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Clinicopathological spectrum of pleomorphic adenoma: A seven-year institutional study

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Abstract
Introduction: Salivary gland tumours (SGT) constitute less than 1%-5% of all head and neck cancers. Among these, Pleomorphic adenoma (PA) is the most common form of benign SGT, accounting for 60-70% of parotid glands, 40-60% of submandibular gland and 40-70% of all minor salivary glands. PA reflects singnificant diversity in histological presentation due to metaplastic transformation of myoepithelial cells in production of extracellular matrix. This pleomorphism, these neoplasms may mimics other SGTs often leading to misdiagnosis by the pathologist and unnecessary aggressive treatment.
Aim: To retrospectively analyze pleomorphic adenoma cases reported over 7 years period focusing on clinical presentation and histopathological findings.
Materials and Methods: 1. Data was collected from diagnosed cases of PA over 7 years period at a Government Dental College and Hospital & Regional Cancer Center, 2. They were analysed for determine demographics patterns, clinical presentation and histopathological variations.
Results: A total of 50 cases of pleomorphic adenoma were identified. The common age of occurrence was 5th to 6th decade with 3 cases in younger patients. A Female predeliction was seen in most cases. The palate was the most common anatomical site. Intraorally the lesion showed as unilateral swelling with solitary mass. Recurrence was frequently observed in younger population.
Conclusion: Early diagnosis of this benign neoplasm is important to avoid misdiagnosis and over treatment as it has high rate of recurrence and chances of malignant transformation.

Keywords: Elastic modulus, flexural strength, provisional restorative materials

1. Introduction
Salivary gland tumors present a wide variety of biological behavior and morphological diversity, often posing challenges difficulties in diagnosis, classification and treatment [1]. These tumors are rare, constituting 5% of all head and neck cancers and 0.5% of total body malignancies, with an annual incidence of 0.5-2 patients/1,00,000 people [2]. Salivary gland tumors (SGTs) may arise in both major salivary glands (parotid, submandibular, and sublingual) as well as in the minor salivary glands.
Pleomorphic adenoma (PA) is the most common benign neoplasm, occurring most frequently in the parotid gland, followed by the minor salivary glands of the palate [3]. PA accounts for approximately 85% of all salivary gland neoplasms, 60% of benign parotid tumors, and about 3% of all head and neck tumors [4]. Typically PA usually arises between the fourth and fifth decade, with a female predilection. No racial predilection has been reported. It generally presents unilaterally, but can also occur bilaterally. According to literature, the majority of PA is found in the superfcial lobe of the parotid gland (90% of lesions), while the deeper lobe is involved in less than 10% of cases [5].
Histologically, PA demonstrate great diversity of morphologic features and growth patterns. Epithelial differentiation manifests as a mix of well-formed duct-like structures associated with myoepithelial cells, which exhibit diverse morphology including spindled, rounded, angular, plasmacytoid, polygonal and mucous appearance [6]. The tumor stroma may consist of myxoid chondroid, myxoid, chondromyxoid, hyaline, fibrous and sclero-hyaline elements. Very rarely, osseous and adipose metaplasia can be observed [7].

Due to this pleomorphism, these neoplasms may mimics other SGTs leading to misdiagnosis by the pathologist and unnecessary aggressive treatment.

The present study aimed to conduct a retrospective analysis of the clinicopathological features of PAs of the salivary glands diagnosed. Emphasizing the morphological diversity of these tumors.

Materials and Methods

The retrospective study included 50 PA cases retrieved from the archives of Department of Oral Pathology and Regional Cancer Center, from January 2019 to July 2025. Histopathological diagnosis of the lesion was mainly based on examination of hematoxylin and eosin-stained tissue sections. Data was retrived related to age, gender and anatomical site of the tumor. Excised tissue specimens were fixed in 10% neutral formalin for a minimum of 24 hours, dehydrated in graded alcohol, and embedded in paraffin. Paraffin-embedded tissue blocks were sectioned serially, stained with hematoxylin and eosin, and subsequently examined under light microscopy. Histopathologically, PA was categorised into subtype on the based on predominant stromal component and cellular content like myxoid, mucoid and chondroid.

Data procured were analysed to determine demographics pattern, clinical presentation and histopathological variations of diagnosed cases of PA over the 7 years study period at Department of Oral Pathology & Regional Cancer Hospital.

Results

During the period from January 2019 to July 2025, a total of 50 cases of pleomorphic adenoma were diagnosed in the Department of Pathology & Regional Cancer Hospital. Among these 61% of cases involved minor salivary glands, palate (40%) being the most common anatomical site. Among major salivary glands, Submandibular gland showed the highest involvement accounting for 14.8% of PA (Graph 1). A marked female predominance was observed with a female-to-male ratio of approximately 2:1 (Graph 2). The patients were distributed in a wide age distribution ranging from the 2nd to 6th decades of life with the peak incidence being 53% in individuals above 60 years of age (Graph 3). Useful follow-up information was obtained for 50 PA patients, recurrence of the lesion was found in 3% of the cases (Graph 4). Histopathologically, there were multiple histiological variants with cystic pattern (29%) being the most prevalent observed in 29% (Graph 5).

Discussion

This study presents a seven-year retrospective analysis of pleomorphic adenoma (PA) cases, shedding light on the clinicopathological characteristics, demographic patterns, and histological variations of this common benign salivary gland tumor. The findings corroborate and expand upon existing literature regarding the epidemiology, clinical presentation, and pathological diversity of PAs, particularly in the context of their frequency occurrence in the minor salivary glands and the variations seen in histological subtypes.

Epidemiology and Demographics

The data revealed a marked female predominance in PA cases, with a female-to-male ratio of approximately 2:1, which aligns with previous studies that suggest a higher incidence of PA in females, generally in the fourth and fifth decades of life. This study further extends the wide age distribution of PA cases ranging, from the second to sixth decades, with the highest peak incidence in the sixth decade, a trend that has been consistently observed in the literature. The incidence observed in this cohort supports the notion that PAs can occur in any age group, they are most commonly diagnosed in adults, with a notable shift toward older populations. The predominance of PAs in minor salivary glands, particularly in the palate (40%), is another significant finding, with 61% of the cases in the study occurring in minor glands. While major glands, particularly the parotid, are the most frequent sites for PA development, the high occurrence in minor salivary glands, especially the palate, is notable. This contrasts with the more commonly cited predilection for the parotid gland in the literature, which is observed in the majority of PA cases (approximately 60%).

Histogenesis

The histogenesis of pleomorphic adenoma (PA) is believed to involve both epithelial and myoepithelial cells, which possess the capacity to differentiation into various tissue types. PAs are classified as mixed tumors because of their biphasic nature, containing both epithelial and mesenchymal components. The epithelial cells can differentiate into duct-like structures, while the myoepithelial cells contribute to diverse stromal elements, including chondroid, myxoid, and fibrous tissues. This tumor's histogenesis is thought to originate from the transformation of a pluripotent progenitor cell population, capable of undergoing metaplasia and differentiating into multiple tissue types. Genetic mutations, particularly those affecting the PLAG1 and HMGA2 genes, are often implicated in the tumor's development, leading to the uncontrolled growth of these bipotent precursor cells. This complex histogenesis is responsible for the pleomorphic nature of the tumor and its varied histological appearance. [11].

Clinical Presentation

Patients with pleomorphic adenomas typically present with a slow-growing, painless, and firm mass most commonly in the region of the parotid gland. The overlying skin remains intact, and facial nerve function is typically preserved unless the tumor is exceptionally large or has undergone malignant transformation. In rare cases, when the deep lobe is affected, the tumor may present as an intraoral swelling or cause displacement of surrounding structures, leading to difficulty in swallowing (dysphagia) or speech disturbances [9].

One of The hallmark features of PA is its histological diversity which is prominently reflected in stromal variation observed. This study highlights multiple stromal subtypes, including myxoid, mucoid, squamous and chondroid. (Figure 1) Among these, the cystic variant (28%) was the most commonly observed histological feature, which reflects the varied morphologic appearances of the tumor. This supports the notion that PAs often present a mix of histologic types, which can complicate diagnosis and management. The stromal variations of PA are critical not only for diagnostic purposes but also for treatment considerations. For example, the myxoid type, with its softer consistency, may pose challenges in surgical removal due to its diffuse boundaries, while the chondroid variety can sometimes present as a more solid mass that is easier to delineate and excise. Squamous metaplasia finding which signifies a potential pitfall in the histopathological diagnosis but squamous metaplasia has also been noted in non-neoplastic pathologies, "like chronic sialadenitis, necrotizing sialometaplasia, and lymphoepithelial cyst. This change is commonly associated with repair following infarction and necrosis of the salivary glands. The

metaplastic process might be triggered by minor trauma. The presumed etiology for this change is ischemia. This etiology is supported experimentally by the induction of squamous metaplasia in rat salivary glands by arterial ligation. Pathogenesis involves squamous metaplasia and keratin pearl formation in PA have been proposed as dedifferentiation of acinar cells and subsequent hyperplasia of acinar, ductal luminal, and myoepithelial cells. Keratin pearl formation and squamous metaplasia are frequently seen involving the minor salivary glands rather than the major glands. Hence, it is proposed that the epithelium of the minor salivary gland duct exposed to various sources of irritants may be the cause for keratin pearl formation in PA". (Hosur *et al*., 2024) In our case, the presence of bony perforation and the presence of squamous metaplasia was considered to be an aggressive lesion, and therefore carcinoma ex pleomorphic adenoma was meant to be ruled out [12]. Microscopically, PAs are composed of epithelial and myoepithelial cells showing a wide array of morphological patterns and mesenchymal differentiation. The epithelial component may appear as plasmacytoid, spindle, clear, squamous, basaloid, cuboidal, oncocytoid, or mucous cells forming structures such as trabecular, ductal, cystic or solid patterns. The stromal components may exhibit myxoid, chondroid, hyaline, calcified tissue characteristics. The total tumour may be myxoid or stroma rich, cellular or cell rich and classic (balanced amount of epithelial and stromal component. PA shows remarkable degree of morphological diversity. According to relative proportion between the stromal and epithelial components of PA varying significantly, allowing classification into following categories 1) stroma accounts for 30-50% of the tumour is classic type, 2) stroma accounts for more than 80% of the tumour stroma rich type, 3) stromal accounts for less than 30% cellular type. 4) Stroma accounts for less than 30% but is predominantly made up of a monomorphic epithelial cellular component of plasmacytoid or hyaline appearance. [10] These histological subtypes underlines the necessity of using advanced diagnostic methods, such as fine needle aspiration (FNA) or intraoperative frozen section, in difficult cases to avoid misdiagnosis or inappropriate treatment.

The histological diversity observed in this current study emphasizes the importance of histopathological classification to guide treatment. Misdiagnosis can occur due to histological similarities with other salivary gland tumors, such as adenoid cystic carcinoma or basal cell adenoma, potentially leading to inappropriate management, making it crucial for pathologists to be aware of the potential variations within PA. In rare instances the presence of osseous and adipose metaplasia can add further completely to diagnosis, reinforcing the need for a thorough histopathological examination.

This institutional study highlights the importance of understanding the clinicopathological diversity of pleomorphic adenomas, particularly in terms of their anatomical sites, demographic characteristic, and histological variations. The findings reinforce that PAs, though generally benign, require careful diagnostic evaluation and precise surgical management to prevent recurrence and ensure optimal patient outcomes. The results advocate for the use of comprehensive diagnostic techniques and emphases the value of individual treatment planning. Further studies with broader and more diverse patient populations are warranted to explore the molecular and genetic factors that may influence the behavior of pleomorphic adenomas, particularly in relation to their recurrence risk and histological heterogenity.

Recurrence

The findings of this study confirms that PAs typically exhibit benign course, with a very low recurrence rate of only 3%. This aligns with the well-established literature, which describe PA as slow-growing and generally non-invasive tumor. The low recurrence rate observed supports the efficacy of standard surgical excision as the preferred treatment modality. However, this study underscores the importance of careful surgical technique to avoid incomplete excision, as it has been reported in other studies that incomplete resection can lead to recurrence. While the study reported a low recurrence rate, it is critical to emphasize the need for long-term follow-up, given the potential for delayed recurrence, particularly in cases of incomplete excision or those with histologically complex variations.

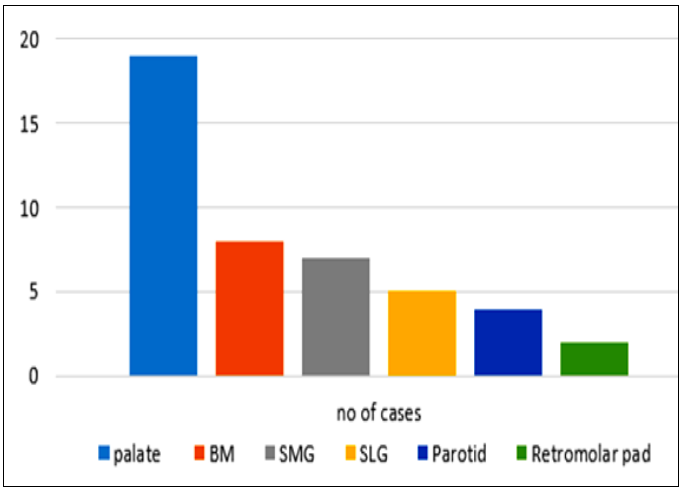
Histological analysis further reveals that the capsule surrounding pleomorphic adenoma is often incomplete. This delicate, thin or partially formed pseudo-capsule allows pseudopodia and satellite tumors to infiltrate the capsule, sometimes leading to herniation. The recurrence of parotid adenoma is believed to result from microscopic lobules or pseudopodia extending beyond the tumor sheath. Enucleation may dislodge tumor nodules, leaving remnants within the normal salivary gland [8].

A key concept in recurrence is the phenomenon of "tumor spill," which occurs when the structural integrity of the tumor is compromised during surgery. This can result in implanting tumor cell within the surgical site, potentially leading to the emergence of multiple new tumors, often around the surgical scar. Consequently, recurrent parotid adenomas may present as multiple nodular outgrowths reported in approximately 5% of cases.

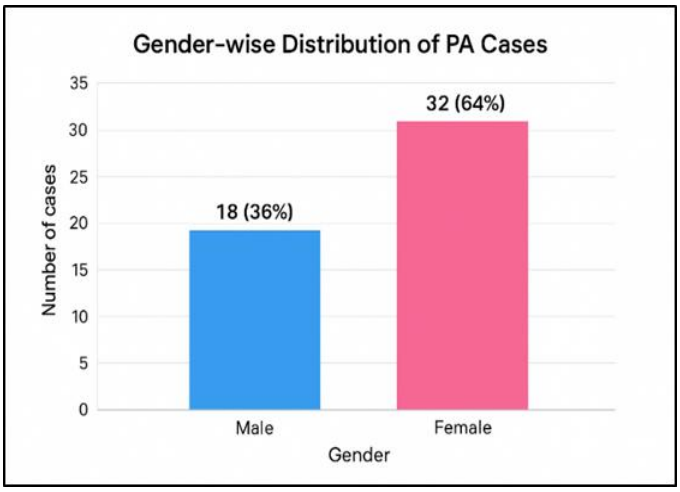
Rather than true recurrence, residual disease may be a more precise term, as the condition appears to persist rather than the tumor reappearing denovo. Attempted enucleation has been associated with an increased likelihood of recurrence. The median age of recurrent pleomorphic adenoma cases is around 33-35 years, approximately a decade earlier than the typical onset (45-50 years) in patients without recurrence [8].

Conclusion

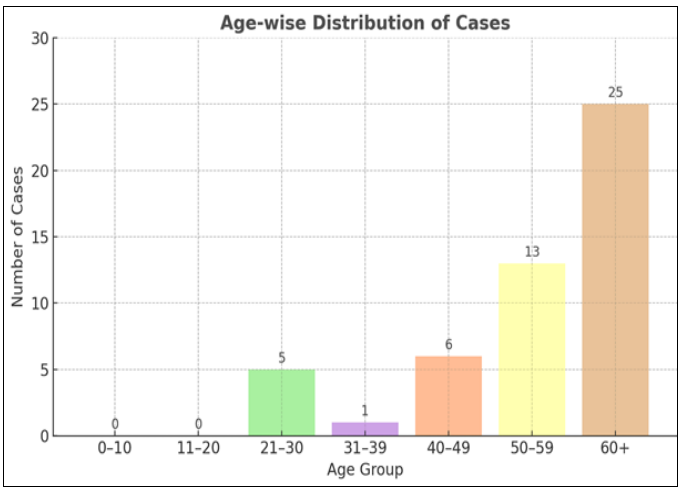
Pleomorphic adenoma remains the most common benign tumor of the salivary glands, with significant histopathological diversity and a potential for both recurrence and malignant transformation. This 7-year retrospective analysis reinforces the importance of early and accurate diagnosis, emphasizing the role of complete surgical excision in minimizing recurrence risks. While the study findings align with existing literature in terms of demographic trends, histological variations, and recurrence rates, continued research into molecular and genetic markers is necessary to enhance diagnostic precision and therapeutic strategies. Integrating both histopathological and molecular assessments will improve prognostic predictions, ultimately leading to more effective and individualized treatment approaches for patients with pleomorphic adenoma.



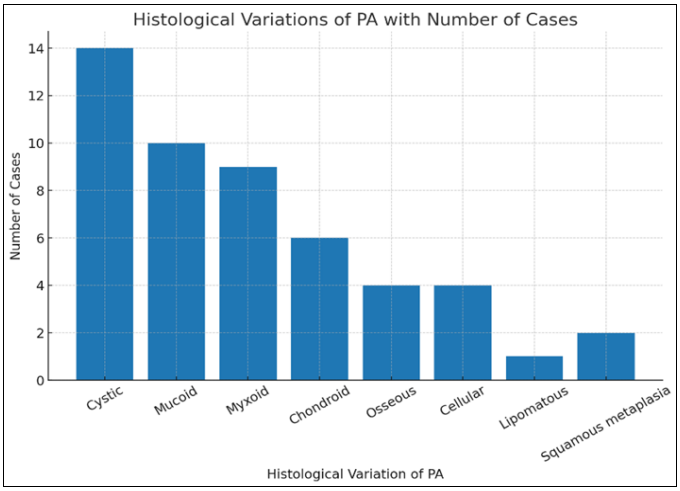
Graph 1: No of cases distribution based on anatomical site



Graph 2: Gender wise distribution of PA Cases

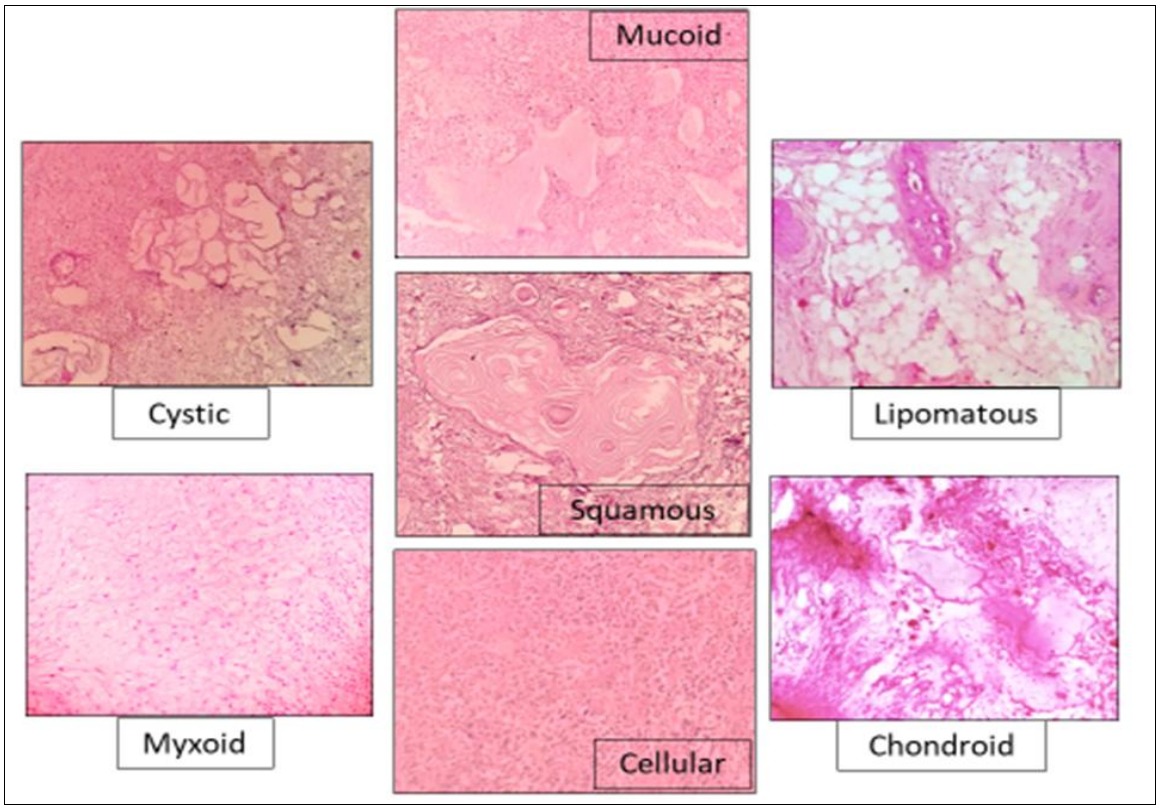


Graph 3: Age wise distribution of Cases



Graph 4: Histiological variants of PA with number of cases

Fig 1: Histological variants



Graph 5: Histological variations in Pleomorphic adenoma

Conflict of Interest
Not available

Financial Support
Not available

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