

Upper Lip Pleomorphic Adenoma: Comparison of Reported Cases between 1990 and 2012

Hamed Mortazavi¹, Somayeh Alirezaei¹, Saranaz Azari-Marhabi¹,
Maryam Baharvand¹, Majid Eshghpour²

¹ Department of Oral Medicine, Dental School, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² Dental Research Center, Faculty of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran

Received 16 April 2013 and Accepted 27 June 2013

Abstract

Introduction: Pleomorphic adenoma of the upper lip is a rare entity and its diagnosis requires a high index of suspicion. The aim of this study was to review the reported cases of pleomorphic adenoma (PA) of the upper lip. **Methods:** This study was performed on the basis of the clinical features of 10 well-documented reported cases of the upper lip pleomorphic adenomas from 1990 to 2012 which have been indexed in the PubMed. The search strategy based on MeSH keywords included "salivary gland tumor", "salivary gland cancer", "pleomorphic adenoma", and "mixed tumor". In the clinical records the following data have been considered: Age, sex, clinical view, complaint time, site, size, texture, pathological view, treatment, recurrence rate, symptom and follow-up period. **Results:** Of the 11 reported cases of PA, 7 (63.7%) were female and 4 (36.3%) were male, with age ranging from 12 to 65 years. 50% of the patients were between 35 and 55 years of age. Only 3 (27.2%) of cases were younger than 20. The main clinical presentation of lesion in all cases was a submucosal nodule. There was a large interval between the first symptoms and diagnosis. The size of the lesions were between 1 and 3 cm. Involvement of the right half of the upper lip was more common than the left side. 63.6% of the lesions showed a firm consistency and bone formation was seen in one (9.09%) case. The follow-up period ranged from 5 to 48 months. There was no evidence of recurrence in any of the reported cases. **Conclusion:** Although rare, pleomorphic adenoma should be considered as a differential diagnosis for the swellings in the upper lip. PA has a potential for malignant transformation.

Therefore this entity should be evaluated carefully by all clinicians.

Key words: Mixed tumor, pleomorphic adenoma, salivary gland cancer, salivary gland tumor.

Mortazavi H, Alirezaei S, Azari-Marhabi S, Baharvand M, Eshghpour M. Upper Lip Pleomorphic Adenoma: Comparison of Reported Cases between 1990 and 2012. *J Dent Mater Tech* 2013; 2(4): 125-9.

Introduction

Salivary gland tumors constitute 3-5% of all head and neck neoplasms and less than 1% of all tumors (1). Pleomorphic adenoma (PA) is the most common tumor of salivary glands, accounting for about 70% of the parotid gland, 50% of the submandibular gland and 45% of the minor salivary glands neoplasms (2,3). PA appears as a painless, firm and slow growing mass that is commonly diagnosed long after the lesion has become present. It mainly affects women in the fourth to sixth decade of life (4,5). The onset of about 5-10% of PAs is at or before the age of 20. In addition, less than 5% of all pediatric head and neck neoplasms have their origin in the salivary glands (3,6). The palate is the most commonly affected site (43-69%), followed by the upper lip (10.1%), cheek (5.5%), throat (2.5%), retromolar region (0.7%), floor of the mouth and the alveolar mucosa (2). The PA of the lips tend to occur at an earlier age than it does at other locations (2,7). The PA of the upper lip is far more common than the PA of the lower lip (6:1) (2). The PA of the upper lip is a rare entity and its diagnosis requires a high index of

suspicion. Therefore the aim of this study was to review of the upper lip PAs in the well-documented reported cases from 1990 to 2012.

Materials and Methods

This study was performed on the basis of the clinical features of 10 well-documented full text reported cases of the upper lip pleomorphic adenomas between 1990 and 2012 which have indexed in the PubMed. The search strategy based on MeSH keywords included "salivary gland tumor", "salivary gland cancer", "pleomorphic adenoma", and "mixed tumor". In the clinical records, the following data was considered: age, sex, clinical view, complaint duration, site, size, texture, pathologic view, treatment, recurrence rate, symptoms and follow-up period. For the studies performed before 1990, we were unable to find the necessary information. Also some of these reports were not in English. Therefore, these studies were excluded.

Results

Of the 11 full text reported cases of PA, 7 (63.7%) were female and 4 (36.3%) were male. The female to male ratio was about 2:1. Although the patients' age ranged from 12 to 65 years, about half of them were between 35 and 55 and only 3 (27.2%) individuals were younger than 20. The main clinical presentation of the lesion in all cases was an asymptomatic nodule. Furthermore, all reported cases were encapsulated and surgery was the accepted treatment. There was a large time gap of 12 to 96 months (mean: 54 months) between the onset of first symptoms and making the diagnosis. The size of the lesions was between 1 and 3 cm, with the average of 2 cm. Involvement of the right half of the upper lip was more common than the left. 63.6% of the lesions had a firm consistency and bone formation was seen in one (9.09%) case. All cases (100%) were capsulated and surgical excision was the treatment of choice. The follow-up period ranged from 5 to 48 months with the average of 28 months. There was no evidence of recurrence in any reported cases. Additional data were summarized in Table 1.

Table 1. Clinical data of 10 upper lip pleomorphic adenomas in the English-language literature indexed in the PubMed from 1990-2012

Author	No. of cases	Age (year)	Sex	Complaint duration (month)	Site	Size (cm)	Texture	Follow-up period (month)
Kataria ² 2011	1	65	female	24	upper lip upper lip/right	1.5×2	Firm	16
Ali ²⁴ 2011	2	33	male	18-19		3×3	rubbery	12
Küçük ⁸ 2011	3	35	Male	84	upper lip/right	1.8×1.5	Firm	-
Debnath ⁵ 2010	4	55	Female	12	upper lip/left	1.5×2	rubbery	12
Pons Vicente ¹ 2008	5	51	Female	120	upper lip	1×1.3	Firm	48
Lotufo ⁶ 2008	6	12	Male	12	upper lip/right	1.5×2	Rubbery	12
Asuquo ²¹ 2009	7	40	Female	120	upper lip	-	Firm	26
Jorge ³ 2002	8	15	Female	24	upper lip	1×3	Firm	5
Jorge ³ 2002	9	18	Female	12	upper lip	1×3	Firm	39
Hamakawa ²² 1997	10	53	Female	24	upper lip/left	1×1	Hard	48
Narita ²³ 1990	11	61	Male	96	upper lip/left	-	Firm	-

Report of a New Case

A 20-year-old female patient attended to the Oral Medicine Department, Dental School, Shahid Beheshti University of Medical Sciences complaining of a swelling in her upper lip. Her history revealed a mass appeared in the left half of her upper lip about 12 months ago which gradually increased in size. The lesion was asymptomatic and did not cause any functional limitation or disability for the patient. Clinical examination showed a freely movable mass of firm consistency with the size of about 1.5×1.8cm. The overlying mucosa was smooth and intact with a pinkish color (Fig. 1). The medical history was unremarkable. Based on the clinical examination the diagnosis of a salivary gland tumor or a benign mesenchymal tumor was made.

Under local anesthesia, the tumor was completely removed by an intraoral excisional biopsy, a common surgical procedure (Fig. 2). Histopathologic examination of the specimen revealed an encapsulated tumor composed of a mixture of glandular epithelium and myoepithelial cells within a mesenchymal-like stroma. The epithelium was arranged in ducts, cystic structures and sheets. There were also nests of epithelial cells with squamous metaplasia and keratin pearl formation. Sheets of plasmacytoid, epitheloid and a few clear myoepithelial cells in a chondroid, mucoid and hyalinized stroma were seen as well. There was no evidence of malignancy. The histopathologic diagnosis of pleomorphic adenoma was established. Subsequent follow-up after 1 year revealed no signs of recurrence.



Figure 1. Clinical presentation of a patient with pleomorphic adenoma



Figure 2. Total surgical excision of the tumor

Discussion

Definition and Etiopathogenesis

Pleomorphic adenoma or benign mixed tumor is the most common salivary neoplasm, accounting for 40% of all minor salivary gland tumors (8,9). Tumors arising from the minor salivary glands are uncommon clinical entities and comprise 10-25% of all salivary gland neoplasms. Malignant transformation may occur in as many as 5% of cases (5,9). The main etiopathogenesis of PA remains unclear. Cytogenic and molecular studies have described that it is of epithelial origin with chromosomal abnormalities at 8q12 and 12q15 (5,6). Exposure to ionizing radiation has been the only known risk factor for cancers of the salivary glands (9-11).

Clinical and Pathological Aspects

Clinically, PA is seen as a painless, slow-growing, soft to firm mass with a normal-color overlying mucosa. This lesion is usually asymptomatic although occasionally it is tender and ulcerated and the patient has difficulty in talking. The lesion is displaceable without any adherence to either superficial or deep layers (1,2). The most common sites of a PA are the palate, lips, buccal mucosa, tongue, floor of the mouth, tonsils, pharynx, retromolar area and the nasal cavity (1,5,12). The size of the tumors varies from 0.8 to 5cm with an average of 2.6cm (3). Most studies showed that PAs are more common in females than in males (the female-male ratio is 7:3). It is also reported that salivary gland tumors are more common in black women while there is no sex predilection in whites (8,13). Minor salivary gland tumors are rare entities in children. However, Jorge et al. (3) and Lotufo et al. (6) reported the PA of the upper lip in three patients under the age of 18. According to Bradley et al. (14), pediatric salivary gland epithelial neoplasms usually occur between 7 and 16 years of age, with an average of 10.5 years. The peak incidence of PA arising from minor salivary glands of the lips is in the third and fourth decades of life, with an average of 33.2 years. In addition, there is a propensity for malignant tumors to occur on the lower lip, whereas

benign lesions predominate on the upper lip. This finding may be related to the differences in embryonic development between the lower and upper lips (2,7). There is a large time interval between the first symptoms and diagnosis of PA, ranging from 2 days to 15 years (3).

Histologically, PA of the extra-major salivary glands is similar to that in the major salivary glands and is composed of a mixture of epithelial and stromal elements. There are three major histologic subtypes; myxoid (80% stroma), cellular (myoepithelial predominant), and mixed (classic) (9,15). Ductal epithelial glands make up glandular and cystic structures of various sizes. Myoepithelial cells are responsible for the production of extra cellular matrix with chondroid, collagenous, mucoid and osseous stroma (3,5). Myxochondroid changes are the most frequent change in the stroma. The cartilaginous differentiation areas are commonly observed in immunohistochemical evaluations in tumors arising from the parotid glands. The ductal epithelial element is positive with keratin and EMA and also, the myoepithelial component stains positively with actin, myosin, keratin, other smooth muscle-specific proteins, fibronectin and S-100 (5,8). A capsule is usually seen in PA. However, it may be incomplete or show infiltration by the tumor cells. This lack of complete encapsulation is more common for minor salivary gland neoplasms. The capsule forms as a result of the fibrosis of the surrounding parenchyma (16).

Diagnosis and Differential Diagnosis of PA

The diagnosis of minor salivary gland tumors is based on the clinical history and physical examination, supported by complementary techniques including computerized tomography (CT), magnetic resonance imaging (MRI), sialography, fine needle aspiration biopsy (FNAB) and incisional biopsy. CT scanning is the best for bony involvement and MRI is better for displaying soft tissue invasion or perineural spread. However, the combination of these methods helps making a tentative diagnosis (1,3). Differential diagnosis of intraoral pleomorphic adenoma includes other minor salivary gland tumors (mucoepidermoid carcinoma, myoepithelioma, basal cell adenoma) and benign and malignant mesenchymal neoplasms (lipoma, neurofibroma, rhabdomyo and sarcoma) (1,3,17-19).

Treatment and Prognosis

Pleomorphic adenomas are usually treated by surgical excision. Superficial parotidectomy and total parotidectomy were suggested for lesions in the superficial and deep lobes of the parotid gland, respectively. Submandibular gland tumors are best treated by total removal of the gland with the neoplasm. Minor salivary gland tumors are usually excised with a safe margin. It is important to know that an inadequate

resection or rupture of the capsule can lead to local recurrence (2,8,9,21).

The prognosis of PA is excellent, with a cure rate of 95%. In addition, tumors with a weak or negative staining for PCNA and P.53 have better prognosis (3,19). According to the literature since 1939, recurrences occur in 2-44% of pleomorphic adenomas. The risk for recurrence seems to be lower for tumors of the minor salivary glands. Inadequate surgery was reported to be the main cause of recurrence (8,9,20-24). Furthermore, it is noted that the chances of recurrence are higher when PA occurs before 30 years of age (6).

Conclusion

Although rare, pleomorphic adenoma should be considered as a differential diagnosis of swellings in the upper lip. This lesion, in most frequent cases, is asymptomatic and the patient may not be aware of its existence and is discovered accidentally by a dentist. Also, it is important to know that pleomorphic adenoma can transform to a malignant lesion.

References

1. Pons Vicente O, Almendros Marqués N, Berini Aytés L, Gay Escoda C. Minor salivary gland tumors: A clinicopathological study of 18 cases. *Med Oral Patol Oral Cir Bucal* 2008;13:E582-8.
2. Kataria SP, Tanwar P, Sethi D, Garg M. Pleomorphic adenoma of the upper lip. *J Cutan Aesthet Surg* 2011;4:217-9.
3. Jorge J, Pires FR, Alves FA, et al. Juvenile intraoral pleomorphic adenoma: report of five cases and review of the literature. *Int J Oral Maxillofac Surg* 2002;31:273-5.
4. Williamson JJ, Meskin LH. Pleomorphic adenoma of the upper lip. *Oral Surg Oral Med Oral Pathol* 1965;20:771-5.
5. Debnath SC, Adhyapok AK. Pleomorphic adenoma (benign mixed tumor) of the minor salivary glands of the upper lip. *J Maxillofac Oral Surg* 2010;9:205-8.
6. Lotufo MA, Júnior CA, Mattos JP, França CM. Pleomorphic adenoma of the upper lip in a child. *J Oral Sci* 2008;50:225-8.
7. Bernier JL. Mixed tumors of the lip. *Ann Dent* 1945;4:125-30.

8. Küçük U, Tan S. Pleomorphic adenoma of the upper lip. *Turk Patoloji Derg* 2011;27:73-6.
9. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. St. Louis: W. B. Saunders, 2009.
10. Otoh EC, Johnson NW, Olosoji H, Danfillo IS, Adeleke OA. Salivary gland neoplasms in Maiduguri, north-eastern Nigeria. *Oral Dis* 2005;11:386-91.
11. Beal KP, Singh B, Kraus D, Yahalom J, Portlock C, Wolden SL. Radiation-induced salivary gland tumors: a report of 18 cases and a review of the literature. *Cancer J* 2003;9:467-71.
12. Yih WY, Kratochvil FJ, Stewart JC. Intraoral minor salivary gland neoplasms: review of 213 cases. *J Oral Maxillofac Surg* 2005;63:805-10.
13. Toida M, Shimokawa K, Makita H, Kato K, Kobayashi A, Kusunoki Y. Intraoral minor salivary gland tumors: a clinicopathological study of 82 cases. *Int J Oral Maxillofac Surg* 2005;34:528-32.
14. Bradley P, McClelland L, Mehta D. Paediatric salivary gland epithelial neoplasms. *ORL J Otorhinolaryngol Relat Spec* 2007;69:137-45.
15. Ogawa Y, Toyosawa S, Ishida T, Ijuhin N. Keratin 14 immunoreactive cells in pleomorphic adenomas and adenoid cystic carcinomas of salivary glands. *Virchows Arch* 2000;437:58-68.
16. Varghese BT, Sebastian P, Abraham EK, Mathews A. Pleomorphic adenoma of minor salivary gland in the parapharyngeal space. *World J Surg Oncol* 2003;25:2.
17. Dalati T, Hussein MR. Juvenile pleomorphic adenoma of the cheek: a case report and review of literature. *Diagn Pathol* 2009; 22:32.
18. Dhanuthai K, Boonadulyarat M, Jaengjongdee T, Jiruedee K. A clinico-pathologic study of 311 intra-oral salivary gland tumors in Thais. *J Oral Pathol Med* 2009;38:495-500.
19. Maynard JD. Management of pleomorphic adenoma of the parotid. *Br J Surg* 1998;75:305-8.
20. Krolls SO, Boyers RC. Mixed tumors of salivary glands. Long-term follow-up. *Cancer* 1972;30:276-81.
21. Asuquo ME, Otei OO, Ekpo R, Abang I, Adams U, Bassey EE. Salivary gland tumor of the lip: report of two cases and literature review. *Cent Afr J Med* 2009;55:43-6.
22. Hamakawa H, Takarada M, Ito C, Tanioka H. Bone-forming pleomorphic adenoma of the upper lip: report of a case. *J Oral Maxillofac Surg* 1997;55:1471-5.
23. Narita H, Kobayashi T, Kanzaki T. Pleomorphic adenoma of the lip. *J Dermatol* 1990;17:710-2.
24. Ali I, Gupta AK, Singh S. Pleomorphic adenoma of the upper lip. *Natl J Maxillofac Surg* 2011;2:219-21.

Corresponding Author:

Majid Eshghpour
 Faculty of Dentistry
 Vakilabad Blvd, Mashhad, Iran
 P.O. Box: 91735-984
 Tel: +98-511-8829501
 Fax: +98-511-8829500
 E-mail: eshghpourm@mums.ac.ir