse histologic patterns demonstrating combination of glandular epithelium and mesenchymal tissue, the proportion of each component varies widely among tumors. Foote and frazell (1954) categorised the tumor into (a) principally myxoid, (b) myxoid and cellular component in equal proportion, (c) predominantly cellular and (d) extremely cellular. The epithelial component forms ducts and small cyst like spaces containing eosinophilic coagulum, the epithelium may also proliferate in the form of sheets, islands, nests and anastomoising cords. Foci of keratinisation may also be seen. Myoepithelial cells make up major component of this tumor and have variable morphology (angular, spindle, ovoid, plasmacytoid). Vacuolar degeneration of myoepithelial cells results in cartilaginous appearance. Areas of hyalinisation, osseous and adipose differentiation can also be noted.[1]Similarly in our case all the features were evident except for osseous differentiation. Additionally squamous metaplasia of the ductal cells and few clear cells were present in this case. (Fig- 3)

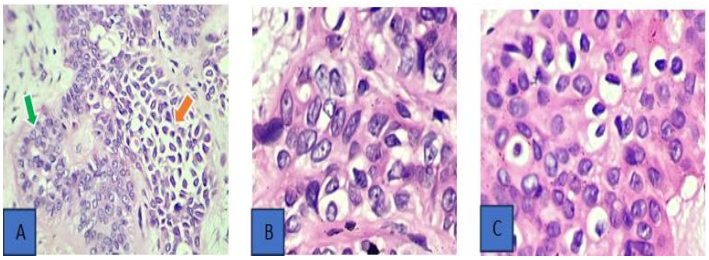


Figure 3: A - shows ductal cells in green colour arrow and angular to ovoid myoepithelial cells in orange colour arrow, B- shows squamous metaplasia and C- shows clear cells.

Squamous metaplasia was observed in this case similar to case reported by Nourwali et al [4]. This is an incidental finding in some benign and malignant tumors. Its origin is not clear, and it has been associated with a traumatic event leading to infarction/ischemia and repair following infarction. Sharma et al reported that fine needle aspiration of the tumor could be a cause of trauma and development of squamous metaplasia later. 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.

In many cases, it is difficult to preoperatively diagnose minor salivary gland tumors, especially in the lip due to the difficulty of image evaluation and the uncertainty of obtaining biopsy findings due to the small size of lip lesion. Additionally, because an incisional biopsy involves incision into the capsule and the possibility of cell seeding, surgical treatment with the assumption of

removal is considered useful. Many PA lesions on the lips are small in size, and if the resection area is larger than necessary, it may cause postoperative scar contracture, deformity of the lips due to tissue loss, and functional impairment. Therefore, if there are no adhesions or infiltrations with surrounding tissues, total removal as the biopsy procedure is better than over-excision including surrounding healthy tissues.[8]

Long-term patient follow-up is crucial to reduce the risk of late recurrence as salivary gland tumors can reoccur after a considerable period. It is recommended that patients are monitored for at least five years after the initial surgery. The most common explanation for PA recurrence is thought to be related to capsule thickness or absence of a capsule. If the capsule ruptures or an incomplete removal is performed during surgery, residual tumor cells will remain, leading to recurrence.[8]Another important reason is nature of its capsule because it is known to have microscopic pseudopod-like extensions into the surrounding tissues consequently leading to recurrence. 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.[4] The prognosis of pleomorphic adenoma is usually good, recurrence rate of PA is 2-8% and according to some clinicians the 5-10 yrs observation period is not sufficient. In study conducted by Valstar et al, the 20-year overall recurrence rate was 6.7% with median time for first recurrence of 7years.[8]

Another important aspect of pleomorphic adenoma is its potential to show cancerous, or metaplastic changes, the latter affecting approximately 25% of pleomorphic adenomas. Carcinoma arising in pleomorphic adenoma is due to transformation of benign lesions into malignancy, and it accounts for approximately 3% of salivary tumors. These carcinomas tend to be larger and longer standing than benign lesions and they tend to affect an older age group with an average age of presentation of 60 years. 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.[4]

Conclusion

Pleomorphic Adenoma occurring in lip is usually painless quiescent nodule and may be present since long duration leading to delay in diagnosis. The diagnosis becomes challenging as it exhibits overlapping clinical features with other labial lesions. However, a definitive diagnosis can only be achieved through histopathological examination. Total surgical excision is recommended as the definitive treatment for pleomorphic adenoma, with an excellent prognosis. However, patients should be closely monitored over an extended period due to the risk of recurrence and the possibility of malignant transformation.

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Legend Table

Table 1: Reported cases of lip pleomorphic adenoma between year 2000 and 2024.[4,6]

Sn.	Authors	Year	Age	Sex	Site	Size (cm)	Disease period	Clinical diagnosis
1	To et al	2002	25	M	L	1.0	3yrs	Bening minor salivary gland tumor
2	Jorge et al	2002	15	F	U	1.0	2 mo	Benign mesenchymal neoplasm, neuroma, neurofibroma
3	Lotufo et al	2008	12	M	U	2.0	1yr	Bening minor salivary gland tumor, lipoma
4	Moritani et al	2008	72	F	U	1.5	1yr	Benign tumor
5	Asuquo et al	2009	50	F	U	16	2yrs	-
6	McNamara et al	2009	55	F	U	1.0	30yrs	-
7	Debnath & Adhyapok	2010	55	F	U	2.0	1yr	Bening minor salivary gland tumor, lipoma
8	Shrestha et al	2010	27	F	U	5.0	3yrs	Bening minor salivary gland tumor
9	Ali et al	2011	33	M	U	3.0	1yr	Granuloma, bening minor salivary gland tumor
10	Kataria et al	2011	65	F	U	2.0	2yr	Pleomorphic adenoma
11	Sengul et al	2011	49	M	L	1.5	-	-
12	Dyalram et al	2012	72	M	U	2.4	5yrs	Pleomorphic adenoma
13	Mitate et al	2013	55	M	U	-	8yr	Pleomorphic adenoma
14	Mariano et al	2013	69	M	U	2.0	4yrs	Pleomorphic adenoma, canalicular adenoma
15	Tzermpos et al	2014	39	F	U	1.0	3yrs	Periapical granuloma, periapical cyst
16	Sood et al	2014	46	M	L	1.5	2yrs	Lipoma, sebaceous cyst
17	Fomete et al	2015	37	F	U	4.0	4yrs	-
18	Singh et al	2015	55	M	U	2.0	1yr	Bening minor salivary gland tumor, mesenchymal tumor

19	Khan et al	2016	60	M	U	4.0	8yrs	-
20	Taniguchi et al	2016	72	F	L	1.5	7yrs	Benign tumor
21	Metgud et al	2016	30	M	U	1.0	5-6 mo	Lipoma, sebaceous cyst
22	Fatahzahed et al	2017	58	M	U	1.5	-	-
23	Ahmedi et al	2017	10	F	U	2.0	3yrs	Lipoma
24	Alves et al	2018	18	M	U	3.0	1yr	-
25	Taiwo et al	2018	33	M	U	4.0	3yrs	Lipoma
26	Yoshimura et al	2018	52	M	U	1.5	1yr	Benign tumor
27	Bhatia	2019	23	F	U	1.8	3mo	Pleomorphic adenoma
28	Nourwali & Dar-odeh	2019	26	M	U	2.3	2yrs	Mesenchymal tumor, PA, sialolithiasis
29	Kazikdas et al	2020	20	M	U	4.0	2yrs	Benign mixed salivary gland tumor
30	Shome et al	2020	25	F	U	3.0	2yrs	Benign salivary gland neoplasm
31	Adiyogi et al	2020	44	M	U	3.0	5yrs	Peripheral giant cell granuloma, minor salivary gland tumor, lipoma
32	Umemori et al	2022	35	F	U	0.7	7yrs	Benign tumor
33	Prakash et al	2022	65	M	U	5.0	5yrs	Benign tumor
34	Jihad Alrehaili	2023	24	F	U	0.5	18mo	-
35	Chidzonga et al	2024	28	M	U	5.0	3yrs	-
36	Saima et al	2024	83	M	U	3.0	2yrs	-
37	Kim et al	2024	82	M	U	1.5	20yrs	-
38	Kumar et al	2024	68	M	U	2.0	1yr	-
39	Rentes et al	2024	61	M	L	3.0	1yr	-