Original Article

"Pleomorphic adenoma in salivary glands: Insights from a 100-patient analysis"

Shazima Sheereen, Mohnish Zulfikar Manva[1], Shamama Sheereen[2], Namrata N. Patil[3], Rawa K. Abdelrahim[4], Mohammed Malik Afroz[5]

Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Mangalore, Karnataka, [2]Department of Pedodontics and Preventive Dentistry, Maharaj Vinayak Global University, Jaipur, Rajasthan, [3]Department of Oral Pathology and Microbiology, Saraswati Dhanwantari Dental College and Hospital, Post Graduation Research Centre, Parbhani, Maharashtra, India, [4]Department of Preventive Dental Sciences, Dar Al Uloom University, [5]Department of Oral Radiology, Dar Al Uloom University, [1]Department of Conservative Dentistry and Endodontics, Cimai Medical centre, Riyadh, KSA

Abstract

Introduction: Pleomorphic adenoma (PA) is a benign epithelial tumour originating from the salivary gland, specifically the parotid gland. This study aims to comprehensively analyse the clinical and pathological features of PA by examining the characteristics of the tumour, including its histological structure and immunohistochemical profile.

Materials and Methods: Over 8 years, beginning in October 2015 and ending in October 2023, an exhaustive retrospective study was conducted in the Department of Pathology, Kasturba Medical College, Mangalore, Manipal University, Karnataka, India. The research focused on 100 cases of pleomorphic adenoma and involved a meticulous examination of the clinical and pathological characteristics obtained by retrieving the pertinent files.

Results: Out of all the primary tumours, the majority ($n = 70$) was found in the parotid gland, followed by PA that developed from the minor salivary glands of the palate ($n = 07$), the submandibular gland ($n = 17$), and the lacrimal gland ($n = 04$). Only two cases had a primary tumour located in the lips. Females were more susceptible to these tumours than males. The parotid gland tumours showed a distinct trend in laterality, with 73 cases observed on the right side. In 85%, the initial symptom of the condition was painless swelling.

Conclusion: Salivary gland PA is typically a benign tumour. However, a subset of these tumours can exhibit a malignant phenotype. The preferred treatment is surgical excision with adequate margins.

Keywords: Benign tumour, parotid, pleomorphic adenoma, salivary glands

Address for correspondence: Dr. Shamama Sheereen, MDS Pedodontist, Department of Pedodontics and Preventive Dentistry, Maharaj Vinayak Global University, Jaipur - 302 028, Rajasthan, India.
E-mail: shamamasheereen@gmail.com

Submitted: 18-Oct-2023, **Revised:** 01-Nov-2023, **Accepted:** 08-Nov-2023, **Published:** 15-Apr-2024

INTRODUCTION

Salivary gland tumours are rare and account for less than 3% of neoplasms in the head and neck region.[1] These tumours possess intricate microscopic features; the most common type is the pleomorphic adenoma (PA). PA constitutes a significant proportion of tumours in the parotid gland, ranging from 60% to 73%, and in the submandibular and minor salivary glands, ranging from

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_452_23

How to cite this article: Sheereen S, Manva MZ, Sheereen S, Patil NN, Abdelrahim RK, Afroz MM. "Pleomorphic adenoma in salivary glands: Insights from a 100-patient analysis". J Oral Maxillofac Pathol 2024;28:42-8.

40% to 60%.[2-4] Pleomorphic adenoma (PA) is a frequently occurring benign tumour in the salivary glands, primarily found in the parotid gland.[5] Most tumours typically arise in the superficial lobe, while the deep lobe of the parotid gland and the parapharyngeal space are only occasionally affected.[6] The highest incidence of minor salivary gland tumours occurs on the palate, with the lip, cheek, tongue, and floor of the mouth being the subsequent most affected sites.[7] PA typically presents as a painless, slow-growing parotid gland swelling without facial nerve involvement.[8] Approximately 75% of parotid tumours are PAs; surgical removal is the preferred treatment option.[9] However, local recurrence can occur due to inadequate pre-operative diagnostics, surgical techniques, and lesions of the pseudo capsule during surgery.[10] Recurrence after primary surgery is difficult to treat, and multiple recurrences are common during long-term follow-up.[11] Post-surgical recurrence of PA is a frequently encountered issue, with the recurrence rates varying between 0.5% and 10%. Certain studies have indicated a greater incidence of up to 48%.[12]

PA is a tumour that exhibits significant morphological diversity at a microscopic level. The tumour comprises luminal (epithelial) and abluminal (myoepithelial) cells with significant variability in the proportion, and its association with the mesenchymal component results in basal lamina and proteoglycan production. Luminal cells typically take on a polygonal, spindle, or stellate shape and can form duct-like structures, sheets, clumps, or interlacing strands. They are recognisable by their cohesive groupings, which usually include a honeycomb pattern.[13-15] When these epithelial cells are present as individual cells, they are indistinguishable from neoplastic myoepithelial cells. Among the parenchymal cells of PA, neoplastic myoepithelial cells are the most relevant in the tumour context because they play a tumour suppressor role with the potential high secretion of tissue inhibitors of metalloproteinases (TIMPs).[16,17] These cells accumulate in large quantities in the extra-cellular matrix and have a variety of appearances, including spindle-shaped (most common), epithelioid, clear-cell, and plasmacytoid.[18] PA can also lead to malignant tumours in both minor and major salivary glands, specifically carcinoma. The risk of malignant transformation of PA is estimated to be between 3% and 4%.

This research aims to comprehensively examine PA's clinical and pathological features, focusing on details that an expert audience can quickly grasp. The study will review the tumour's histological structure and immunohistochemical profile. By providing a comprehensive understanding of the technicalities of PA, we aim to enhance healthcare practitioners' knowledge. The ultimate goal of this study is to improve diagnosis, treatment, and outcomes for patients suffering from this ailment.

MATERIALS AND METHODS

A comprehensive retrospective study spanning over 8 years, from October 2015 to October 2023, was conducted after approval from the institutional ethical committee in the Department of Pathology at Kasturba Medical College in Mangalore, Karnataka, India. The study focused on 100 PA cases and thoroughly examined the clinical and pathological characteristics retrieved from relevant files. The study focused exclusively on PA cases accompanied by detailed demographic and clinical information and biopsy or specimen samples obtained via excision. Cases lacking such detailed records were excluded from the analysis. The specimens received were fixed in 10% formalin, followed by routine tissue processing and sectioning of 5μ thickness using a paraffin-embedded technique. Haematoxylin and eosin staining was performed on tissue sections and analysed under a light microscope at ×4, ×10, and ×40 magnifications. Multiple sections from different regions were evaluated based on the size of the lesion, with a total of 3–5 sections examined.

Scoring criteria: 0

Based on the proportion of parenchymal and stromal tumour components, the cases were classified into four sub-types as proposed by Foote and Frazell:[19]

- Type I: Principally myxoid
- Type II: Myxoid and cellular
- Type III: Predominantly cellular
- Type IV: Extremely cellular

"Morphological patterns", "cellular patterns", "capsular alterations", and "stromal components" were analysed.

RESULTS

Our study showed that women were more susceptible to parotid gland tumours than men, especially those between 30 and 60 years of age. Among the tumours, the majority (n = 70) was found in the parotid gland, followed by a PA, which developed from the minor salivary glands of the palate (n = 07), the submandibular gland (n = 17), and the lacrimal gland (n = 04). Interestingly, there was a distinct trend in laterality for the parotid gland tumours, with 73 cases observed on the right and only 27 on the left. In addition, only two cases had a primary tumour in the lips. The initial symptom of the condition was painless swelling in 85% of cases, followed by a pressure sensation in 10% and pain in 5% of cases across all sites.

This was often associated with pain (5%) and pressure sensation (3%) [Tables 1-5].

Upon histopathological examination, the cases were categorised into four sub-types based on the Foote and Frazell[19] classification system. All cases demonstrated a type II pattern characterised by a myxoid and cellular appearance. The cellular components of the cases were primarily composed of spindle cells (90%), followed by cuboidal cells (85%), plasmacytoid cells (50%), squamous cells (40%), and mucous cells (20%). The ductal morphological pattern was observed in all cases, with 40% demonstrating a cystic pattern and 25% showing a cribriform pattern. The stromal components of the cases were composed of an 85% hyalinised matrix and a 15% chondroid matrix. Encapsulation was observed in 40% of the cases, with 20% demonstrating satellite nodules within the capsule. A summary of the various morphological patterns and cellular and stromal components can be found in Table 6.

The outer surface appears clearly defined, enclosed, and thin on gross examination. Meanwhile, the inner surface showcases a tan-to-white colouration and a noticeably firm consistency, as depicted in Figure 1. The analysed sample reveals a tumour that originates from a salivary gland. The tumour is clearly defined and consists of both epithelial and myoepithelial elements. The epithelial elements are mainly present in ducts, interspersed with myxoid components in the stromal tissue, as depicted in Figure 2. Upon examination of the smear, it was observed that myoepithelial cells were arranged in sheets. Some of these cells exhibited a clear cytoplasm, as depicted in Figure 3.

Upon histochemical staining of Pleomorphic Adenoma, it was observed that there were areas positive for Periodic-Acid-Schiff within the duct lumen, which indicates neutral mucins, as depicted in Figure 4. The ductal (epithelial) cells were typically positive for cytokeratins 14, as depicted in Figure 5. Myoepithelial cells were positive for P63, as

Table 1: Gender distribution of PA

Gender	No of cases	Percentage
Female	65	65%
Male	35	35%

Table 2: Age distribution of PA

Age	No of cases	Percentage
<20 years	03	03%
21-30 years	20	20%
31-40 years	24	24%
41-50 years	26	26%
51-60 years	14	14%
61-70 years	08	08%
>70 years	05	05%

Figure 1: Gross finding of Pleomorphic Adenoma. Outer Surface - Well circumscribed, encapsulated and thin surface. Cut Surface - Tan to white, firm in consistency

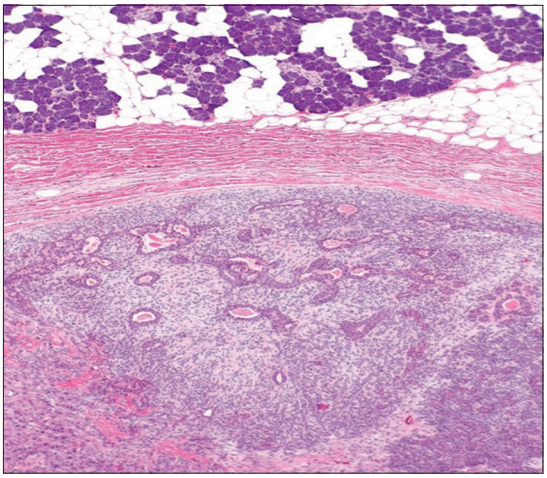

Figure 2: Histopathological image shows Histopathological examination of Pleomorphic Adenoma. Sections show a tumour with a salivary gland which is well-circumscribed and composed of epithelial and myoepithelial elements. Epithelial elements are arranged predominantly as ducts along with myxoid components in the stroma

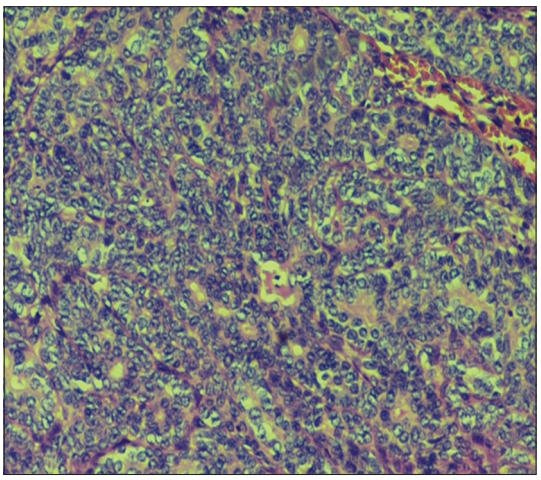

Figure 3: Histopathological image shows Histopathological examination of Pleomorphic Adenoma. The studied smear shows myoepithelial cells arranged in sheets. Few of these cells has clear cytoplasm

depicted in Figure 6. The ductal component, on the other hand, was positive for the epithelial markers Epithelial Membrane Antigen and Carcinoembryogenic antigen, as depicted in Figure 7. Staining for S100 protein often highlights most abluminal cells and those lying in the matrix, as depicted in Figure 8. Calponin stain highlights the myoepithelial and modified myoepithelial cells, as depicted in Figure 9.

Recurrence: Out of the total number of patients, 25 individuals suffered from recurring tumours. Most of these patients (16 individuals) were between 45 and 70. Five patients had a second relapse, while four experienced a third relapse.

Of the patients, 7% were diagnosed with a carcinoma inside a PA, as depicted in Figure 10. The primary therapy for these patients included local resection in five, conservative parotidectomy in one, and partial resection of the soft palate in one. Further interventions were carried out in all cases, including dissection of efferent lymphatics of the neck and additional local resections. Reconstruction was done using various methods such as palatine flaps, pharynx-palatine flaps, microvascular radial forearm flaps, and latissimus dorsi-flaps. In one patient, the facial nerve was adhering to the tumour and had to be removed. Sural

Table 3: Laterality of PA

Laterality	No of cases	Percentage
Right-sided	73	73%
Left-sided	27	27%
Total	100	100%

Table 4: Site distribution of PA

Site	No of cases	Percentage
Parotid gland	70	70%
Submandibular gland	17	17%
Palate	07	07%
Lacrimal gland	04	04%
Lip	02	02%
Total	100	100%

Table 5: Presenting complaints in PA

Presenting complaints	No of cases	Percentage
Painless swelling	85	85%
Pressure sensation	10	10%
Pain	05	05%
Total	100	100%

Table 6: Various morphological patterns and cellular and stromal components

Cellular component	Morphological pattern	Stromal component
Category Percent	Category Percent	Category Percent
Plasmacytoid 50	Ductal 100	Hyalinised 85
Spindle 90	Myxoid 100	Trabecular 20
Cuboidal 85	Cystic 40	Chondroid 15
Squamous 40	Cribriform 25	Osteoid 20
Mucous 20	Solid 05	-

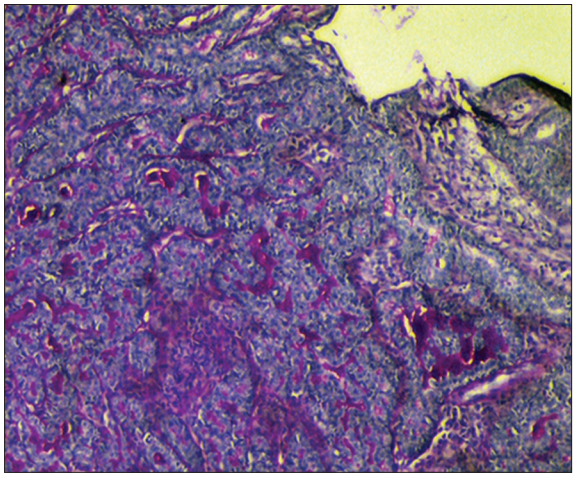

Figure 4: Histopathological image shows Periodic-Acid-Schiff – Positive. The histochemical staining of Pleomorphic Adenoma revealed Periodic-Acid-Schiff -positive areas within the lumen of ducts indicative of neutral mucin

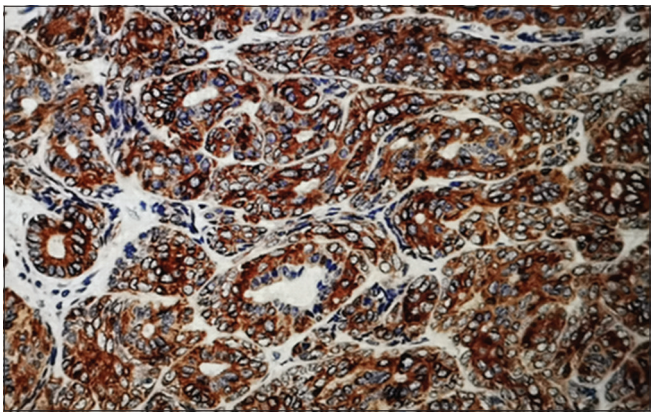

Figure 5: Histopathological image shows Immunohistochemistry: Cytokeratin 14 – Positive. The ductal (epithelial) cells are typically positive for cytokeratins

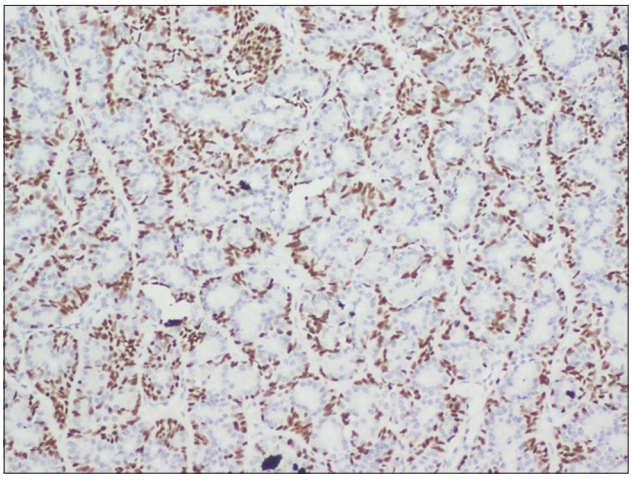

Figure 6: Histopathological image shows Immunohistochemistry: P63 –Positive. Myoepithelial cells are positive for P63

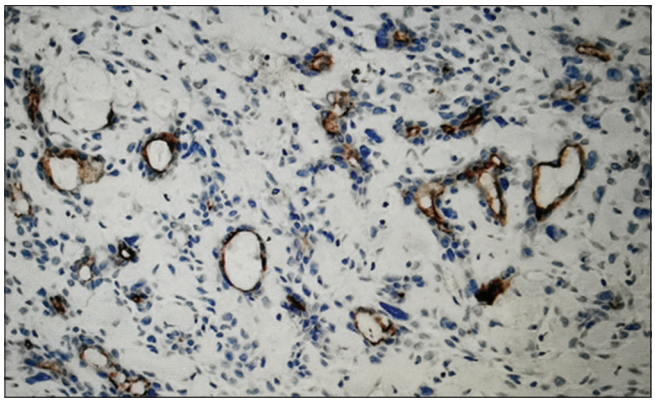

Figure 7: Histopathological image shows Immunohistochemistry: Epithelial Membrane Antigen – Positive. The luminal cells are Epithelial Membrane Antigen positive and, consistent with an epithelial origin. This is a benign lesion

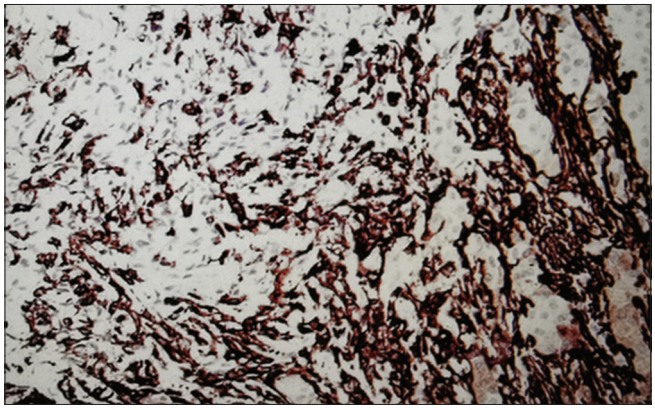

Figure 9: Histopathological image shows staining for calponin Positive. Calponin stain highlights the myoepithelial and modified myoepithelial cells

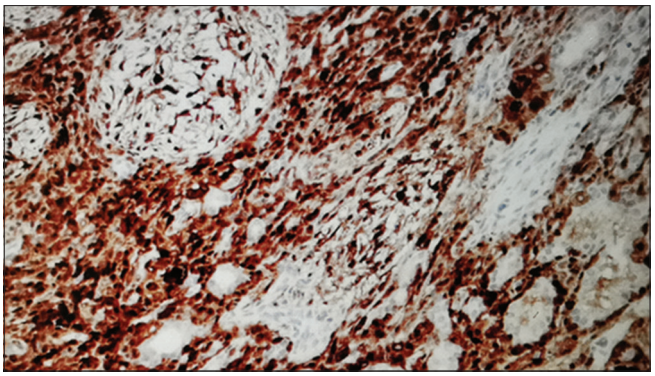

Figure 8: Histopathological image shows S-100 Positive. Staining for S100 protein often highlights most abluminal cells, as well as those lying in the matrix

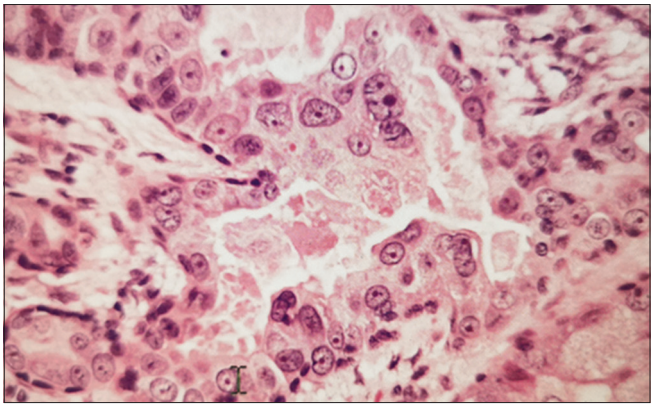

Figure 10: Histopathological image shows carcinoma *in situ* ex PA. The preexisting pleomorphic adenoma's luminal (ductal) cells are replaced by atypical large cells with apocrine cytoplasm

nerve interposition grafts were employed to restore facial animation. None of the patients were given post-operative radiation therapy.

DISCUSSION

The research study highlights a crucial observation that PA, a type of tumour found in the salivary gland, can lead to the development of carcinoma, a cancerous tumour.[9] PA is a benign tumour that consists of cells capable of differentiating into multiple types of cells, including epithelial and mesenchymal cells. According to Dardick I *et al*.,[20] neoplastically altered myoepithelial cells with multi-directional differentiation properties may be responsible for the histogenesis of this tumour. Additionally, the mucin 1 gene (MUC1) is associated with the recurrence of PA and its malignant transformation, with carcinoma cells overexpressing mucin 1 gene.[21,22] Immunohistochemistry markers such as cytokeratin, Epithelial Membrane Antigen, P63, alpha smooth-muscle actin, calponin, h-caldesmon, vimentin, and S-100-protein can aid in diagnosing this tumour.[23,24] The study on the proportion of parenchymal and stromal tumour components revealed that all the cases belonged to Type II (myxoid and cellular variant), which is inconsistent with Satpathy Y *et al*.'s findings in 2014.[25] This could be due to geographic differences. Usually, PA of the major salivary glands falls under the type I or II categories, while minor salivary gland tumours are more cellular in nature.[26] The epithelial component of the studied cases displayed a range of patterns, including ductal, trabecular, tubular, solid, cystic, and papillary architectures. In all cases with ductal patterns, two layers of cells merged with the stromal component, and the myoepithelial cells modified the stromal component, sometimes undergoing osteoid or chondroid metaplasia, as noted in Dardick I *et al*.'s 1982 study.[20] The present study revealed that 40% of cases exhibited cystic areas with squamous metaplasia, leading to diagnostic challenges similar to those observed in Nonitha S *et al*.'s 2019 study.[27] It is important to note that extensive squamous metaplasia does not necessarily indicate malignant transformation unless accompanied by capsular invasion, haemorrhage, and necrosis. Misdiagnosis

as malignant tumours can occur, leading to unnecessary aggressive therapy.[27]

The myoepithelial tumour cells can take on different shapes, including spindle-shaped, epithelioid, clear-cell, and plasmacytoid.[18] Similar to the present study, studies showed the most common cellular pattern was spindle cell in all the cases, followed by cuboidal cells (85%) and plasmacytoid cells (50%); this was not in concordance with Fabio Augusto Ito FA *et al.* 2009 and Ellis and Auclair 1996, stating that plasmacytoid cells are more common, followed by spindle cells which appear to be in transition from one form to the others.[28,29] Cuboidal cells are typically epithelial and found in less dense tumour areas. The tumour stroma or supportive tissue is essential for tumour growth and can have varying compositions, such as increased collagen synthesis, blood vessel growth, and myofibroblast production.[30] The mesenchymal component, derived from modified myoepithelial cells, can take several forms, including myxoid, hyaline, chondroid, myxochondroid, or osseous. This study found myxoid to be the most common variant, followed by hyalinised stroma and chondroid. This finding is similar to a hypothesis that myxoid variants may express more acidic mucins and, due to lack of differentiation, have a higher recurrence rate and poorer prognosis. Some studies have suggested that hyalinised stroma may have a greater propensity for malignant change.[31] Our study observed that excisional PA had a thick fibrous capsule in 40% of cases. This may be due to the complete excision of the tumour as a treatment plan. Additionally, 20% of the cases had satellite nodules within their capsule, which may suggest that recurrence of the tumour may occur if simple enucleation is performed. In some rare cases, the PA can coexist with other salivary gland tumours or develop in different sites simultaneously, adding complexity to investigating and managing such cases.[11] Therefore, surgical therapy should consider the possibility of multi-focal origin and the potential for a transformed phenotype. The insights presented in the preceding text are important for identifying and treating PA.[12] These observations underscore the critical significance of scrupulous scrutiny and tumour management to forestall the onset of further complications. The findings shed light on the need for careful and comprehensive assessment and management of this type of tumour for successful outcomes.[32-35]

CONCLUSION

PA is a neoplasm that arises from the salivary gland and is characterised by a heterogeneous mixture of epithelial and mesenchymal elements. Despite being classified as a benign tumour, it has been reported to display local invasiveness and poses a significant risk of re-occurrence in cases where the removal is incomplete. Therefore, it is imperative to exercise caution when managing such cases and prioritise complete surgical resection. In addition, surgical treatment planning should consider the potential for malignant transformation in PA, which further highlights the importance of careful monitoring and follow-up.

Abbreviations

O/S = Outer surface
C/S = Cut surface
HPE = Histopathological examination
PA = Pleomorphic adenoma
PAS = Periodic-Acid-Schiff
EMA = Epithelial membrane antigen
CK = Cytokeratin
H and E = Haematoxylin and eosin
IHC = Immunohistochemistry

Author contribution

Shazima Sheereen: Wrote the largest share of report; Mohnish Zulfikar Manva: Drafting the work; Shamama Sheereen: Assisted in writing the manuscript; Namrata N Patil: Final approval of the version; Rawa Kamal Abdelrahim: Contributed towards the manuscript revision; Mohammed Malik Afroz: Substantial contributions to the revisions of the report.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. van der Wal JE, Leverstein H, Snow GB, Kraaijenhagen HA, van der Waal I. Parotid gland tumors: Histologic reevaluation and reclassification of 478 cases. Head Neck 1998;20:204-7.
2. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. J Pathol 1985;146:51-8.
3. Spiro RH. Salivary neoplasms: Overview of a 35-year experience with 2,807 patients. Head Neck Surg 1986;8:177-84.
4. Ito FA, Ito K, Vargas PA, de Almeida OP, Lopes MA. Salivary gland tumors in a Brazilian population: A retrospective study of 496 cases. Int J Oral Maxillofac Surg 2005;34:533-6.
5. Almeslet AS. Pleomorphic adenoma: a systematic review. International journal of clinical pediatric dentistry 2020;13:284.
6. Morita N, Miyata K, Sakamoto T, Wada T. Pleomorphic adenoma in the parapharyngeal space: Report of three cases. J Oral Maxillofac Surg 1995;53:605-10.
7. 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.

8. Sergi B, Limongelli A, Scarano E, Fetoni AR, Paludetti G. Giant deep lobe parotid gland pleomorphic adenoma involving the parapharyngeal space. Report of three cases and review of the diagnostic and therapeutic approaches. Acta Otorhinolaryngol Ital 2008;28:261-5.
9. Seifert G, Donath K. [Morphology of salivary gland diseases]. Arch Otorhinolaryngol 1976;213:111-208.
10. Maran AG, Mackenzie IJ, Stanley RE. Recurrent pleomorphic adenomas of the parotid gland. Arch Otolaryngol 1984;110:167-71.
11. Pires FR, Alves Fde A, de Almeida OP, Lopes MA, Kowalski LP. Synchronous mucoepidermoid carcinoma of tongue and pleomorphic adenoma of submandibular gland. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95:328-31.
12. Tischendorf L, Luttermann T, Hermann PK. Entartungswahrscheinlichkeit des operativ behandelten pleomorphen Adenoms. Dtsch Z Mund Kiefer Gesichtschir 1992;16:10-2.
13. Gündüz AK, Yeşiltaş YS, Shields CL. Overview of benign and malignant lacrimal gland tumors. Curr Opin Ophthalmol 2018;29:458-68.
14. Xiao HD, Bifulco CB. Cellular and molecular pathology. Oral, Head and Neck Oncology and Reconstructive Surgery 2018:57-78. http://dx.doi.org/10.1016/b978-0-323-26568-3.00002-6.
15. Yabuuchi H, Fukuya T, Tajima T, Hachitanda Y, Tomita K, Koga M. Salivary gland tumors: Diagnostic value of gadolinium-enhanced dynamic MR imaging with histopathologic correlation. Radiology 2003;226:345-54. doi: 10.1148/radiol. 2262011486.
16. Han W, Chen S, Yuan W, Fan Q, Tian J, Wang X, *et al*. Oriented collagen fibers direct tumor cell intravasation. Proc Natl Acad Sci U S A 2016;113:11208-13. doi: 10.1073/pnas. 1610347113.
17. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. J Pathol 1985;146:51-8.
18. Monica K, Sandhya PR. Analysis of Various Histopathological Patterns in Pleomorphic Adenoma-An Institutional Case Study. J Oral MaxillofacPathol 2023;14:29-32.
19. Rajwanshi A, Gupta K, Gupta N, Shukla R, Srinivasan R, Nijhawan R, *et al*. Fine-needle aspiration cytology of salivary glands: diagnostic pitfalls—revisited. Diagnostic cytopathology 2006;34:580-4.
20. Dardick I, van Nostrand AW, Phillips MJ. Histogenesis of salivary gland pleomorphic adenoma (mixed tumor) with an evaluation of the role of the myoepithelial cell. Hum Pathol 1982;13:62-75. doi: 10.1016/s0046-8177 (82) 80140-8.
21. Kashyap B, Kullaa AM. Regulation of mucin 1 expression and its relationship with oral diseases. Archives of Oral Biology 2020;117:104791.
22. Soares AB, Demasi AP, Altemani A, de Araújo VC. Increased mucin 1 expression in recurrence and malignant transformation of salivary gland pleomorphic adenoma. Histopathology 2011;58:377-82.
23. Nishimura T, Furukawa M, Kawahara E, Miwa A. Differential diagnosis of pleomorphic adenoma by immunohistochemical means. J Laryngol Otol 1991;105:1057-60. doi: 10.1017/s0022215100118183.
24. Furuse C, Sousa SO, Nunes FD, Magalhães MH, Araújo VC. Myoepithelial cell markers in salivary gland neoplasms. Int J Surg Pathol 2005;13:57-65. doi: 10.1177/106689690501300108.
25. Satpathy Y, Spadigam AE, Dhupar A, Syed S. Epithelial and stromal patterns of pleomorphic adenoma of minor salivary glands: A histopathological and histochemical study. J Oral Maxillofac Pathol 2014;18:379-85.
26. Alsanie I, Rajab S, Cottom H, Adegun O, Agarwal R, Jay A, *et al*. Distribution and frequency of salivary gland tumours: an international multicenter study. Head and neck pathology 2022;16:1043-54.
27. Nonitha S, Yogesh TL, Nandaprasad S, Maheshwari BU, Mahalakshmi IP, 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: JOMFP 2019;23:356.
28. 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:E57-61.
29. 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:E57-61.
30. Hoying JB, Utzinger U, Weiss JA. Formation of microvascular networks: Role of stromal interactions directing angiogenic growth. Microcirculation 2014;21:278-89.
31. Auclair PL, Ellis GL. Atypical features in salivary gland mixed tumors: Their relationship to malignant transformation. Mod Pathol 1996;9:652-7.
32. Zeebregts CJ, Mastboom WJ, van Noort G, van Det RJ. Synchronous tumours of the unilateral parotid gland: Rare or undetected? J Craniomaxillofac Surg 2003;31:62-6.
33. Friedrich RE, Li L, Knop J, Giese M, Schmelzle R. Pleomorphic adenoma of the salivary glands: Analysis of 94 patients. Anticancer Res 2005;25:1703-5.
34. Sandhya MK, Ramani P. Analysis of various histopathological patterns in pleomorphic adenoma-An institutional case study. Oral and Maxillofac Pathol J 2023;14:28-32.
35. Valstar MH, de Ridder M, van den Broek EC, Stuiver MM, van Dijk BAC, van Velthuysen MLF, *et al*. Salivary gland pleomorphic adenoma in the Netherlands: A nationwide observational study of primary tumor incidence, malignant transformation, recurrence, and risk factors for recurrence. Oral Oncol 2017;66:93-9.