

Clinical and Histopathological Comparison of Pleomorphic Adenoma in Major and Minor Salivary Glands

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Abstract

Objectives: Pleomorphic adenoma is the most common benign salivary gland tumor. Since the studies conducted on the histopathology of pleomorphic adenoma have different results and this tumor can mimic other salivary gland tumors, and due to the high prevalence of this lesion, this study was conducted to investigate the clinical and histopathological differences of pleomorphic adenoma in the major and minor salivary glands.

Methods: A total of 72 cases with the diagnosis of pleomorphic adenoma were reviewed by the oral and maxillofacial pathologists, and the findings were analyzed using Fisher's Exact and Pearson chi-square tests to compare the frequency distribution of variables between major and minor salivary gland lesions with the first type error of 0.05.

Results: The most common age group was 41-50 years old, and the gender preference was for women. The clinical symptoms were mostly painless swelling. The most common locations for the major and minor salivary glands were in the parotid and in palate, respectively. The most common histopathological classification was classic; and the most common cells observed in the major and minor salivary glands were squamous and plasmacytoid, respectively. The most common microscopic pattern was solid, the most common stromal subtypes in the major and minor salivary glands were myxoid and hyalinized, respectively; and the most common capsular forms in the major and minor salivary glands were thin and partial, respectively. Keratin pearls were observed in both major and minor salivary gland lesions.

Conclusion: The findings of this study are consistent with previous studies in many cases. Osteoid and fatty changes in stroma were seen in this study which are remarkable findings. Partial encapsulation is more common in minor salivary glands, which could be associated with recurrence.

Keywords: Pathology; Salivary glands; Adenoma; Pleomorphic

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Introduction

Pleomorphic adenoma is the most common salivary gland tumor, which is also known as a mixed tumor.¹ Salivary gland tumors are generally uncommon and make up less than 3% of head and neck tumors.² Willis first expressed the term "pleomorphic," which indicated the unusual histopathological appearance of the lesion.³ The microscopic variation in this tumor from one lesion to another and also in different parts of the same lesion is very high, and the names "pleomorphic" and "mixed" tumors indicate this. Of course, it should be noted that none of the names are completely correct because true pleomorphic cells were rarely found, and the origin of the lesion is not from more than one embryonic layer.¹ From a clinical point of view, this lesion appears as a firm mass with slow and painless growth and can be seen at any age, but it is more common in 30 to 60 years and has a slight gender tendency in women.^{1,4-6}

From the histopathological point of view, this lesion has well-defined borders and is usually encapsulated.⁶ The histopathological classification of the lesion can be divided into three general types based on the epithelial and stromal components.^{2,7}

1- Stroma-rich (with dominant stromal component)

2- Cellular (with a dominant cellular component)

3- Classic (with a balance between cellular and stromal components)

Usually, a large part of the lesion is formed by myoepithelial cells, which can be shaped spindle, round, or angular. Diversity in the stroma is also attributed to these cells. Lesions that have a myxoid stroma in the microscopic view will recur with a higher probability.³

In terms of capsules, it has been estimated in previous studies that the prevalence of incomplete capsules is higher in lesions of minor salivary glands, especially in the palatal region.^{3,4}

Misdiagnosis that leads to a wrong treatment plan may lead to the lesion in place, which increases the risk of malignancy that is proportional to the years that the tumor is present.¹

Considering the high prevalence, wide histopathological diversity, and possibility of recurrence and malignancy, it is necessary to make every effort to correctly diagnose pleomorphic adenoma, and this is the purpose of the present study.

Methods

The available records of patients with the diagnosis of pleomorphic adenoma referred to the oral and maxillofacial pathology department at School of Dentistry; Shahid Beheshti University of medical sciences; between 1994 and 2023 were reviewed. A total of 72 samples were selected, and their slides were examined with a Leica DM-500 optical microscope under X40, X100, and X400 magnifications by two oral and maxillofacial pathologists.

The obtained results were classified according to the classification in Nonitha's study³ and entered into SPSS.26 software for analysis. The frequency distribution of demographic and clinical variables such as age, gender, location, clinical symptoms, and histopathologic variables such as histopathological classification, cell type, microscopic pattern, stromal subtype, and capsule, was compared between major and minor salivary gland lesions, using Fisher's Exact and Pearson chi-square tests. The first type error of the test in this research was considered to be $\alpha = 0.05$, so probability values lower than that were considered statistically significant.

The present study was reviewed by the medical ethics committee of Shahid Beheshti University of Medical Sciences and approved under the code IR.SBMU.DRC.REC.1402.036. The confidentiality of all the information in patient records was respected.

Results

The study included a total of 72 cases, 25 of which were in the major salivary glands (two in the submandibular gland and 23 in the parotid), 47 in the minor salivary glands (42 in the palate, and five in other parts of the oral cavity).

The mean age was 44.36, ranging from 15 to 76 years, with the peak incidence in the fifth and fourth decades of life in major and minor salivary glands, respectively. ($p < 0.001$) (Table 1)

Table 1- Frequency distribution of different age groups in pleomorphic adenoma of major and minor salivary glands

Age group	Major	Minor	Total
15-30	3 (12%)	9 (19.1%)	12 (16.7%)
31-40	0 (0%)	13 (27.7%)	13 (18.1%)
41-50	22 (88%)	7 (14.9%)	29 (40.3%)
51-60	0 (0%)	10 (21.3%)	10 (13.9%)
61-76	0 (0%)	8 (17%)	8 (11.1%)
total	25 (100%)	47 (100%)	72 (100%)

Slight female predilection was seen in pleomorphic adenoma lesions of both major and minor salivary glands. (54.2% of all cases occurred in females) ($p = 0.788$) (Table 2).

The most common location for the lesions of major and minor salivary glands was in the parotid and in palate, respectively.

Table 2- Frequency distribution of gender in pleomorphic adenoma of major and minor salivary glands

Gender	Major	Minor	Total
female	13 (52%)	26 (55.3%)	39 (54.2%)
male	12 (48%)	21 (44.7%)	33 (45.8%)
total	25 (100%)	47 (100%)	72 (100%)

The clinical symptoms were mostly painless swelling, but lesions with painful swelling were only observed in minor salivary glands. ($p < 0.05$) (Table 3)

Table 3- Frequency distribution of clinical symptoms in pleomorphic adenoma of major and minor salivary glands

clinical symptoms	Major	Minor	Total
No symptom	0 (0.0%)	2 (4.3%)	2 (2.8%)
Swelling	25 (100%)	38 (80.9%)	63 (87.5%)
Pain and swelling	0 (0.0%)	7 (14.9%)	7 (9.7%)
Total	25 (100%)	47 (100%)	72 (100%)

The most common histopathological classification was classic but stroma-rich and cellular type were more common in major and minor salivary glands, respectively. ($p < 0.001$) (Table 4)

Table 4- Frequency distribution of histopathological classification in pleomorphic adenoma of major and minor salivary glands

histopathological classification	Major	Minor	Total
Classic	16 (64%)	25 (53.2%)	41 (56.9%)
Stroma rich	7 (28%)	2 (4.3%)	9 (12.5%)
Cellular	2 (8%)	20 (42.6%)	22 (30.6%)
total	25 (100%)	47 (100%)	72 (100%)

The most common cell types were squamous and plasmacytoid, among major and minor salivary gland lesions, respectively. Basaloid and clear cells were found in a few cases (note that clear cells were only observed in minor salivary glands) ($p = 0.148$)

The most common cells seen together as a group in pleomorphic adenoma of major salivary glands were plasmacytoid/spindle/squamous complex. The most common cells seen together as a group in pleomorphic adenoma of minor salivary glands were the plasmacytoid/spindle/cuboidal complex. ($p < 0.001$) (Table 5)

The most common microscopic pattern was solid (76% in major and 95.7% in minor salivary glands), and the next most frequent patterns were ductal, cystic, and trabecular, respectively. ($p=0.228$)

Table 5- Frequency distribution of cell types in pleomorphic adenoma of major and minor salivary glands

Cell types	Major	Minor
plasmacytoid	19 (76%)	43 (91.5%)
Spindle	19 (76%)	34 (72.3%)
cuboidal	6 (24%)	18 (38.3%)
squamous	21 (84%)	17 (36.2%)
mucous	10 (40%)	17 (36.2%)
clear	0 (0%)	2 (4.2%)
basaloid	2 (8%)	2 (4.2%)

The most common microscopic patterns together as a group in both minor and major salivary glands pleomorphic adenoma were solid/ductal/cystic complex. ($p<0.05$) (Table 6).

Table 6- Frequency distribution of microscopic pattern in pleomorphic adenoma of major and minor salivary glands

Microscopic pattern	Major	Minor
solid	19 (76%)	45 (95.7%)
ductal	18 (72%)	34 (72.3%)
trabecular	10 (40%)	8 (17%)
cystic	18 (72%)	28 (59.6%)

In pleomorphic adenoma of major salivary glands, the most common stromal subtypes were myxoid, hyalinized, and chondroid, respectively. In pleomorphic adenoma of minor salivary glands, the most common stromal subtype was hyalinized, myxoid, and chondroid, respectively. ($p<0.05$) Osteoid was only found in minor salivary glands (14.9%), but Fatty stroma was observed in both major and minor salivary glands. (20% in major and 6.4% in minor salivary glands)

Keratin pearls were also observed in both major and minor salivary glands. (8% in major and 14.9% in minor salivary glands) (Table 7)

Table 7- Frequency distribution of stromal subtypes in pleomorphic adenoma of major and minor salivary glands

Stromal subtypes	Major	Minor
myxoid	23 (92%)	34 (72.3%)
hyalinized	18 (72%)	42 (89.4%)
chondroid	12 (48%)	7 (14.9%)
osteoid	0 (0%)	7 (14.9%)
fatty	5 (20%)	3 (6.4%)
Keratin pearl	2 (8%)	7 (14.9%)

Lesions without a capsule or with partial encapsulation were more common in minor salivary glands, and capsular

lesions (either thick or thin capsules) were more common in major salivary glands. ($p<0.001$)

Most of the lesions in major and minor salivary glands had a thin capsule (52%) and partial encapsulation (51.1%), respectively. (Table 8)

Table 8- Frequency distribution of capsular types in pleomorphic adenoma of major and minor salivary glands

Capsular types	major	minor	total
non capsulated	1 (4%)	7 (14.9%)	8 (11.1%)
partially encapsulated	1 (4%)	24 (51.1%)	25 (34.7%)
Thin capsule	13 (52%)	10 (21.3%)	23 (31.9%)
thick capsule	10 (40%)	6 (12.8%)	16 (22.2%)
total	25 (100%)	47 (100%)	72 (100%)

Discussion

Pleomorphic adenoma is the most common salivary gland tumor. The microscopic variation of this tumor from one lesion to another and also in different parts of the same lesion is high, which causes the correct histopathological diagnosis of pleomorphic adenoma to be challenging. Several attempts were made to understand the clinical and microscopic changes in pleomorphic adenoma of the major and minor salivary glands.³

The present study focused on comparing clinical and histopathological features of this lesion between major and minor salivary glands.

Pleomorphic adenoma can occur at all ages; however, the age group most commonly affected is the fifth decade⁴⁻⁶, which is in line with the results of the present study.

In this study, one of the pleomorphic adenomas in the minor salivary glands was found in a 15-year-old person, but Pati et al.⁸ reported the pleomorphic adenoma even in a 7-year-old patient.

Similar to the present study, previous investigations reported a female predilection in pleomorphic adenoma⁴⁻⁶, although one exception is Nonitha's et al. study³ that reported a slight male predilection (male-to-female ratio of 1.06:1) in both major and minor salivary gland tumors.

The majority of cases reported in previous studies and the present one occur in major salivary glands, especially parotid, and the cases that occur in minor salivary glands mostly affect the palatal region.^{3-6,9}

The locations that were less frequently reported in previous studies but were observed in this study included minor salivary gland tumors of the parapharynx, upper lip, maxillary vestibule, and floor of the mouth.

In the Ordonez et al. study⁶, the prevalence of painful pleomorphic adenoma in minor salivary glands was reported to be 16.6%, which is close to the result of the present study, which obtained the reported number of 14.9%.

Almeslet et al.'s systematic review generally reported pleomorphic adenomas without symptoms, and pain was only observed in one case of minor salivary gland pleomorphic adenoma, which was located on the left side of the palate.⁵

In the Lopes et al. study, the most common histopathological classification was classical, with a prevalence of 50%⁴, which is close to the present study, with a 56.9% prevalence as the most common histopathological classification. In this study, the most common histopathological classification in both lesions of major (64%) and minor (53.2%) salivary glands was classic, unlike the Attarbashi et al. study, which observed the most common histopathological classification as cellular⁷ with a frequency of 38% for all their cases (without minor and major segregation).

Harney et al. reported that pleomorphic adenomas of the superficial lobe of the parotid had more stromal components than the deep lobe.¹⁰ They also found no significant difference between predominant cell types in tumors of the superficial and deep lobes of the parotid.

In this study, the most frequent cell types in pleomorphic adenomas of major and minor salivary glands were spindle and plasmacytoid, respectively. In the study by Augusto et al.², the most common cell types were plasmacytoid and then spindle. Attarbashi et al. reported⁷ that the most common cell types were spindle (90%) and plasmacytoid (80%). Nonitha et al.³ reported that the most common cell type was cubic in major salivary glands, and in the minor salivary glands, the cubic basaloid and spindle cells were more abundant in all cases. Augusto et al. reported that different cell types could be in transition from one to another.²

The existence of mucous cells could be associated with abnormal differentiation¹¹, which means increased luminal cell synthesis and glycoprotein retention.

In the Attarbashi et al. study, the most common microscopic patterns were solid and ductal⁷, which is in line with the present findings. In Khandker et al. and Augusto et al. studies, unlike the present study, the most common microscopic pattern was trabecular.^{2,12}

Nonitha et al. reported that solid and ductal patterns were found in all cases without any cystic pattern being observed. Furthermore, the trabecular pattern was observed only in one case of minor salivary glands pleomorphic adenoma.³ However, in the present study, both cystic and trabecular patterns were observed in lesions of both major and minor salivary glands.

In the present study, the most common stromal subtype in major salivary gland lesions was myxoid, followed by hyalinized and chondroid; and in minor salivary glands were hyalinized, followed by myxoid and chondroid. In the studies of Attarbashi et al. and Khandker et al., the most

common stromal subtypes were myxoid and hyalinized, respectively.^{7,12}

In the study by Nonitha et al., contrary to this study, myxoid stroma was observed in all pleomorphic adenomas of major and minor salivary glands. Also, there was less hyalinized stroma in minor salivary gland lesions than in major salivary gland lesions.

Pleomorphic adenomas with myxoid stroma have more tendency to become recurrent¹³, and hyalinized stroma is related to aggressive behavior and malignant transformation of the tumor.¹⁴

The frequency of keratin pearl in the pleomorphic adenomas of minor salivary glands was higher, which is in line with the study of Nonitha et al.³ Squamous metaplasia and keratin pearl formation could be mistaken for malignancies such as mucoepidermoid carcinoma and squamous cell carcinoma; in addition, pleomorphic adenoma and polymorphous low-grade adenocarcinoma could be mistaken with each other.¹⁵

Osteoid and fatty changes were also found in the present investigation.

Cases without capsules in the present study were found in contrast to the previous studies^{3,4,6} (14.9% in minor salivary gland lesions and 4% in major salivary gland lesions).

The relationship between the capsule and microscopic features has been investigated by Stennert et al., and they found that many stroma-rich PAs present partial encapsulation; therefore, conservative surgery for pleomorphic adenomas especially for those that are stroma-rich, is indicative of recurrence.¹³

Conclusion

Pleomorphic adenoma shows variable histopathologic features. Areas of hyalinization, keratin pearls, and osteoid were more evident in minor salivary gland tumors. Fatty changes in stroma were more evident in major salivary gland tumors. Partial encapsulation was more common in minor salivary gland tumors, which may be associated with recurrence.

A pleomorphic adenoma can be a diagnostic challenge for pathologists; therefore, it is important to be familiar with its histopathological variations for accurate diagnosis.

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obtained from all subjects involved in the study

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References

1. Neville BW, Damm DD, Allen CM, Chi AC. Oral and Maxillofacial Pathology-E-Book: Elsevier Health Sciences; 2023.chapter 11 and page 444 to 447
2. Ito FA, Jorge J, Vargas PA, Lopes MA. Histopathological findings of pleomorphic adenomas of the salivary glands. *Med Oral Patol Oral Cir Bucal*. 2009;14(2):E57-61.
3. Nonitha S, Yogesh T, Nandaprasad S, Maheshwari BU, Mahalakshmi I, Veerabasavaiah BT. Histomorphological comparison of pleomorphic adenoma in major and minor salivary glands of oral cavity: A comparative study. *Journal of Oral and Maxillofacial Pathology: J Oral Maxillofac Pathol*. 2019;23(3):356-62.
4. Lopes MLDdS, Barroso KMA, Henriques ÁCG, Dos Santos JN, Martins MD, de Souza LB. Pleomorphic adenomas of the salivary glands: retrospective multicentric study of 130 cases with emphasis on histopathological features. *Eur Arch Otorhinolaryngol*. 2017;274(1):543-51.
5. Almeslet AS. Pleomorphic adenoma: a systematic review. *Int J Clin Pediatr Dent*. 2020;13(3):284-7.
6. Ordóñez JS, Arévalo MA, Torres MF. Pleomorphic adenoma of minor salivary glands: Review of the literature. *World J Adv Res Rev*. 2023; 18(02):365–74.
7. Nezhad MJ, Moghadam SA, Mokhtari S, Taravati S. Different histopathologic features of pleomorphic adenoma in salivary glands. *International Journal of Oral & Maxillofacial Pathology*. 2013;4(2):7-12.
8. Pati AR, Giraddi GB, Singh C. Benign pleomorphic adenoma of minor salivary gland of palate. *J Dent Oral Hyg*. 2011;3(6):82-8.
9. Yamamoto H, Fukumoto M, Yamaguchi F, Sakata K, Oikawa T. Pleomorphic adenoma of the buccal gland in a child. *Int J Oral Maxillofac Surg*. 1986;15(4):474-7.
10. Harney MS, Murphy C, Hone S, Toner M, Timon CV. A histological comparison of deep and superficial lobe pleomorphic adenomas of the parotid gland. *Head Neck*. 2003;25(8):649-53.
11. Triantafyllou A. Degenerative nuclear atypia in pleomorphic adenoma of salivary glands: Histological and immunohistochemical observations. *Pathol Res Pract*. 2021;224:153482.
12. Khandker MNH, Sadat SA, Rahman T, Haider IA, Mohiuddin A. Clinical presentation and histological variation of pleomorphic adenoma of salivary glands. *J Bangladesh Coll Phys Surg*. 2019; 37:72-7.
13. Stennert E, Guntinas-Lichius O, Klussmann JP, Arnold G. Histopathology of pleomorphic adenoma in the parotid gland: a prospective unselected series of 100 cases. *Laryngoscope*. 2001; 111(12):2195-200..
14. Auclair PL, Ellis GL. Atypical features in salivary gland mixed tumors: their relationship to malignant transformation. *Mod Pathol*. 1996;9(6):652-7.
15. El-Naaj IA, Leiser Y, Wolff A, Peled M. Polymorphous low grade adenocarcinoma: case series and review of surgical management. *J Oral Maxillofac Surg*. 2011;69(7):1967-72.