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Histopathological Characteristics of Pleomorphic Adenoma; A Retrospective Analysis of 120 Cases

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Abstract

Background The salivary gland pleomorphic adenoma (PA) is a benign epithelial neoplasm, histologically characterized by a great diversity of morphological aspects. It is the most common neoplasm of salivary gland origin.

Objective Studying the histopathological characteristics of PA with special attention to the various morphological features of the epithelial cells and stromal components of this neoplasm.

Methods Hematoxylin and Eosin (H&E) stained tissue sections of 120 cases of PA were reviewed. The tumors were classified according to their histological subtypes as described by Seifert *et al*. The epithelial components were analyzed considering the type of cells and the morphological pattern. The stromal components were analyzed according to the presence of myxoid, hyaline, chondroid or calcified tissue.

Results This study revealed that most of the tumors were located in the parotid gland (44%). Myxoid or stroma-rich was the most frequent histological subtype (43%). Plasmacytoid cells were the most commonly seen epithelial component (100%), followed by cuboidal cells in (80%) of the cases. Trabecular pattern was the predominant epithelial morphological pattern (90 %), and the myxoid component was the most frequent stromal component (80%).

Conclusion PA of the salivary glands demonstrates a wide variety of cells, stromal components, and morphological characteristics. Since it is the most frequent salivary gland neoplasm that can resemble other salivary gland tumors, the knowledge about these variations is essential for a correct diagnosis.

Keywords Histopathology, pleomorphic adenoma, salivary gland neoplasms

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List of abbreviations: H&E = Hematoxylin and eosin, PA = Pleomorphic adenoma

Introduction

Pleomorphic adenoma (PA) is a benign mixed tumor, and it is the most common salivary gland tumor. It occurs predominantly in females at a premenopausal age [(1)]. PA represents 60% to 73% of the parotid gland tumors, and 40% to 60% of the submandibular and minor salivary glands tumors [(2)].

These tumors consist of excretory ductoacinar units and associated myoepithelial cells, which are believed to originate from totipotential stem cells. This may explain the morphologic diversity in parotid gland neoplasms [(3)]. They are characterized by a biphasic growth of both epithelial cells and myoepithelial cells that are

arranged with various morphological patterns and subtypes[4].

Histologically, PA is characterized by a great diversity of morphological aspects. Its structural pleomorphism is given both by the epithelial component, as a result of the cytological differentiations and the growing patterns, and by the stromal component because of its rich morphological and quantitative diversity [5].

Epithelial cells typically form duct-like structures associated with nonductal cells presenting variable shapes and forms. The stromal element demonstrates varying degrees of myxoid, hyaline, cartilaginous, or osseous differentiation [2]. Among these morphological aspects, one aspect is usually predominant in variable proportion [6]. The pathognomonic stromal feature of pleomorphic adenoma is the presence of chondro-myxoid stroma.

PA usually presents as a slow progressing asymptomatic, parotid gland swelling without facial nerve involvement [7]. Up to 10% of cases show malignant transformation and features predictive of malignant change include advancing age, massive tumor size, a long duration of the mass, occurrence in the submandibular salivary gland, and hyalinized connective tissue [8].

The best treatment option is a wide local excision with good safety margins and follow-up for few years.It had been suggested that focal infiltrations of the tumor capsule of the pleomorphic adenoma could be left behind if the lesion was simply enucleated. Moreover, multicentricity of pleomorphic adenoma has been recorded in up to 11% of the examined tissue specimens [9]. Currently, it is generally accepted that these histopathological features of pleomorphic adenoma explain tumor recurrence after simple enucleation. Therefore, it is well recognized that the best surgical treatment option for a pleomorphic adenoma of the superficial parotid gland is a wide local excision with good safety margins and follow-up for few years. A better option is a lateral lobectomy [7]. Adopting these procedures, the recurrence rate has declined to a figure less than2.5% in recent years.Nevertheless, there is still a debate about the optimal treatment option of parotid pleomorphic adenoma. Some authors have propagated a local dissection or a subtotal superficial parotidectomy as an alternative to superficial parotidectomy[10].

In this study, we describe the histopathological characteristics of 120 cases of PA with special reference to the morphology of the epithelial cells and stromal components.

Methods

This retrospective study included 120 formalin-fixed, paraffin embedded biopsy specimens of PA obtained from the archives of the Department of Pathology AL KindiHospital and the Department of Oral Pathology, College of Dentistry, Baghdad University.

The ethical approval was obtained from the authority of these medical institute to facilitate this work and obtaining the materials from histopathological archives.

The clinicopathological information regarding age, gender, lesion sites, clinical presentation, in addition to any other pertinent information were obtained from the case sheets presented with the surgical specimen. Sections of 5µm thickness were cut from each tissue specimen. All H&E-stained tissue sections were reviewed by two Pathology specialists to confirm the diagnosis.

Data regarding age, site distribution and histological subtypes in regard to different salivary glands, various cellular types of the epithelial component in addition to the morphological pattern of epithelial and stromal components of PAs, were considered.

The tumors were classified as myxoid or stroma-rich, cellular or cell-rich and classic (balanced amount of epithelial and stromal components) as described by Sergi *et al*. [7]. The epithelial components were analyzed taking into consideration the types of cells (plasmacytoid, spindle, clear, squamous, basaloid, cubic, oncocytoid and mucous cells) and the morphological pattern (trabecular, ductal, cystic and solid). The stromal

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components were analyzed according to the presence of myxoid, hyaline, chondroid or calcified tissue.

The statistical data were analyzed using SPSS software (version 21). P value < 0.005 was considered.

Results

The study sample consisted of 120 pleomorphic adenomas of the salivary glands, of which 72 cases were females (60%), and 48cases were males (40%), with a M/F ratio of 1/1.2. The age range was 15-70 years, with a mean age of 38 years. The majority of the tumors were found within the (30-40) age group (Table1).

Table1. Incidence of PA in different age groups

Age groups(yrs)	No.	%
10-20	8	6.6
21-30	28	23.3
31-40	41	34.16
41-50	19	15.83
51-60	15	12.5
61-70	9	7.5

All patients were presented with a unilateral lesion, with slightly dominant left side occurrence (63 on the left, 57 on the right). The majority of the cases were located in the parotid gland 53 cases (44%), the second most common location was the minor salivary glands 38 cases (32%), distributed as follows; the palate (15cases), the oral mucosa (13cases) and the lower lip (10 cases).Followed by 28 cases in the submandibular gland (24%). No cases were recorded in the sublingual salivary gland (Table 2).

Table 2. Site distribution of 120 cases of PA

Location	No.	%
Parotid	53	44
Minor salivary glands	38	32
Submandibular salivary gland	28	24
Total	120	100

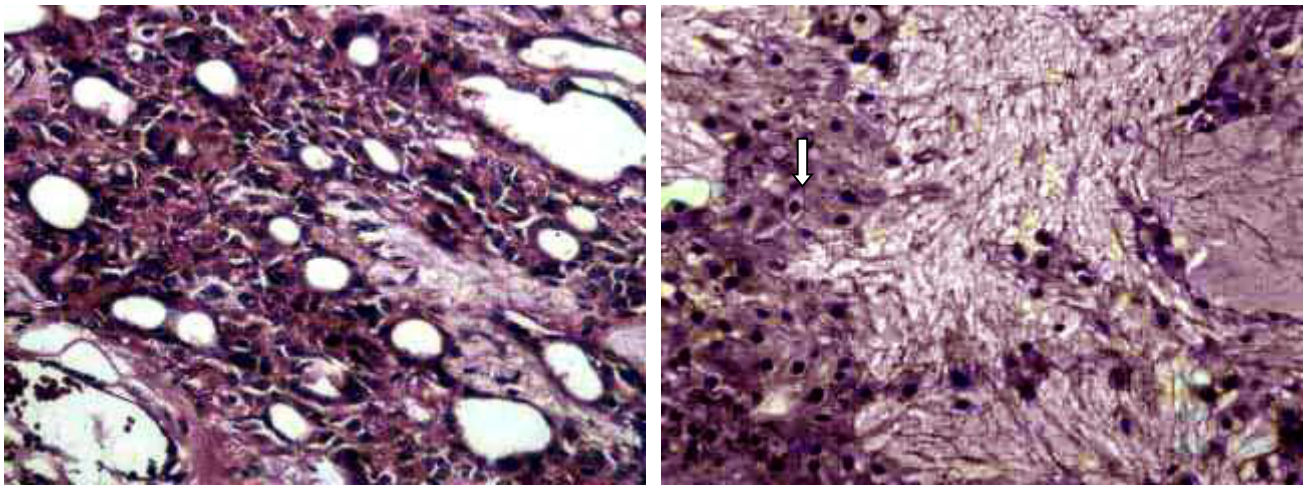
The study revealed that myxoid or stroma - rich is the most frequent histological subtype found in the examined specimens (43%), followed by the cellular or stroma-poor and classic subtypes, in (38%) and (19%) of the tumors respectively (Table 3).

Plasmacytoid cells were the most commonly presented epithelial component, as they were present in all of the examined cases (100%)(Figure 1). Spindle cells were the second most common cell type presented in 90 cases (75%), followed by cuboidal cells in (63%) of the cases.The other components presented in a descending manner as follows: basaloid cells (60%), squamous and clear cell types (32% & 29 %) respectively. On the other hand, oncocytoidand mucous cells were the least found epithelial components, they are

considered as occasional findings, (2% and 1%) respectively (Table-4).

Table 3. The histological classification of 120 cases of PA

Histological classification	No.	%
Stroma-rich	52	43.3
Stroma-poor	45	37.5
Classic	23	19.1
Total	120	100



A **B**

Figure1. A: PA with predominant plasmacytoid cell(arrow head) and ductal morphological pattern (H&E,4X), B: PA plasmacytoid epithelial cell(arrow) (H&E 10 X)

Table 4. Various epithelial cell types present in the studied sample of PAs

Histological cell types	No.	%
Plasmacytoid	120	100
Spindle cell	90	75
Cuboidal cell	76	63
Basaloid cell	72	60
Squamous cell	32	26.6
Clear cell	29	24.1
Oncocytic cell	2	1.6
mucous cells	1	0.8

Regarding the morphological patterns of the epithelial component, trabeculae formation was found in 90% of the cases, the next common morphological pattern was ductal formation it was found in 78% of the cases (Figure 2), followed by solid and cystic formation, found in 42% and 23% of the cases respectively.

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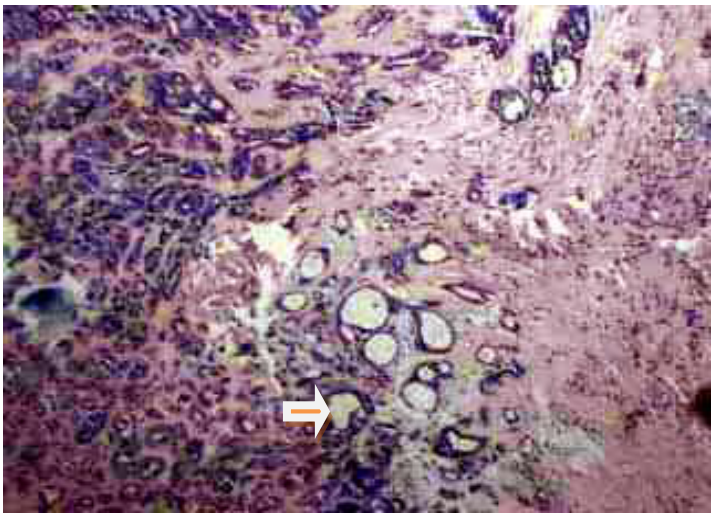

Figure2. PA shows trabeculae(arrow head) and ductal morphological patternarrow (H&EX4)

Concerning the stromal components, myxoid component was the commonly seen component (Figure 3), it was found in (80%) of the cases, followed by chondroid (Figure 4) and hyaline components (Figure 5), they were found in (54% and 48%) of the cases. On the other hand, calcified component was considered as an occasional finding; it was found in 7 cases only, as shown in (Table5).

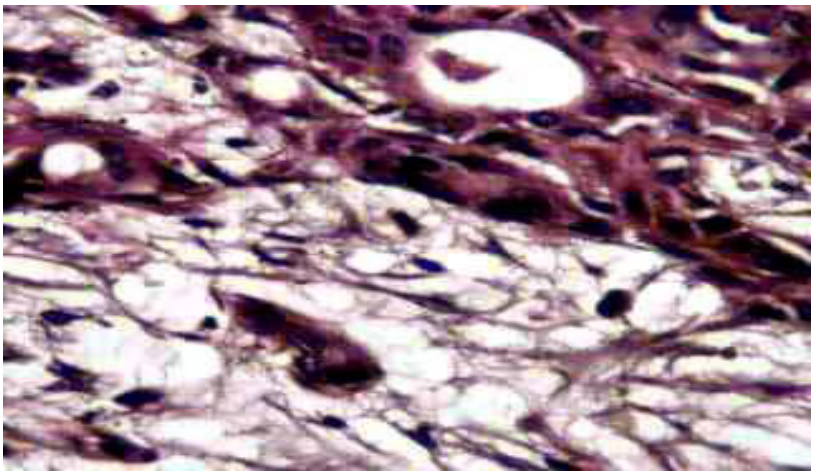

Figure3. PA showing myxoid background (H&E 20X)

Table 5. The morphological pattern of the epithelial and the stromal components of the study sample

Morphological pattern				Stromal components			
Trabeculae No. (%)	Ductal No. (%)	Solid No.(%)	Cystic No.(%)	Myxoid No.(%)	Chondroid No.(%)	Hyaline No.(%)	Calcified No.(%)
108(90)	91(76)	50(42)	28(23)	96(80)	65(54)	57(48)	7(6)

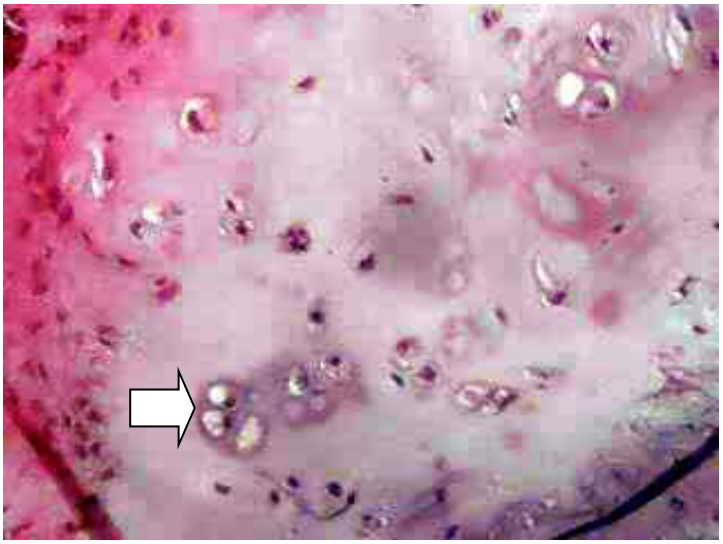

Figure4. PA showing chondroid background (H&E 10X)

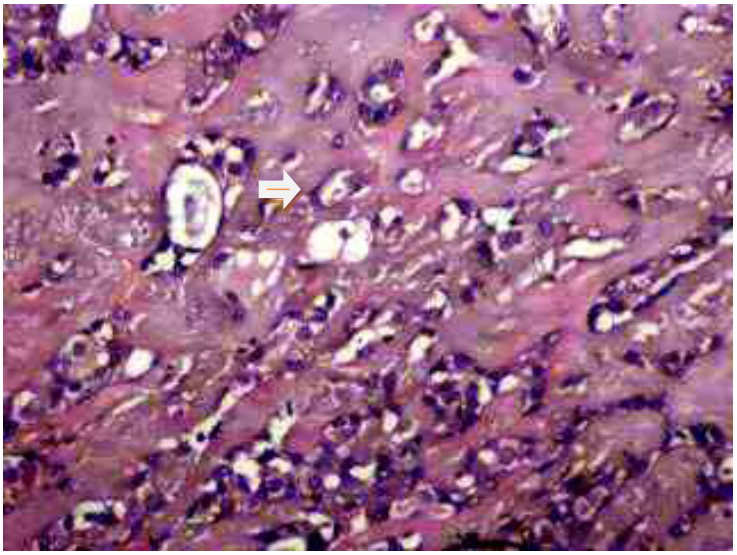

Figure5. PA shows hyaline background(H&E10X)

Discussion

PA is regarded as a slow-growing benign tumor that can affect all the salivary gland groups. Most commonly arising in the parotid gland, less frequently affecting the minor salivary glands and the submandibular glands, and occasionally affecting the sublingual group of salivary glands [11].

The present study showed that PA was more frequent in the parotid gland than the other salivary glands. Females were more frequently affected than males and the peak incidence was in the third-fifth decades of life, similar findings were reported in several previous related studies [12-15].

Inspite of the presence of a large variety of histological elements, the diagnosis of PA depends mainly on the presence of epithelial and mesenchymal like tissue as a major diagnostic feature. The relative proportion of these two elements has been used to subclassify PA into stoma – rich, cellular rich and classic types, however, this classification

doesn't imply any therapeutic or diagnostic importance [16].

In this study, stroma-rich subtype corresponded to (43%) of the cases, cell-rich (38%) and classic type (19%), interestingly, these results are close to those reported by Stennert *et al.* [17] and Paris *et al*. [18].

The current study revealed plasmacytoid cells predominance followed by cuboidal cells and spindle cells predominance respectively. Similar findings were reported by Ito *et al*, 2009 [19]. They explained the predominance of these cells over the other types that these cells appear to be in transition from one form to the other. Moreover, oncocytic and mucoid cells were the least presented cell types and were considered occasional findings, this again comes in accordance to the findings of Ito *et al,* 2009 and Takeda *et al*. [19,20].

Concerning the stromal components, in the present work myxoid component was the commonly seen area, it was found in (80%) of the cases, followed by chondroid & hyaline components respectively. On the other hand, calcified components were considered as occasional findings, as they were found in only 7 cases. These findings agree with those recorded by Ito *et al.*[19] who explained the presence of hyalinization to be related to an aggressive behavior or malignant transformation of PA. In summary, the present study demonstrated a wide variety of cells, stromal components and, morphological characteristics present in PA of the salivary glands. Since PA is the most frequent salivary gland neoplasm and can resemble other salivary gland tumors, the knowledge about these variation is essential for a correct diagnosis. However, these histological and morphological variations have no therapeutic or prognostic value.

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Authors Contribution

Dr.Sarkis and Dr.Al-Drobie: Selection, sectioning and processing of the studytissue specimen, pathological microscopic examination of the tissue section. Dr.Majeed: Data collection regarding clinico-pathological information, article editing regarding writing,organization and clinical information. Dr.Al-Marzooq: Data collection, clinical information, references, statistical analysis.

Conflict of interest

The authors have no conflict of interest to declare.

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