Clinicopathological study of 74 palatal pleomorphic adenomas

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Background/purpose: Pleomorphic adenoma (PA) is the most common salivary gland tumor and the palate is the most common intraoral site for PA. This study aimed to present the clinicopathological features of a series of 74 palatal PAs.

Methods: Seventy-four palatal PAs were collected from 1993 to 2009. The clinical and histopathological features of these 74 PAs were reviewed and analyzed.

Results: The 74 palatal PA patients showed a marked female predilection (49:25, ~2:1) and were nearly evenly distributed from the 3rd to 8th decades of life with a mean age of 47 years. All palatal PAs were treated by wide surgical excision and recurrence was noted in one PA. Histopathologically, there were 47 classic and 27 cellular PAs. Of the 74 PAs, 12 were completely encapsulated, 40 partially encapsulated, and 22 nonencapsulated. The duct-like structures and myxoid stroma were more or less found in every palatal PA. Plasmacytoid myoepithelial cell, clear cell, squamous epithelial nest, keratin pearl, hyalinized stroma, osteoid area, and chondroid area were found in 50, 19, 29, 19, 49, eight, and six PAs, respectively.

Conclusion: We conclude that the palatal PA patients show a prominent female predilection (2:1) and are nearly evenly distributed from 20 years to 79 years of age. Plasmacytoid myoepithelial cell is the most characteristic type of tumor cell in PAs. Wide surgical excision is treatment of choice for PAs. Although ~84% of palatal PAs are partially or nonencapsulated, recurrence of the lesion is rarely encountered after total surgical removal of the tumors.

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Introduction

In humans, there are three pairs of major salivary glands including parotid, submandibular, and sublingual glands and 600–1000 minor salivary glands located mainly in the submucosa of oral mucosae except the gingiva and anterior hard palate. The minor salivary glands include labial, buccal, glossopalatine, palatine, anterior lingual (glands of Blandin and Nuhn), posterior lingual mucous, and posterior lingual serous (von Ebner’s glands) glands. The pleomorphic adenoma (PA) is the most common benign tumor in both major and minor salivary glands. The palate is the most common intraoral site for PA. Therefore, it desired to study the clinicopathological features of the palatal PAs.

In this study, 74 palatal PAs were retrieved from the files of Department of Pathology, National Taiwan University Hospital (NTUH), Taipei, Taiwan from 1993 to 2009. The clinical and histopathological features of these 74 PAs were reviewed, analyzed, and compared with those reported in previous studies.

Methods

The study group included 74 palatal PAs retrieved from the files of Department of Pathology, NTUH from January 1993 to December 2009. All lesions > 1 cm in greatest diameter and suspected of being palatal PAs received an incisional biopsy. The whole lesion was then excised after the histopathological diagnosis was confirmed. If the tumors were < 1 cm in greatest diameter, they were surgically excised without doing the incisional biopsy in the beginning. The histopathological diagnosis of the lesion was mainly based on an examination of hematoxylin and eosin-stained tissue sections. Immunohistochemical staining was performed to identify the specific cells if needed.

The patients’ data on age, sex, tumor size, treatment, and recurrence were obtained by reviewing the dental and medical charts. The excised specimens were fixed in 10% neutral formalin for at least 24 hours, dehydrated in graded alcohol, and then embedded in paraffin. If bony fragments were included, decalcification was also performed. The paraffin-embedded tissue blocks were cut in series sections of 5 μm, which were then stained with hematoxylin and eosin and examined by light microscopy.

The PA could be classified into myxoid, classic, and cellular types depending on the amount of stroma and the proportion of cellular components. The myxoid PA had myxoid stroma > 80% of the tumor, the classic PA was composed of some duct-like structures and myoepithelial cells within a myxomatous and hyalinized stroma, and the cellular PA was predominantly cellular with little amount of stromal tissue. We also assessed the encapsulation of the PAs to see whether they were completely encapsulated, partially encapsulated, or nonencapsulated. In addition, the presence of duct-like structure, plasmacytoid myoepithelial cell, clear cell, squamous epithelial nest, keratin pearl, myxoid stroma, hyalinized stroma, osteoid area, and chondroid area in PAs was searched and recorded.

Results

During the period from January 1993 to December 2009, 133 palatal minor salivary gland tumors were diagnosed in the Department of Pathology, NTUH. Of the 133 cases, 78
Figure 2  Histopathological microphotographs of pleomorphic adenoma (PA). (A) A classic PA composed of duct-like structures in a myxomatous stroma. (B) A cellular PA made up of aggregates of plasmacytoid myoepithelial cells and a few duct-like structures lined by inner ductal cells and outer clear myoepithelial cells in a little hyalinized stroma. (C) A classic PA encapsulated by a thin layer of dense fibrous capsule. (D) A PA showing a sheet of characteristic plasmacytoid myoepithelial cells. (E) A PA exhibiting a few duct-like structures and many clear myoepithelial cells. (F) A PA with nests of squamous epithelia showing prominent intercellular bridges. (G) Several keratin pearls in a classic PA. (H) Nests of myoepithelial cells in a dense hyalinized stroma. (I) A PA showing osteoid structures with osteocyte-like cells in the lacunae. (J) A PA showing chondroid area with none or vacuolated chondrocytes in the lacunae. Hematoxylin and eosin stain; original magnification: A, B, D, E, H, I, and J, 20×; C, 4×; F and G, 10×.
(58.6%) were benign and 55 (41.4%) were malignant tumors. Only two types of benign salivary gland tumors, PA (74 cases, 55.6%) and myoepithelioma (4 cases, 3.0%), were found. Because PA was the most commonly occurring minor salivary gland tumor in the palate, this study concentrated on the presentation of clinicopathological features of 74 palatal PAs.

Palatal PA patients showed a marked female predominance with a female-to-male ratio of 49:25 (≈ 2:1). The palatal PA patients were distributed in a wide age range from the 3rd to 8th decades with a peak incidence being in the 5th decade of life (22%). The mean age of palatal PA patients was 47 (range, 11–83) years (Table 1). All the 74 PAs were located in the posterior lateral aspect of the palate and presented as smooth-surfaced and dome-shaped swellings or masses clinically (Figure 1). Trauma-induced focal surface ulceration was noted in two PAs. The mean greatest diameter of 74 palatal PAs was 1.9 ± 0.9 cm (range, 1–4 cm). Thirteen PAs (17.6%) ≤ 1 cm in greatest diameter were treated by excisional biopsy without initial incisional biopsy. The remaining 61 PAs (82.4%) were treated by wide surgical excision after incisional biopsy. Useful follow-up information was obtained for 38 PA patients (51.4%), local recurrence of the lesion was found in one PA after a follow-up period ranging from 5.8 years to 21.3 years.

Histopathologically, there were 47 classic (Figure 2A) and 27 cellular PAs (Figure 2B). There was no myxoid-type PA in this study. Of the 74 palatal PAs, 12 were completely encapsulated (Figure 2C), 40 partially encapsulated, and 22 nonencapsulated. Duct-like structures and myxoid stroma were more or less found in every PA. Plasmacytoid myoepithelial cell (Figure 2D), clear cell (Figure 2E), squamous epithelial nest (Figure 2F), keratin pearl (Figure 2G), hyalinized stroma (Figure 2H), osteoid area (Figure 2I), and chondroid area (Figure 2J) were found in 50, 19, 29, 19, 49, eight, and six PAs, respectively.

**Discussion**

It is of no doubt that PA is the most common benign minor salivary gland tumor in the palate. Among all palatal minor salivary gland tumors, the frequency of the benign neoplasm ranges from 53% to 58%. Most of them are PAs, accounting for 39.8–51.9% of all palatal minor salivary gland tumors.2–6 PAs constitute 40–70% of all minor salivary gland tumors.2–6,11,12 In our previous study, PAs accounted for 55.6% of 133 benign and malignant minor salivary gland tumors of the palate.10 For the intraoral regions, the palate is the most common site for minor gland tumors (42–54% of all cases), followed by the lips (21–25% of all cases) and the buccal mucosa (11–15% of all cases).3–6

PAs of all salivary glands show a female predominance with a female-to-male ratio of 1.9:1.4 Friedrich et al.13 examined 94 PAs of all salivary glands and found that the parotid PAs occur more often in women (n = 45) than in men (n = 28) with a female-to-male ratio of 1.6:1. Stennert et al.4 also demonstrated a slight female preponderance with a female-to-male ratio of 1.3:1 for 100 parotid PAs. Our palatal PA patients showed a marked female predilection with a female-to-male ratio of 2:1. Becelli et al.14 also found a significant female predilection for 11 patients with palatal PAs. Jorge et al.15 also demonstrated that four out of five patients with juvenile intraoral PAs were female. However, Kuo et al.16 examined 37 patients with PAs of extra-major salivary glands and discovered that 22 were male and 15 female, with a male-to-female ratio of 1.5:1. In addition, Chau and Radden17 also showed a slight male predilection (1:0.8) for 53 intraoral PAs.

Regarding the histological types of PAs, the myxoid, classic, and cellular PAs were found in 0, 33, and four of 37 PAs of extra-major salivary glands;10 in two, five, and 19 PAs of minor salivary glands; in 51, 14, and 35 of 100 PAs of the parotid glands; and in zero, 47, and 27 of 74 palatal PAs in the present study, respectively. These findings suggest that there are more myxoid PAs in parotid glands than in minor salivary glands.

Stennert et al.8 studied 100 parotid PAs and discovered that 97 had focally very thin capsule, 46 had focal absence of encapsulation, and 28 had pseudopodia projecting into the surrounding tissue or satellite nodules outside the capsule. Margaritescu et al.17 studied 103 PAs of both major and minor salivary glands and found that 53 of 77 PAs of parotid gland and 10 of 16 PAs of submandibular gland were completely encapsulated. Moreover, 24 parotid PAs, six submandibular PAs, and two sublingual PAs were partially encapsulated. In addition, all the eight intraoral PAs were nonencapsulated.17 Chau and Radden16 examined 53 intraoral PAs and demonstrated that 12 (23%) were encapsulated, 31 (59%) partially encapsulated, five (9%) nonencapsulated, and five (9%) indeterminate. Of our 74 palatal PAs, 12 (16%) were completely encapsulated, 40 (54%) partially encapsulated, and 22 (30%) nonencapsulated. The results of the aforementioned studies indicate that the majority (68–100%) of PAs of intraoral minor salivary glands are either partially encapsulated or nonencapsulated. Furthermore, although a relatively high proportion of PAs of major salivary glands are encapsulated, focally very thin capsule, focal absence of encapsulation, and pseudopodia projecting into the surrounding tissue or satellite nodules outside the capsule are not uncommonly found in PAs of major salivary glands.

Histologically, PA contains both epithelial and mesenchymal (or stromal) components. The epithelial component may appear as ducts, tubules, strands, trabeculae, and solid sheets. The ducts of a PA are lined by inner duct-lining cells and outer myoepithelial cells. The presence of ducts or duct-like structures in a PA is the reason why PAs are called adenomas. Myoepithelial cells in a PA may appear as plasmacytoid, spindled, or clear cells. Squamous metaplasia, sometimes with the formation of keratin pearls, can be seen in both ducts and sheets of epithelial cells.18 The mesenchymal component may appear as myxoid and/or hyalinized connective tissue and occasionally as cartilage and/or bone. All these mesenchymal tissues are believed to be the result of metaplasia or actually products of the tumor myoepithelial cells.18 In this study, plasmacytoid cell, clear cell, squamous epithelial nest, keratin pearl, myxoid stroma, hyalinized stroma, osteoid area, and
chondroid area were found in 50, 19, 29, 19, 74, 49, eight, and six of 74 palatal PAs, respectively. Satpathy et al\(^8\) showed plasmacytoid cell, squamous epithelial nest, myxoid stroma, hyalinated stroma, osteoid area, and chondroid area in 17, four, 19, one, two, and two of 26 PAs of minor salivary glands (including 24 palatal PAs). Moreover, Mârgăritescu et al\(^7\) demonstrated myxoid, fibro-hyaline, chondroid, and osteoid stroma in 103, 20, 45, and one, respectively, of 103 PAs of both major and minor salivary glands. The plasmacytoid cells are highly characteristic of a PA and almost never found in other salivary gland tumors.

Immunohistochemical staining is a useful technique to identify a specific cell type in tissues or tumors.\(^{19-31}\) For example, anti-CD1a and anti-S-100 protein immunostains can be used to recognize Langerhans cells in the lining epithelia of cyst or in tumors.\(^{19-26}\) When PA histological sections are immunostained, the inner ductal cells in the tubular or glandular structures are positive for cytokeratins 3, 6, 10, 11, 13, and 16, but the neoplastic myoepithelial cells are irregularly positive for cytokeratins 13, 14, and 16.\(^{18}\) The neoplastic myoepithelial cells coexpress pan-cytokeratin and vimentin and are variably positive for S-100 protein, calponin, CD10, glial fibrillary acidic protein, \(\alpha\)-smooth muscle actin, and muscle-specific actin.\(^{18}\) Because neoplastic myoepithelial cells may have morphological diversity, sometimes they may need multiple immunostains to identify their cell origin.

In conclusion, the palatal PA patients show a prominent female predilection (2:1) and are nearly evenly distributed from 20 years to 79 years of age. Plasmacytoid myoepithelial cell is the most characteristic type of tumor cell in PAs. Wide surgical excision is the treatment of choice for PAs. Although ~84% of palatal PAs are partially- or nonencapsulated, recurrence of the lesion is rarely encountered after total surgical removal of the tumors.

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