

Original Research

## Different Histopathologic Features of Pleomorphic Adenoma in Salivary Glands

Mahmood Jahangir Nezhad, Saedeh Atarbashi Moghadam, Sepideh Mokhtari, ShirinTaravati

### Abstract

**Back ground:** Pleomorphic adenoma is the most common salivary gland tumor. It is composed of varying proportions of epithelial and myoepithelial cells that are arranged in a great variety of morphological patterns. Therefore, it has a diverse histological presentation that may cause diagnostic problems with other salivary gland tumors. **Purpose of Study:** The objective of this study was to assess the different histopathological features of pleomorphic adenoma in salivary glands. **Materials and Methods:** Fifty specimens of pleomorphic adenoma were analyzed. All the cases were primary neoplasms and excisional biopsies. The tumors were classified as stroma-rich, cell-rich and classic (balanced amount of epithelial and stromal component). The mesenchymal component was divided into myxoid, chondroid, hyaline, fatty and calcified tissue. The parenchymal component was analyzed according to presence of spindle, plasmacytoid, basaloid, squamous, cubic, mucous and oncocytoid cells. The architectural pattern was divided into ductal, solid and trabecular. Presence of capsule was also analyzed. **Results:** The most common pattern was cell-rich (38%). Myxoid (78%) and Hyalinized (56%) stroma were the most frequent mesenchymal tissues. Spindle shaped (92%) and plasmacytoid (86%) cells were also the most common cell types. Ductal (72%) and solid (66%) structures were the most frequent patterns. All specimens had capsule. There was no evidence of cellular atypia or necrosis in all cases. **Conclusion:** The knowledge about various microscopic patterns of pleomorphic adenoma is essential and helps to have a proper diagnosis and better treatment.

**Key words:** Complex and Mixed Neoplasms; Histopathology; Mixed Tumor; Myoepithelial Tumor; Pleomorphic adenoma; Salivary Gland Tumors;

*Mahmood Jahangir Nezhad, Saedeh Atarbashi Moghadam, Sepideh Mokhtari, ShirinTaravati. Different Histopathologic Features of Pleomorphic Adenoma in Salivary Glands. International Journal of Oral & Maxillofacial Pathology; 2013;4(2):07-11. ©International Journal of Oral and Maxillofacial Pathology. Published by Publishing Division, Celesta Software Private Limited. All Rights Reserved.*

Received on: 12/02/2013 Accepted on: 24/07/2013

### Introduction

Pleomorphic adenoma (PA) is a benign neoplasm with remarkable degree of morphological diversity. It is the most common tumor of salivary glands and mainly affects the parotid.<sup>1</sup> Clinically PA presents as a slow growing firm mass, which is usually encapsulated. It is more frequent in adults aged 30 to 50 years, with a slight predominance among females.<sup>2</sup> These tumors are composed of epithelial and myoepithelial cells. Epithelial cells typically form ductal structures. The stroma demonstrates varying degrees of myxomatous, hyaline, cartilaginous and osseous differentiation.<sup>3</sup> Recurrence rate is 20 - 45% after the simple procedure of tumor enucleation.<sup>4</sup> The purpose of this study was to evaluate the various microscopic features of PA and determine the diversity of histopathological features in this tumor.

### Materials and methods

Fifty specimens of PA were collected from the archives of pathology department of Ahvas University of Medical Sciences. All

the cases were excisional biopsies and primary tumors. Clinical data were recorded. Histopathological features were assessed by using hematoxylin and eosin (H & E) stained sections.

An average of four slides was analyzed for per patient. The tumors were classified as stroma-rich (myxoid), cell-rich (cellular) and classic (balanced amount of epithelial and stromal components) as described by Seifert et al.<sup>3</sup> The stromal changes were analyzed according to the presence of myxoid, hyaline, chondroid, fatty and osseous tissue. The parenchymal component was analyzed according to presence of spindle, plasmacytoid, basaloid, squamous, cubic, mucous and oncocytoid cells. The architectural pattern was divided into ductal, solid and trabecular. Presence of capsule was analyzed. The sections were observed with Olympus CX21 light microscope. SPSS (Statistical Package for Social Science) software (Version 16) was used to analyze the data.

## Results

The majority of cases were located in the parotid (68%). The male to female ratio was 1:1 (25 persons in each group). The mean age was 39 years ranging from 19 to 75 years and the peak of incidence was in the fourth and sixth decades. Tumors were classified as cell-rich, classic and stroma-rich (Table 1).

Spindle cells were the most common cell type, being present in 92% of studied neoplasms. Plasmacytoid and Cubic cells were present in more than 80% of cases representing the next most frequent cell types. Squamous and basaloid cells were found in few cases. There was no evidence of mucous or oncocytic metaplasia in the specimens (Table 2).

In one case, keratin pearl formation was evident (Fig 1). Concerning the morphological patterns of parenchymal component, duct formation (72%) was the most frequent pattern (Table 3). Myxoid change (78%) was the most common stromal change (Fig 2). In addition, Hyalinized stroma was most frequent in cell-rich PAs (Fig 3). Chondroid change and fatty stroma (Fig 4 & 5) were less common (Table 4). All specimens had capsule. There was no evidence of calcified material, atypical cells or necrosis in all cases.

Histopathological pattern	Number	Percent
Stroma-rich	15	30
Cellular	19	38
Classic	16	32
Total	50	100

**Table 1:** Histological classification of pleomorphic adenoma in 50 cases

Cell type	Plasmacytoid	Spindle	Cubic	Basaloid	Squamous
Number	43	46	40	2	7
	(86%)	(92%)	(80%)	(4%)	(14%)

**Table 2:** Cellular types present in the parenchymal component of pleomorphic adenoma

Morphological pattern of epithelial component	Duct	Solid	Trabecular
Tumors number	36	33	28
	(72%)	(66%)	(56%)

**Table 3:** Morphology of epithelial components of pleomorphic adenoma

Type of stroma	Myxoid	Hyalinized	Chondroid	Fatty
Total	39	28	12	2
	(78%)	(56%)	(24%)	(4%)

**Table 4:** Stroma subtypes in pleomorphic adenoma

## Discussion

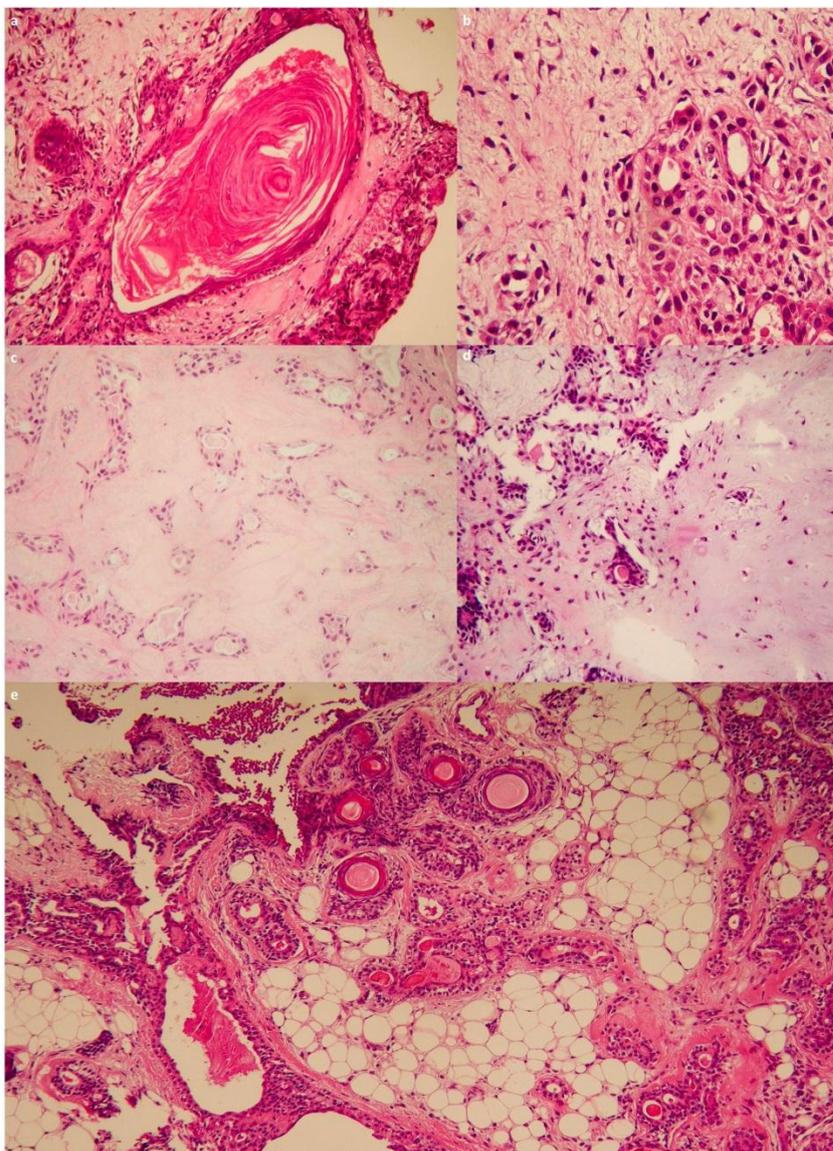
Pleomorphic adenomas are the most common neoplasms of salivary glands. These benign tumors are composed of epithelial and myoepithelial cells with various morphological patterns and subtypes.<sup>4,5</sup> The capsule varies in presence and thickness, and many tumors show finger-like processes projecting into the capsule. Naeim et al has divided the PAs, according to their cellularity, into 3 groups as hypocellular, moderately cellular and hypercellular (similar to Seifert definition).<sup>6</sup> Here, cell-rich subtype was the most common pattern followed by classic and stroma-rich architecture; however, the results were close to each other. Stroma-rich pattern has been the most common subtype in few other studies.<sup>3,4</sup> Bullerdiek et al states that the majority of classic tumors have 8q12 rearrangement whereas myxoid PAs demonstrate normal karyotype. 12q13-15 rearrangement is also more common in cellular PAs.<sup>7</sup>

Harney et al research revealed that PAs of the superficial lobe of parotid had more stromal component than tumors of the deep lobe. They also found no significant difference in predominant cell types between tumors of superficial and deep lobes.<sup>8,9</sup> In our study, spindle and plasmacytoid cells were the most frequent cell types that was in accordance with other studies.<sup>3,4</sup> Ellis et al suggests that these cells appear to be in transition from one form to the other form.<sup>3</sup> Interestingly, recent studies show that plasmacytoid cells in PA originate from luminal cells rather than myoepithelial cells.<sup>10</sup> Here, similar to other studies, cubic cells were the third most common cell type. Squamous cells were in the fourth grade. Extensive squamous metaplasia and keratin pearl formation could be mistaken for malignant tumors such as mucoepidermoid carcinoma and squamous cell carcinoma. In addition, pleomorphic adenoma and polymorphous low-grade adenocarcinoma are frequently mistaken with each other.<sup>11</sup>

In our specimens, no mucous and oncocytic cells were found. Triantafyllou et al suggest that mucous cells in PA reflect an abnormal line of differentiation.<sup>12</sup> This abnormality is an increased synthesis of luminal cells or

retention of glycoproteins.<sup>10</sup> Development of oncocytes is most associated with acini and striated duct cells.<sup>13</sup> Oncocytoid variant of PA has also been reported in the literature.<sup>14</sup>

In this study, ductal and solid structures were the most frequent patterns followed by trabecular architecture. However, in Ito et al study the trabecular and ductal patterns were the most common features.<sup>3</sup>



**Figure 1:** The photomicrograph of pleomorphic adenoma shows various histopathological patterns like keratin pearl formation (a, x200), ductal structures with in the myxoid stroma (b, x400), hyalinization (c,x200), chondroid areas (d,x200) and fatty changes in the stroma(e,x40).

The present investigation demonstrates the predominance of myxoid and hyalinized stroma which is similar to Ito et al results.<sup>3</sup> Some studies show that prominent zones of hyalinization are related to the aggressive behavior or malignant transformation of the tumor in future. This feature has also been found in long standing neoplasms.<sup>15</sup> We found no evidence of atypical cells or necrotic areas in our specimens. Atypical cells could be found in benign pleomorphic adenomas.<sup>3,16</sup> Ohtake et al observed cellular atypia in fifty one percent of their analyzed

cases.<sup>17</sup> Ethunandan et al also reported atypical histological features in some cases of benign pleomorphic adenoma.<sup>18</sup> Atypical cells are frequently associated with previous manipulation of tumor by biopsy or fine needle aspiration.<sup>16</sup>

Here, sebaceous cells were found in 4% of cases. Cutaneous adnexal differentiation could be present in PA and may present diagnostic pitfalls. This variation must not be misinterpreted as carcinoma.<sup>19</sup>

Many histological and immunohistochemical studies have been done to predict the recurrence rate of PA.<sup>4,20-23</sup> Some histopathological features are related to the recurrence of tumor after conservative surgery.<sup>4</sup> Soares et al confirm that MUC-1 is related to the recurrence of PA. They also mention that this protein is associated with malignant transformation of tumor.<sup>23</sup> In Stenert et al investigation, myxoid subtype was predominant in recurrent tumors.<sup>4</sup> However, this relation was not found in other studies.<sup>20</sup> Kazanceva et al suggest that recurrent PAs are frequently hypocellular. They also state that the amount of chondro-myxoid stroma increases with the duration of neoplasm.<sup>24</sup>

The relation between histopathological features in PA and the presence of capsule has also been investigated. Most recurrences of PAs are multi-nodular.<sup>21</sup> Stenert et al state that many stroma-rich tumors and some of other type PAs show a focal absence of the capsule. They conclude that conservative surgery, especially in tumors of stroma-rich type, is a major risk factor of recurrence.<sup>4</sup>

### Conclusion

The numerous phenotypic features of pleomorphic adenoma may challenge the pathologists. As many PAs may resemble some malignant salivary gland tumors which can lead to misdiagnosis and unnecessarily lead to aggressive therapy. Therefore, histopathological variations in PA should be well-known and this is essential for correct diagnosis and better treatment.

### Acknowledgement

We would like to acknowledge all the staff members for their support and guidance.

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Source of Support: Nil, Conflict of Interest: None Declared.