REVIEW ARTICLE

Pleomorphic Adenoma: A Systematic Review

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Abstract

Background: Pleomorphic adenoma (PA) is a commonly occurring benign tumor originating in the salivary glands.

Objective: The aim was to carry out a systematic literature of reports on pleomorphic adenoma from 2000 to 2018 to determine patient's age spread, gender, anatomical location, capsular invasion, histopathology, treatment and patient outcome.

Materials and methods: A PubMed search was conducted with the following key words: adenoma, pleomorphic adenoma, and mixed salivary tumor.

Results: Twenty-two articles in English were read in full after fulfilling the eligibility criteria. The mean age of PA occurrence was 44.14 years with a definite female predilection (M:F ratio = 13:8). It most commonly occurred in the facial region (42.85%), and surgical approach is the preferred intervention.

Conclusion: Pleomorphic adenomas are benign salivary gland neoplasms that can grow into extensive sizes if left untreated and hence need to be diagnosed early. Complete excision of the tumor is the definitive treatment, as enucleation can result in recurrence. Facial nerve has to be preserved if PA occurs in the parotid gland.

Keywords: Case report, Pleomorphic adenoma, Salivary gland, Tumor.

International Journal of Clinical Pediatric Dentistry (2020): 10.5005/jp-journals-10005-1776

Introduction

Pleomorphic adenoma (PA) ranks as the commonly occurring tumor and constitutes up to two-thirds of all salivary gland neoplasms.[1] Pleomorphic adenoma was first termed by Willis.[2] In the earlier years, it was also referred as mixed tumor, enclavoma, branchioma, endothelioma, endochroma, etc.[3] The occurrence is mostly situated parotid glands (85%) followed by minor salivary glands (10%) and the submandibular glands (5%).[4] Adult females in the third to fifth decade are most commonly affected with PA. The World Health Organization defines PA as a tumor which is localized and presents pleomorphic or mixed characteristic of epithelial origin which is interwoven with mucoid tissue, myxoid tissue, and chondroid masses.

Adenomas mostly originate in the superficial lobe but may occasionally invade the deeper tissues of the gland and the parapharyngeal space. Pleomorphic adenoma generally presents as a slowly progressing swelling, nonsymptomatic, and not involving facial nerve.[5] Although PA principally manifests in the parotid glands, it can also be located in hard palate and soft palate glands of saliva, upper lip, cheek, tongue, and floor of the mouth.[6]

The term "pleomorphic adenoma" is derived due to morphological complexity of the tumor between individuals and glands. Pleomorphic adenoma presents pathognomic histopathologic features. It is a single cell that differentiates into either epithelial or myoepithelial cell and not just concurrent multiplication of carcinogenic cells of epithelium and myoepithelium.

The tumor has three components: an epithelial component, myoepithelial cell component, and mesenchymal component. The recognition of PA is conceptualized on the identification of these three components. Histological presentation of PA shows a variable pattern of epithelium in a loose fibrous stroma of myxoid, chondroid, or mucoid type. Myoepithelial cells are of polygonal shape with a pale eosinophilic cytoplasm. The diagnosis of pleomorphic adenoma with certainty is microscopic identification.[7]

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How to cite this article: Almeslet AS. Pleomorphic Adenoma: A Systematic Review. Int J Clin Pediatr Dent 2020;13(3):284–287.

Source of support: Nil

Conflict of interest: None

Materials and Methods

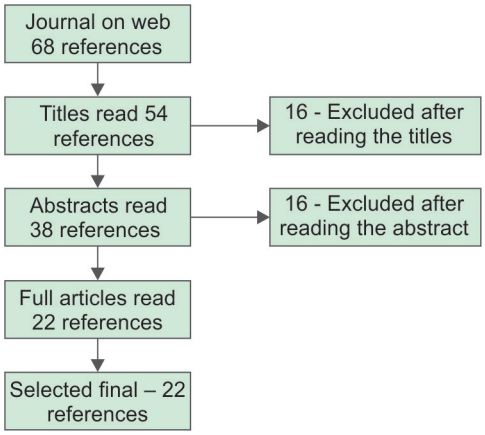
A literature search in English was carried out utilizing PUBMED the databases in identification of cases regarding PA. Synonyms such as mixed tumor and salivary gland tumors were also used. The terms used for literature search were PA, mixed tumor, reviews, and case reports. Case reports before the year 2000 were not included for the present review. An independent researcher searched the databases and identified 68 relevant studies. Reference checks of the cases identified were also made to help snowballing or networking of the cases.

The outcome criteria were not predefined but were built as the literature review progressed. A table was tabulated regarding author, year of publication, age, gender, lesion associated with pain, location, encapsulation, multinodular, invasion into surrounding tissues, and treatment opted for each of the case report included (Flowchart 1).

Inclusion Criteria

- All case reports regarding PA
- Literature reviews of articles on PA
- Reports or literature documented in English language.

Flowchart 1: Literature search flowchart for systematic review on PA



Exclusion Criteria

- Reports documented in languages other than English.
- Dissertation or pages of textbook relating to PA.

Results

Our search obtained 68 articles in Journal of Web of which 16 were excluded after reading the abstracts. Twenty-two full-text articles published in the English language were included for the review purpose, which met the inclusion criteria of the reviewers. Studies included in the review were Tandon et al.,[8] Taiwo et al.,[9] Farhat et al.,[10] Panda et al.,[11] Celik,[12] Balan et al.,[13] Kaul et al.,[14] Mittal et al.,[15] Kamala et al.,[16] Bagga et al.,[17] Modak et al.,[18] Jain et al.,[19] Verma et al.,[20] Dhir et al.,[21] Saito et al.,[22] Swarnagowri et al.,[23] Nagaraj et al.,[24] Rahnama,[25] Sunil,[26] Aggarwal et al.,[27] Kumar et al.,[28] and Shrestha et al.[29]

Mean age of PA occurrence was 44.14 years (range: 13–75 years). Pleomorphic adenoma definitely showed a female predilection with male–female ratio of 8:13. The most commonly located site was among the reports reviewed were on the left and right side of the neck (42.8%), followed by its occurrence in the palate, upper lip, soft palate, nasopharynx, right submandibular region, external auditory canal, and left ear lobule (Table 1).

Discussion

The cause of PA is still obscure. The exact etiology is obscure although the incidence increases from 15 to 20 years after exposure to radiation. Few studies have suggested an association of the tumor with simian virus 40 (SV 40). Use of tobacco, genetical predisposition, and exposure to chemicals are also thought to play a role in the disease etiology.[30] Molecular studies and cytogenetics have postulated chromosomal aberration of 8q12 and 12q15.

Pleomorphic adenomas mostly occur in the young- and middle-aged adults, between 30 and 60 years. The literature reports suggest female predilection. Location of occurrence is predominantly in the parotid gland occurring in the superficial lobe and presenting as a swelling on the ramus of the mandible in front of the ear. Fewer lesions grow in a medial direction between the ascending ramus and the stylomandibular ligament that shows in the lateral pharyngeal wall or soft palate. It appears as an irregular nodular lesion that is firm in consistency. Areas of cystic degeneration can be palpated if it is superficial and does not show any fixation. Pleomorphic adenoma in the minor salivary glands mostly occurs in the palate followed by upper lips and buccal mucosa.[2,31] It is generally asymptomatic, with no pain and facial nerve involvement. If not intervened in the early stages, PA can grow to grotesque proportion. A few cases may transform into malignancy.

In cut section, the mass appears as an irregular ovoid mass with well-defined borders, which may be covered by an incomplete fibrous capsule or remain unencapsulated. The consistency may be rubbery, fleshy, or mucoid interspersed with areas of hemorrhage and infarction.[24]

The tumor confirmation is made by computed tomography (CT) and Magnetic resonance imaging (MRI). MRI is preferred as it presents better delineation, elaborate tumor margin, and the tumor location with respect to its surrounding tissues. But for differentiating malignancy and benign lesions, Fine-needle aspiration biopsy (FNAB) is used. Although these tumors are encapsulated, they still are excised with adequate margins involving surrounding normal tissues. This is because of pseudopodic exhibits microscopic extensions into the surrounding tissues because of dehiscences in false capsule. For this reason, incisional biopsy is avoided to prevent spillage of tumor cells.[5]

Pleomorphic adenomas generally present as a rounded, well-demarcated mass, or masses which is less than 6 cm in its greatest dimension. The clinical presentation of PA is generally a slow-growing, asymptomatic, and unilateral firm mass that can enlarge in size if not treated. Pleomorphic adenomas of the minor salivary glands mostly occurs in the soft and hard palate due to greater concentration of salivary glands in these location and typically presents as a firm or rubbery submucosal mass either without ulceration or surrounding ulceration.[32]

Although PA presents as an asymptomatic mass, facial nerve weakness may be found in chronic neglected parotid gland tumors.[33,34] In case of deep lobe involvement, an oral retrotonsillar mass/parapharyngeal space tumor may emerge.[35] Although they are encapsulated, some parts of the capsule may not be fully developed. This can cause expansible growth-producing protrusions into the surrounding gland that renders enucleation of the tumor at recurrence risk.[36]

Surgical excision of the mass is the most opted treatment. Only one report[15] treated PA with enucleation. In PA occurring in the superficial lobe of parotid gland, superficial parotidectomy with facial nerve preservation is done. Total parotidectomy is done if tumors involve the deep lobe. Pleomorphic adenoma in minor salivary glands is treated with wide local excision along with involved periosteum or bone. Enucleation is not the treatment of choice as it can lead to high local recurrence. Prognosis of PA is good with 95% cure rate. As the tumor is radio resistant, radiotherapy is not indicated.[37,38]

Clinically, PA can have differential diagnosis of palatal abscess, odontogenic cyst, nonodontogenic cyst, soft tissue tumors-like fibroma, lipoma, neurofibroma, neurilemmoma, lymphoma, or other salivary gland tumors. Palatal abscess can be differentiated by identifying the source of palatal abscess which would be a nonvital tooth in the immediate surroundings. Odontogenic and nonodontogenic cyst do not exhibit a cystic nature during exploration into the mass.[39]

Because of its varied histopathological presentation, it may be confused with myoepithelioma, adenoid cystic carcinoma, mucoepidermoid carcinoma, and basal cell adenoma. Myoepithelioma lacks the typical feature of glanduloductal differentiation and the absence of chondromyxoid or chondroid foci. Adenoid cystic carcinoma can be identified because of its infiltrative growth

Table 1: The list of case reports reviewed on pleomorphic adenoma

Investigator	*Pain*	*Location*	*Age (years)*	*Gender*	*Encapsulated*	*Multinodular*	*Invasion into adjacent tissues*	*Treatment opted*
Tandon et al., 2018[8]	Present	Left side of palate	28	M	No	No	No	Surgical excision
Taiwo et al., 2018[9]	Absent	Upper lip	33	M	No	No	No	Surgical excision
Farhat et al., 2018[10]	Absent	Left side of neck	53	M	Yes	No	No	Surgical excision
Panda et al., 2018[11]	Absent	Soft palate	72	M	Yes	No	No	Complete excision
Celik et al., 2018[12]	Absent	Nasopharynx	51	F	Yes	No	No	Lateral rhinotomy with transnasal endoscopic approach
Balan et al., 2017[13]	Absent	Left maxillary labial mucosa	72	F	Yes	Yes	No	Surgical excision
Kaul et al., 2017[14]	Absent	Cheek	36	F	Yes	No	No	Surgical excision
Mittal et al., 2017[15]	Absent	Left side of the face	26	M	Yes	No	No	Enucleation
Kamala et al., 2016[16]	Absent	Palate	40	F	Yes	No	No	Surgical excision
Bagga et al., 2016[17]	Absent	Right submandibular region	50	M	Yes	No	No	Excision of sub-mandibular gland with mass
Modak et al., 2016[18]	Absent	Right side of the face	39	F	Yes	No	No	Surgical excision
Jain et al., 2015[19]	Absent	Left side of the face	50	F	Yes	No	No	Excision
Verma et al., 2014[20]	Absent	Left side of the cheek	42	F	Yes	No	No	Surgical excision
Dhir et al., 2014[21]	Absent	Left lower one third of face	35	M	Yes	No	No	Superficial parotidectomy of left parotid gland
Saito et al., 2014[22]	Absent	External auditory canal	40	M	Yes	No	No	Retroauricular surgical approach
Swarnagowri et al., 2014[23]	Absent	Hard palate	13	F	Yes	No	No	Not known
Nagaraj et al., 2014[24]	Absent	Left side of the face	75	F	Yes	Yes	Yes	Excision with removal of periosteum and bone involved
Rahnama et al., 2013[25]	Absent	Hard palate	47	F	Yes	No	No	Surgical excision
Sunil et al., 2013[26]	Absent	Angle of the mandible (right side)	62	F	Yes	No	No	Surgical excision
Aggarwal et al., 2012[27]	Absent	Right side of face	55	F	Yes	No	No	Surgical excision
Kumar et al., 2011[28]	Absent	Left ear lobule	28	F	Yes	No	No	Surgical excision
Shrestha et al., 2010[29]	Absent	Upper lip	27	F	No	No	No	Surgical excision with lip splitting incision

pattern and tendency for perineural invasion. The intermediary cells are a common feature in mucoepidermoid carcinoma and pleomorphic adenoma. Although the intermediary cells have of the mucoepidermoid carcinoma produce extracellular material, they do not have the ability to create myxochondroid stroma.

Malignancy of PA occurs as three forms: carcinoma ex-pleomorphic adenoma (CEPA), carcinosarcoma, and metastasizing pleomorphic adenoma (MPA), of which the last two rarely occur.[40,41]

A systematic review conducted by Knight et al. which included a total of 81 cases of MPA reported that the most common sites for MPA were bone, lung, and cervical lymph nodes with an occurrence of 36.6% (28 cases), 33.8% (26 cases), and cervical lymph nodes 20.1% (17 cases), respectively. Other sites included kidneys (8.6%), cutaneous (8.6%), hepatic (4.9%), and brain (3.7%).[42]

The risk of recurrence of PA is generally associated with inadequate surgical procedure, which could have been spillage of tumor or tumor capsule. Recurrent PA occurs as multiple, separate nodules. Surgical risks involved are pseudopodia, capsular penetration, and tumor rupture.[43]

The study included articles on English language only, incorporating an element of selection bias.

Conclusion

Pleomorphic adenomas are benign salivary gland neoplasms that can grow into extensive sizes. They need to be diagnosed early. Complete excision of the tumor is the definitive treatment, as enucleation can result in recurrence. Facial nerve has to be preserved if PA occurs in the parotid gland. Even after removal, a long-term follow-up is necessary to check for recurrence.

References

1. Califano J, Eisele DW. Benign salivary gland neoplasms. Otolaryngol Clin North Am 1999;32(5):861–873. DOI: 10.1016/S0030-6665(05)70178-X.
2. Rajendran S, Sivapathasundaram S. Shafer's Textbook of Oral Pathology. 6th ed., New Delhi: Elsevier; 2009. pp. 219–224.
3. Regezi JA, Batsakis JG. Histogenesis of salivary gland neoplasms. Otolaryngol Clin North Am 1977;10(2):297–307.
4. Luna MA. Salivary glands. In: Pilch BZ. Head and neck surgical pathology. Philadelphia: Lippincott Williams and Wilkins; 2001. pp. 284–349.
5. Sergi B, Limongelli A, Scarano E, et al. Giant deep lobe parotid gland pleomorphic adenoma involving the parapharyngeal space. report of three cases and review of the diagnostic and therapeutic approaches. Acta Otorhinolarngol Ital 2008;28(5):261–265.
6. Vincente OP, Marques NA, Aytes LB, et al. Minor salivary gland tumors: a clinicopathological study of 18 cases. Med Oral Patol Oral Cir Buccal 2008;13(9):582–588.
7. Zarbo RJ. Salivary gland neoplasia: a review for the practicing pathologist. Modern Pathology 2002;15(3):298–323. DOI: 10.1038/modpathol.3880525.
8. Tandon A, Jaiswal R, Siddiqui S, et al. Keratininzing pleomorphic adenoma: an unusual case report. J Oral Maxillofac Pathol 2018;22(Suppl 1):69–72. DOI: 10.4103/jomfp.JOMFP_200_17.
9. Taiwo AO, Akinshipo A, Braimah RO, et al. Pleomorphic adenoma of the upper lip: a case report. Saudi J Med Sci 2018;6(1):32–35. DOI: 10.4103/sjmms.sjmms_109_16.
10. Farhat F, Asmir RA, Yudhistra A, et al. An uncommon occurrence of pleomorphic adenoma in the submandibular salivary gland: a case report. Open Access Maced J Med Sci 2018;6(6):1101–1103. DOI: 10.3889/oamjms.2018.248.
11. Panda S, Manjunath NML, Panda K. Pleomorphic adenoma of the soft palate: a case report with literature review. Oncol J India 2018;2:13–15. DOI: 10.4103/oji.oji_4_18.
12. Celik S, Kilic O, Kinet TZ, et al. Nasopharyngeal pleomorphic adenoma: a rare case report and review of literature. Case Rep Otolaryngol 2018;2018:2481370. DOI: 10.1155/2018/2481370.
13. Balan N, Mani MS, Ahamed SY, et al. Pleomorphic adenoma: case report and review of literature. J Indian Acad Dent Spec Res 2017;4:61–64. DOI: 10.4103/jiadsr.jiadsr_17_17.
14. Kaul D, Rajput AK, Ahmed Z, et al. Pleomorphic adenoma in the cheek, a rare finding. J Int Clin Dent Res Organ 2017;9:79–81. DOI: 10.4103/jicdro.jicdro_18_17.
15. Mittal G, Aggrawal A, Garg R, et al. Pleomorphic adenoma: a case report. Int J Appl Dent Sci 2017;3(2):154–155.
16. Kamala R, Kallali BN, Gokul K, et al. Pleomorphic adenoma of the palate: a case report and review of a rare entity. J Indian Acad Oral Med Radiol 2016;28:329–333. DOI: 10.4103/0972-1363.195655.
17. Bagga MB, Bhatnagar D, Bhatnagar D. An unusual presentation of pleomorphic adenoma. A case report. J Indian Acad Oral Med Radiol 2016;28:191–194. DOI: 10.4103/0972-1363.195146.
18. Modak R, Hebbale M, Mhapuskar A, et al. Pleomorphic adenoma of right parotid gland: a case report and review of literature. Int J Curr Med Pharm Res 2016;2(8):626–629.
19. Jain S, Hasan S, Vyas N, et al. Pleomorphic adenoma of the parotid gland: report of a case with review of literature. Ethiop J Health Sci 2015;25(2):189–194. DOI: 10.4314/ejhs.v25i2.13.
20. Verma P, Sachdeva SK, Verma KG, et al. Pleomorphic adenoma of cheek. A rare case report and review of literature. Indian J Dent Res 2014;25(1):122–124. DOI: 10.4103/0970-9290.131166.
21. Dhir P, David CM, Dhaduti KG. Pleomorphic adenoma of the parotid gland with cystic degeneration: a rare case report. J Indian Acad Oral Med Radol 2014;26(4):450–453. DOI: 10.4103/0972-1363.155661.
22. Saito C, Kanazawa T, Yamaguchi T, et al. Primary pleomorphic adenoma of external auditory canal: a case report and review of literature. Case Rep Otolaryngol 2014;2014:975151. DOI: 10.1155/2014/975151.
23. Swarnagowri BN, Sharma G, Bhuyan M. Pleomorphic adenoma of the hard palate: a cytology case report. Int J Adv Med 2014;1:55–57. DOI: 10.5455/2349-3933.ijam20140514.
24. Nagaraj H, Raikar RN, Taj RA, et al. The world's biggest benign parotid tumor "Plemorphic adenoma": a rare case report. IOSR J Dent Med Sci 2014;13(2):8–12. DOI: 10.9790/0853-13220812.
25. Rahnama M, Ovzedata-Koszel U, Czupketto L, et al. Pleomorphic adenoma of the palate: a case report and review of literature. Contemp Oncol (Pozn) 2013;17(1):103–106.
26. Sunil S, Gopakumar D. Pleomorphic adenoma. A case report and review of literature. Int J Odontostomat 2013;7(2):171–174. DOI: 10.4067/S0718-381X2013000200001.
27. Aggarwal A, Singh R, Sheikh S, et al. Pleomorphic adenoma of minor salivary gland—a case report. RSBO 2012;9(1):97–101.
28. Kumar R, Sagar P, Sharma SC, et al. Auricular pleomorphic adenoma: case report and review of literature. Indian J Otol 2011;17(4):181–182. DOI: 10.4103/0971-7749.94502.
29. Shrestha A, Reddy NS, Ganguly SN. Pleomorphic adenoma of the upper lip: a case report. J Coll Med Sci Nepal 2010;69(1):51–53. DOI: 10.3126/jcmsn.v6i1.3603.
30. Martinelli M, Martini F, Rinaldi E, et al. Simian virus 40 sequences and expression of the viral large T antigen oncoprotein in human pleomorphic adenomas of parotid glands. Am J Pathol 2002;161(4):1127–1133. DOI: 10.1016/S0002-9440(10)64389-1.
31. Friedrich RE, Li L, Knop J, et al. Pleomorphic adenoma of the salivary glands: analysis of 94 patients. Anticancer Res 2005;25(3):1703–1705.
32. Silva SJ, Costa GT, Filho ACB, et al. Metachronous bilateral pleomorphic adenoma of the parotid gland. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101(3):333–338. DOI: 10.1016/j.tripleo.2005.07.025.
33. Takahama Jr. A, Perez DEC, Magrin J, et al. Giant pleomorphic adenoma of the parotid gland. Med Oral Patol Oral Cir Bucal 2008;13(1):58–60.
34. Hakeem AH, Hazarika B, Pradhan SA, et al. Primary Pleomorphic adenoma of minor salivary gland in the parapharyngeal space. World J Surg Oncol 2009;7(80):1–4. DOI: 10.1186/1477-7819-7-85.
35. Ledesma-Montes C, Garces-Ortiz M. Salivary gland tumors in a mexican sample. A retrospective study. Med Oral 2002;7:324–330.
36. Kaur S, Thami GP, Nagarkar NM. Pleomorphic adenoma of the hard palate—case report. Indian J Dermatol Venerol Leprol 2003;69(7):75.
37. Auclair PL, Ellis GL. Atypical features in salivary gland mixed tumors: their relationship to malignant transformation. Mod Pathol 1996;9(6):652–657.
38. Yamamoto Y. Clinical signs and histology of carcinoma in pleomorphic adenoma. Otologia 1994;87:1320–1324.
39. Sreenivas SD. Pleomorphic adenoma of the palate—a case report. JIDA 2011;5:4.
40. Auclair PL. Sarcomas and sacromatoid carcinomas of major salivary gland regions: a clinicopathological and immunohistochemical study of 67 cases and review of literature. Cancer 1986;58:1305–1315. DOI: 10.1002/1097-0142(19860915)58:6<1305::AID-CNCR2820580621>3.0.CO;2-K.
41. Ghosh A, Arundhati, Asthana AK. Pleomorphic adenoma of the parotid gland metastasizing to the scapular region. Acta Cytol 2008;52(6):733–735. DOI: 10.1159/000325632.
42. Knight J, Ratnasingham K. Metastasising pleomorphic adenoma: systematic review. Int J Surg 2015;19:137–145. DOI: 10.1016/j.ijsu.2015.04.084.
43. Patrick J, Bradley M. Recurrent salivary gland pleomorphic adenoma: etiology, management and results. Curr Opin Otolaryngol Head Neck Surg 2001;9(2):100–108. DOI: 10.1097/00020840-200104000-00008.