นิพนธ์ต้นฉบับ

# Malignant tumors of major salivary glands during the past ten years at King Chulalongkorn Memorial Hospital

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**Objective** : *To determine the occurrence rates of malignant tumors of major salivary glands according to location, histological cell types, sex, and age.*

**Study design** : *Retrospective descriptive study*

**Settings** : *Department of Pathology, Faculty of Medicine, Chulalongkorn University.*

**Method** : *The data was collected from pathology record files from the department of pathology of King Chulalongkorn Memorial Hospital over a ten year period from January 1989 to December 1998. All available histologic materials were reviewed. The histological classification of salivary gland tumors was based on the World Health Organization's criteria, second edition.*

**Results** : *Of the total of 86 cases, in 66 cases (76.7 %) the neoplasms were located in the parotid glands, in 19 cases (22.1 %) in the submandibular and in 1 case (1.2%) in the sublingual glands. Mucoepidermoid carcinoma was the largest group with 20 cases (23.3 %) followed by adenoid cystic carcinoma (14 cases,16.3 %). Most tumors showed a female preponderance except for squamous cell and metastatic carcinomas which were more common in males and with male: female ratios of 5:0 and 5:2 respectively. The number of cases*

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*in the sixth decade of life was greatest (21 cases), followed by the seventh decade (16 cases).*

**Conclusions** : *Among the major salivary glands, the parotid glands are the most common site for malignant tumors while the sublingual glands are the least common location. Mucoepidermoid carcinoma is the most frequent histological cell type among the different kinds of neoplasms. The tumors tend to be more common in females except for squamous cell carcinoma and metastatic carcinoma. The diseases occur more often in the elderly (sixth to seventh decades).*

**Key words** : *Malignant tumors, Major salivary glands.*

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**ธนภัทร ไพสุนทรสุข, สมบรูณ์ คีลาวัฒน์, จุลินทร สำราญ, จุไรอร อุณหสูต, ศยามล ฆารไสว. มะเร็งต่อมน้ำลายหลักในช่วงสิบปีที่ผ่านมาในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2542 ส.ค; 43(8): 523-32**

**จุดประสงค์** : *เพื่อหาอัตราการเกิดของมะเร็งในต่อมน้ำลายหลักเกี่ยวกับเรื่องตำแหน่งที่เกิด, ชนิดของเซลล์มะเร็ง, เพศ, และ อายุ*

**รูปแบบการศึกษา** : *การศึกษาเชิงพรรณนาชนิดย้อนกลับ*

**สถานที่ศึกษา** : *ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

**วิธีการ** : *ทำการรวบรวมข้อมูลจากแฟ้มบันทึกทางพยาธิวิทยาจากภาควิชาพยาธิวิทยา โรงพยาบาลจุฬาลงกรณ์ในช่วงเวลา 10 ปี นับตั้งแต่ มกราคม 2532 ถึงธันวาคม 2541 โดยนำสไลด์เท่าที่จัดหาได้มาศึกษาอีกครั้งด้วยกล้องจุลทรรศน์ และ จัดแบ่งชนิดของมะเร็งตามหลักเกณฑ์ขององค์การอนามัยโลกซึ่งตีพิมพ์ครั้งที่สอง*

**ผลการศึกษา** : *จำนวนเนื้องอกชนิดร้ายแรงของต่อมน้ำลายหลักทั้งหมดมี 86 ราย โดยพบในต่อมน้ำลาย parotid มากที่สุดเป็นจำนวนถึง 66 ราย (76.7%) รองลงมาพบที่ submandibular gland จำนวน 19 ราย (22.1%) ส่วน sublingual gland พบเพียง 1 ราย (1.2%) Mucoepidermoid คือชนิดที่พบมากสุดจำนวน 20 ราย (23.3%) และ Adenoid cystic พบรองลงมาเป็นจำนวน 14 ราย (16.3%) โดยส่วนมากเนื้องอกชนิดร้ายแรงพบบ่อยในเพศหญิง ยกเว้นชนิด Squamous cell carcinoma และ Metastatic tumor จะพบในเพศชายมากกว่าในสัดส่วนเพศชายต่อเพศหญิง 5:0 และ 5:2 ตามลำดับ ช่วงอายุที่พบเนื้องอกได้มากที่สุดคือ 51 ถึง 60 ปี จำนวน 21 ราย รองลงไปคือช่วงอายุ61-70 ปี จำนวน 16 ราย*

**สรุป** : *ระหว่างต่อมน้ำลายหลักด้วยกัน parotid gland เป็นต่อมที่มีอัตราการเกิดของมะเร็งมากที่สุด และ sublingual gland พบได้น้อยที่สุด Mucoepidermoid carcinoma เป็นชนิดของเซลล์มะเร็งที่พบบ่อยที่สุด พบมีแนวโน้มของการเกิดมะเร็งชนิดต่าง ๆ ในเพศหญิงมากกว่าเพศชาย ยกเว้นใน squamous cell carcinoma และ Metastatic carcinoma และอายุที่พบได้บ่อยสุดคือช่วง 51 ถึง 70 ปี*

Malignant tumors of the salivary glands are less frequently encountered in comparison with benign tumors. Among the major glands, malignant tumors are more commonly found in the parotid glands than in the submandibular and sublingual glands. Age, sex and clinical presentation of the patients also vary depending on histologic types.[1]

In Thailand, studies of these tumors have not been widely done. The available data about the neoplasms in this country comes from a few centers, all of which are medical schools.[1-4] No study about salivary gland tumors in King Chulalongkorn memorial hospital had been previously done. This report provides basic data about proportion, age, sex and other available information of various malignant neoplasms of major salivary glands recorded in the pathology record files from the Department of Pathology of King Chulalongkorn Memorial Hospital from January 1989 to December 1998.

## Materials and Methods

The data was collected from the pathology record files from the Department of Pathology of King Chulalongkorn Memorial Hospital for the ten year period from January 1989 to December 1998. All available histologic materials were reviewed. The histological classification of salivary gland tumors were based on the World Health Organization's criteria.[5]

## Results

The total number of malignant tumors of all major salivary glands was 86 cases. The parotid glands were the most frequent locations of the neoplasms with 66 cases (76.7%). The submandibular glands were the second most common site with 19 cases (22.1%). The least common location was the sublingual gland with only 1 case (1.2%) recorded.

Among the different kinds of tumors, mucoepidermoid carcinoma (Figures 1A and B) was

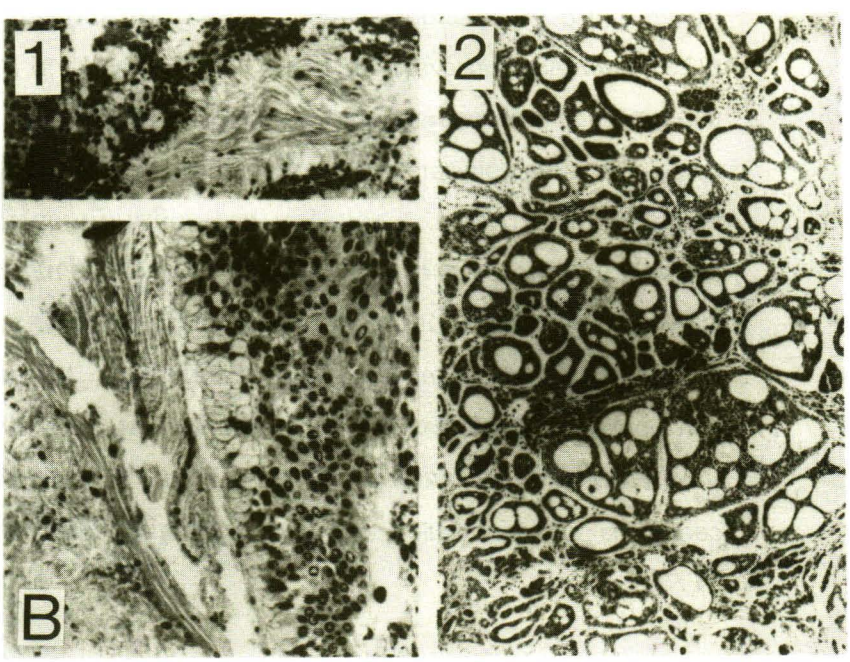


**Figure 1.** Mucoepidermoid carcinoma (A) low power, (B) high power.

**Figure 2.** Adenoid cystic carcinoma. The tumor cells show cribiform appearances.

the most frequent with 20 out of the total number of 86 cases (23.3%) followed by adenoid cystic carcinoma (Figure 2) with 14 cases (16.3%). Malignant mixed tumors which had both histologic patterns, namely carcinoma ex pleomorphic adenoma (Figures 3A and B) and carcinosarcoma, were the third most common tumors with 11 cases. For carcinosarcoma, the carcinomatous and sarcomatous were undifferentiated carcinoma and chondrosarcoma, respectively, there was only one case found. Malignant lymphoma (Figures 4A and B) were found in 10 cases. Acinic cell carcinoma (Figure 5) occurred in 9 cases followed by 7 cases of metastatic carcinoma. Next to metastatic carcinoma was squamous cell carcinoma (Figures 6A and B) with 5 cases. There were 4 cases of undifferentiated carcinoma (malignant lymphoepithelial lesion). Salivary duct carcinoma and adenocarcinoma, not otherwise specified, had 2 cases each. Papillary cystadenocarcinoma and epithelial-myoepithelial carcinoma were the two rarest tumors in this series with 1 case each.

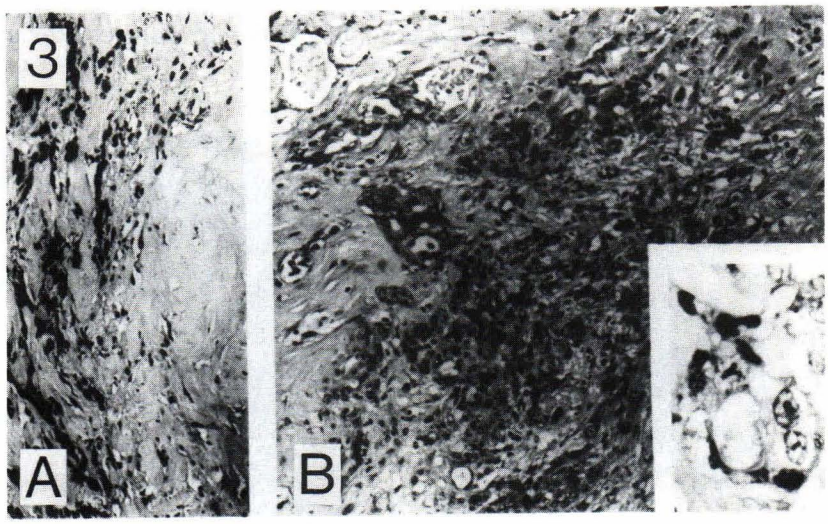


**Figure 3.** Carcinoma ex pleomorphic adenoma. The epithelial part shows adenocarcinoma (inset).

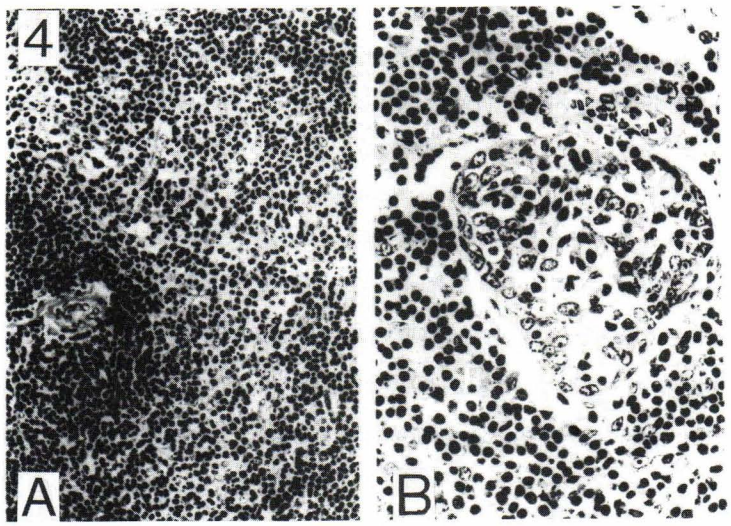


**Figure 4.** Malignant lymphoma (MALT). Lymphoepithelial are demonstrated.

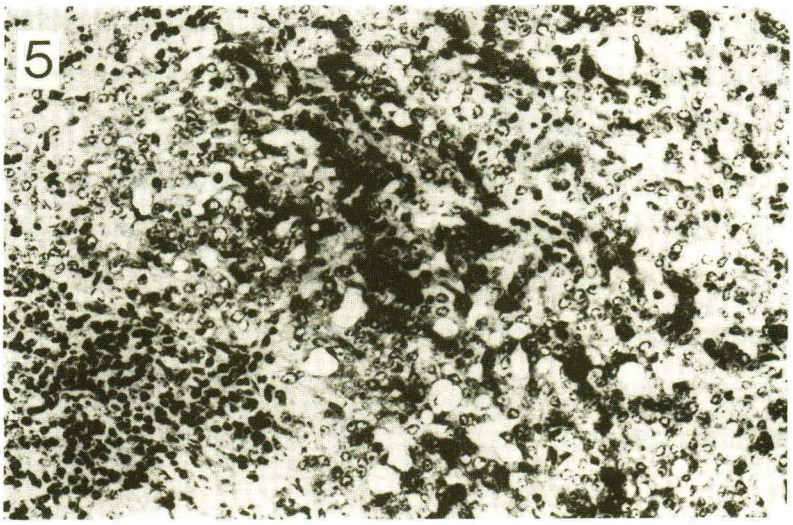


**Figure 5.** Acinic cell carcinoma. The tumor cells contain zymogen granules like normal acinar.

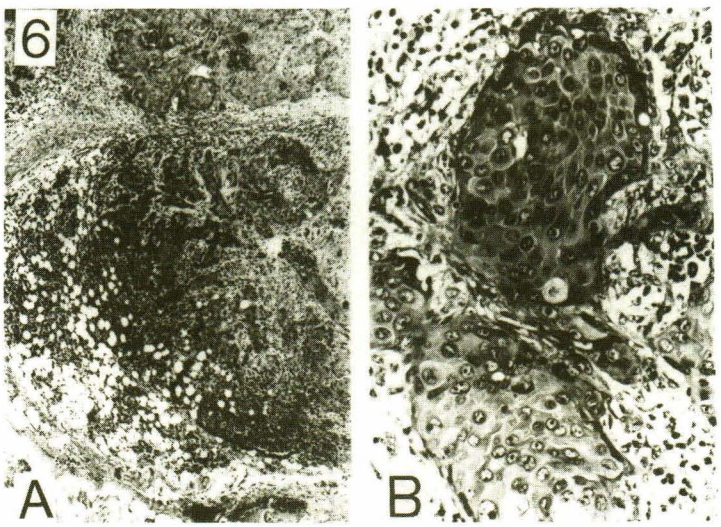


**Figure 6.** Squamous cell carcinoma. The tumor cells are arranged in sheets. They have distinct cell borders with prominent intercellular bridges.

The tumor locations are illustated in table 1. The majority of the tumors occurred in the parotid glands except for adenocarcinoma, not otherwise specified, of which 1 case was found in the parotid and 1 case in submandibular glands. For mucoepidermoid carcinoma, 17 cases were located in the parotid glands and only 3 cases were found in the submandibular glands. Similarly, 8 cases of adenoid cystic carcinoma were in the parotid, 5 cases in the submandibular, and1 case in the sublingual glands. All 9 of the acinic cell carcinoma cases occurred in the parotid glands. There were 8 cases of malignant mixed tumors in the parotid glands and 3 cases of in the submandibular glands. Malignant lymphoma were also more

common in the parotid with 8 out of 10 cases there while only 2 cases were in the submandibular glands. Of 7 cases of metastatic carcinoma, 4 cases were in the parotid while the other 3 cases were in the submandibular glands. Three cases of squamous cell carcinoma were located in the parotid while 2 cases were detected in the submandibular glands. All 4 cases of undifferentiated carcinoma were discovered in the parotid glands. Salivary duct carcinoma, epithelial-myoepithelial carcinoma and papillary cystadenocarcinoma all occurred in parotid glands.

The male to female sex ratio was 8:9 (males 40 cases, females 46 cases) for the tumors overall. For each group of tumors, the ratios were different. Table2 shows the sex distribution of the tumors. Mucoepidermoid carcinoma had a 7:13 male to female sex ratio. Adenoid cystic carcinoma had 6:8, acinic cell carcinoma 4:5, adenocarcinoma, not otherwise specified, 1:1, squamous cell carcinoma 5:0, malignant mixed tumors 4:7, epithelial-myoepithelial carcinoma 1:0, papillary cystadenocarcinoma 1:0, salivary duct carcinoma 2:0, undifferentiated carcinoma 1:3, malignant lymphoma 3:7 and metastatic carcinoma had 5:2.

The number of cases was highest in the $6^{th}$ decade of life. The incidence was low in the $1^{st}$, $2^{nd}$, $9^{th}$ and $10^{th}$ decades. The number of cases in different age groups for each tumor is illustrated in table 3.

**Table 1.** Illustrate location of tumors.

| Type of tumor | Site of tumor | | |
|---|---|---|---|
| | Parotid gland | Subman. gland | Sublingual gland |
| Mucoepidermoid CA | 17 | 3 | - |
| Adenoid cystic CA | 8 | 5 | 1 |
| Acinic cell CA | 9 | - | - |
| Adenocarcinoma | 1 | 1 | - |
| Squamous cell CA | 3 | 2 | - |
| Malignant mixed tumor | 8 | 3 | - |
| Epithelial – myoepithelial CA | 1 | - | - |
| Papillary cystadenocarcinoma | 1 | - | - |
| Salivary duct CA | 2 | - | - |
| Undifferentiated CA | 4 | - | - |
| Malignant lymphoma | 8 | 2 | - |
| Metastatic CA | 4 | 3 | - |
| **Total** | 66 | 19 | 1 |

Table 2. Sex distribution of tumors.

| Type of tumor | Sex | |
|---|---|---|
| | Male | Female |
| Mucoepidermoid CA | 7 | 13 |
| Adenoid cystic CA | 6 | 8 |
| Acinic cell CA | 4 | 5 |
| Adenocarcinoma | 1 | 1 |
| Squamous cell CA | 5 | - |
| Malignant mixed tumor | 4 | 7 |
| Epithelial-myoepithelial CA | 1 | - |
| Papillary cystadenocarcinoma | 1 | - |
| Salivary duct CA | 2 | - |
| Undifferentiated CA | 1 | 3 |
| Malignant lymphoma | 3 | 7 |
| Metastatic CA | 5 | 2 |
| Total | 40 | 46 |

## Discussion

As indicated by the findings in this study, malignant salivary gland tumors tend to occur in the parotid glands more than in the other major salivary glands. The sublingual glands were the least common locations.

Mucoepidermoid carcinoma was the most common malignant tumor and comprised 23.3 percent of all the malignant neoplasms in the major salivary glands followed by adenoid cystic carcinoma (16.3 percent). Malignant mixed tumors were the third most common disease at 11.8 percent. Rare tumors were epithelial-myoepithelial carcinoma, papillary cystadenocarcinoma, adenocarcinoma, not otherwise specified, and salivary duct carcinoma.

Table 3. Age distribution of tumors.

| Type of tumor | Age ( years) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 81-90 | 91-100 | Total |
| Mucoepidermoid CA | 1 | 1 | 6 | 2 | 1 | 5 | 3 | 1 | - | - | 20 |
| Adenoid cystic CA | - | - | 1 | 3 | 4 | 1 | 5 | - | - | - | 14 |
| Acinic cell CA | - | - | 2 | 3 | - | 4 | - | - | - | - | 9 |
| Adenocarcinoma | - | - | - | - | 1 | 1 | - | - | - | - | 2 |
| Squamous cell CA | - | - | - | - | 1 | 2 | 1 | - | 1 | - | 5 |
| Malignant mixed tumor | - | - | 1 | 3 | 1 | 2 | 2 | 1 | - | - | 10* |
| Epithelial – myoepithelial CA | - | - | - | - | - | - | 1 | - | - | - | 1 |
| Papillary cystadenocarcinoma | - | - | - | - | - | - | - | 1 | - | - | 1 |
| Salivary duct CA | - | - | - | - | - | - | 1 | 1 | - | - | 2 |
| Undifferentiated CA | - | 1 | - | 1 | - | - | 1 | 1 | - | - | 4 |
| Malignant lymphoma | - | - | 1 | 2 | 1 | 4 | - | 2 | - | - | 10 |
| Metastatic CA | - | - | - | - | - | 2 | 2 | 2 | - | 1 | 7 |
| Total | 1 | 2 | 11 | 14 | 9 | 21 | 16 | 9 | 1 | 1 | 85* |

*One case of malignant mixed tumor lost age information.

In general, there was no sex preponderance but some tumors showed distinct differences between the sexes such as squamous cell carcinoma, all of which occurred in males. Mucoepidermoid carcinoma, malignant mixed tumors and malignant lymphoma were more common in females.

For mucoepidermoid carcinoma, there were two patients whose ages were below 20 but it is common in patients from the 3rd to the 7th decades of life. Adenoid cystic carcinoma is common in age the 4th to the 7th decades. Acinic cell carcinoma occurs in a slightly younger age group, the 3rd to the 6th decades. Malignant mixed tumors have a wide age range from the 3rd to the 8th decades. Malignant lymphoma was from the 3rd to the 8th decades. Squamous cell carcinoma, adenocarcinoma, metastatic carcinoma, epithelial-myoepithelial carcinoma, papillary cystadenocarcinoma and salivary duct carcinoma tended to occur in the older age group in the 5th to 8th decades of life. Another tumor which can occur in both the young and the elderly is undifferentiated carcinoma. The youngest such patient was in the 2nd decade and the oldest in the 8thdecade of life.

Most of our findings were similar to those reported in other series. In this study, we found that the most common site for the neoplasms were the parotid glands followed by the submandibular glands and sublingual glands. In general, and all malignant salivary gland tumors are considered, they are more commonly located in the parotid and minor salivary glands than in the submandibular and sublingual glands. But which glands are the most frequent location depends on the series.[6,7] However, we did not include the minor salivary glands in this analysis, therefore we do not have the information on them to compare with the others.

For adenoid cystic carcinoma, the sites of distribution of this study differ from other studies that is, they are found more in the parotid glands while, in general, they are more usual in the submandibular and sublingual glands than they are in the parotid glands. [8]

Mucoepidermoid carcinoma is reported by most series to be the most common tumor among malignant tumors of the salivary glands [8,9] as in our report. The occurrence rates of adenoid cystic carcinoma, acinic cell carcinoma, malignant mixed tumor and adenocarcinoma differ from series to series.

Usually, salivary gland tumors, regardless of being benign or malignant tumors, tend to occur more often in females except for squamous cell carcinoma which is more common in males.[10,11] Our findings also had these trends. Most of the tumors from our study showed a female preponderance except for squamous cell carcinoma and metastatic carcinoma which have male predominance.

Generally, the average age for malignant tumors is higher than for benign neoplasms which most often appear in the 5th to 7th decades of life.[7,8,12] Our data showed that the most common age group for malignant tumors was in the 6th decade followed by 7th decade. However, the youngest patient in this series was 2 years old and had a mucoepidermoid carcinoma.

The small population of our study was the main disadvantage.Thus some figures do not represent the real nature of the diseases, especially in cases of the rare entities. This problem results from the rarity of the tumors themselves and from the ineffectiveness of data collection. Data missing

including medical records and histological materials (slides and blocks) and is the main barrier for increasing the population size by using longer periods of study.

It is difficult to conduct such studies in large populations, but if many centers do their own studies, their results can be compared and the data made more complete.

## Conclusion

A study of malignant tumors of the major salivary glands in King Chulalongkorn Memorial Hospital from January 1989 to December 1998 was conducted. Most findings were similar to other series. The parotid glands were the most common sites for these neoplasms while the sublingual glands were the least common locations for them. This excepts adenoid cystic carcinoma which in most series is more common in the submandibular and sublingual glands and less frequent in the parotid glands.

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