

ORIGINAL RESEARCH

The Influence of Demographic Factors and Histopathological Variants in Survival Analysis of Malignant Minor Salivary Gland Tumors

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ABSTRACT

Minor salivary gland tumors account for 2 to 4% of all head and neck cancers. These tumors are classically slow growing with patients being aware of their presence over months or even years. They are usually innocuous, asymptomatic and do not interfere with function till they attain large size.

This retrospective study of malignant minor salivary gland tumors seen at Regional Cancer Center, Thiruvananthapuram, India over a period of 24 years included 84 cases.

Aims: To assess the history, clinical presentation, pathological types of cases involving malignant minor salivary gland tumors and their influence on survival.

Methods: The study was carried out in the division of surgical oncology, Regional Cancer Center, Thiruvananthapuram, India. A retrospective study design was adopted to assess the history, clinical presentation, pathological types. The cases were extracted from the electronic database by using International Classification of Diseases of Oncology (ICD-O) (1st edition) codes of histology and sites. All patients were restaged using American Joint Committee on Cancer (AJCC) Tumor, Node and Metastasis (TNM) classification (2002). Demographic factors, clinical, histopathological findings were displayed with frequency tables. Survival was estimated by Kaplan-Meier method (Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. *J Amer Statist Assn* 1958;53:457-81).

Results: Mucoepidermoid carcinoma was the most common histopathological variant followed by adenoid cystic carcinoma. Mean age of the patients was 46.7 years. The overall disease free survival observed at 2 and 5 years in the present study was 73.3 and 59.7% respectively.

Conclusion: The histological type of minor salivary gland tumor was found to significantly influence survival. Gender and habits had no significant influence on survival.

Keywords: Malignant, Minor, Salivary gland tumors, Histopathology.

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INTRODUCTION

As many as 80% of minor salivary gland tumors are malignant. Histological differentiation and classification, clinical presentation, gender predilections and topographical site are the factors that mainly influence the efficacy of

different therapy's. The minor salivary gland tissues begin their embryologic development as solid buds from the oral epithelium. As the epithelial buds proliferate, solid cords appear and develop into double layer of cuboidal progenitor cells under the influence of surrounding mesenchymal tissue. Progenitor cells differentiate into various ducts, acini and myoepithelia.

Tumors arising in the minor salivary glands are rare.¹ In terms of salivary gland malignancy, it is a generally accepted norm that the smaller the gland in which the tumor arises, the greater the likelihood of its being malignant.² There is a remarkable variation in clinical presentation, behavior and histology of these neoplasms.³ The malignant salivary gland tumors deviate from the other malignant tumors being classically slow growing, with patients being aware of its presence late. They are usually innocuous, asymptomatic and do not interfere with function. Ulceration, a classical diagnostic feature only seen secondarily from either masticatory or denture trauma or pressure.⁴ Although both major and minor salivary gland shares the same histogenesis and function, there are distinct differences in their neoplastic patterns. Adenoid cystic carcinoma is the most common malignancy in the minor salivary gland and mucoepidermoid carcinoma has the highest propensity for lymphatic metastasis.⁴

The percentage of malignant or potentially malignant tumors in minor salivary glands is much higher than in major glands. Adenoid cystic carcinoma is the most prevalent histological type and palate the most common site.⁵ Tumor size, histology and site are the most important prognostic factors in malignant minor salivary gland tumors. Resection with good margin is adequate treatment for small lesions and large, poorly differentiated tumors require a combined approach (surgery and radiation therapy).⁶ Early diagnosis and treatment of minor salivary gland carcinoma likely leads to have a better outcome.⁷

This paper aims to assess the history, clinical presentation, pathological types of cases involving malignant minor salivary gland tumors and their influence on survival.

METHODS

The study was carried out in the division of surgical oncology, Regional Cancer Center, Thiruvananthapuram,

India. A retrospective study design was adopted to assess the history, clinical presentation, pathological types. Eighty-four cases of malignant minor salivary gland tumors of the upper aerodigestive tract, viz. palate, buccal mucosa, tongue, nasopharynx and oropharynx treated between 1982 and 2005 were included in the study. All the tumors were malignant, had histological confirmations and were exclusively confined to minor salivary glands.

The cases were extracted from the electronic database by using International Classification of Diseases of Oncology (ICD-O) (1st edition) codes of histology and sites. All patients were restaged using American Joint Committee on Cancer (AJCC) tumor, node and metastasis (TNM) classification (2002).

Demographic factors, clinical, histopathological findings were displayed with frequency tables. Survival was estimated by Kaplan-Meier method.

RESULTS

This retrospective study on malignant minor salivary gland tumors between the period 1982 and 2005 included 84 cases. Mean age of the patients was 46.7 years (range 8-76 years).

Table 1 shows the gender distribution in the present study. There were nearly equal number of patients in both the genders. No gender predilection was observed.

Of the 84 patients, 22 (26.2%) patients had no habits, while only eight (9.5%) had current habits and one had past habits (Table 2). History of habits included either smoking, alcoholism, pan chewing. Gutkha chewing was associated as a common habit with one of the above mentioned habit in all of them.

The majority 35 patients (41.7%) were mucoepidermoid carcinomas, followed by adenoid cystic carcinoma

representing (38.1%) adenocarcinoma (16.7%), and one patient had epidermoid carcinoma (Table 3).

Table 3: Distribution of patients by histopathological variant

	Histopathological variant	
	Frequency	Percentage
Mucoepidermoid carcinoma	35	41.7
Adenoid cystic carcinoma	32	38.1
Adenocarcinoma	14	16.7
Epidermoid carcinoma	1	1.2
Do not know	2	2.4
Total	84	100

Survival Analysis

The mean follow-up was 100 months and ranged from 1 to 350 months (median 86 months) while mean disease free time was 83.4 months (90.9 months) ranging from 1 to 350 months (median 45.5 months).

Disease free survival calculated using Kaplan-Meier method. The time of analysis was from the date of pathologic diagnosis to the date follow-up or death.

The overall disease free survival observed at 2 and 5 years in the present study was 73.3 and 59.7% respectively. As shown in Table 4, the disease free survival at the end of 2 years was 66.2% for males and 87.2% for females. At the end of 5 years the disease free survival for males decreased to 50.7% and for females 69.7%. Statistically this difference was not significant (0.12).

Patients with no habits had a survival of 70.8 and 53.9% at the end of 2 and 5 years respectively. Those with current habits had 64.8% survival at 2 years, however, all the patients died by the end of 5 years. Patients whose habits were not known had a survival of 72.6 and 66% at the end of 2 and 5 years respectively. This difference too was not significant.

Table 1: Distribution of patients by gender

	Sex	
	Frequency	Percentage
Male	43	51.2
Female	41	48.8
Total	84	100

Table 2: Distribution of patients by habits

	Habits	
	Frequency	Percentage
No	22	26.2
Current	8	9.5
Past	1	1.2
Others	12	14.3
Do not know	41	48.8
Total	84	100

Table 4: Survival analysis

Variable	2 years	5 years	p-value
Disease free survival	73.3	59.7	—
Sex			
Male	66.2	50.7	0.12
Female	87.2	69.7	—
Habits			
No	70.8	53.9	0.55
Current	64.8	0.0	—
Do not know	72.6	66.0	—
Histopathological variant			
Mucoepidermoid carcinoma	83.2	70.7	0.02*
Adenoid cystic carcinoma	81.7	55.9	—
Adenocarcinoma	51.5	0.0	—
Epidermoid carcinoma	0.0	0.0	—

*Significant

Survival was highest in patients with mucoepidermoid carcinoma followed by adenoid cystic carcinoma (83.2 and 70.7 vs 81.7 and 55.9 at 2 and 5 years respectively) (Table 4). Adenocarcinoma had a survival of 51.5% at the end of 2 years that fell to zero at 5 years. The difference was statistically significant (0.02).

DISCUSSION

The management of patients with neoplasms of the salivary glands involves multidisciplinary approach. Oral and maxillofacial surgery and oral pathology are distinct yet synergistic disciplines. Due to this, the number of patients studied over a period of time are relatively small and it is difficult to ascertain the prognostic factors with accuracy. This study, though spans over a period of 24 years, includes only 84 patients which is significantly less when compared to other pathologic disease states.

In terms of salivary gland malignancy, it is a generally accepted norm that the smaller the gland in which the tumor arises, the greater the likelihood of its being malignant.² The minor salivary gland tumors deviate from the other malignant tumors being classically slow growing, with patients being aware of its presence late. They are innocuous, asymptomatic, and do not interfere with function. Ulceration, a classical diagnostic sign only seen secondarily from either masticatory or denture trauma.⁴

Age and Gender

Pogrel MA stated that most salivary gland tumors are slightly more common in females and more frequently encountered in the third to fifth decades of life.⁸ Anderson JA et al reviewed 95 patients of minor salivary gland cancer and found mean age of patients with this malignancy as 55 years.⁹ In the present study, no gender predisposition was found, while the mean age at 46.7 years was a decade younger than other series.

No statistically significant difference in relation to sex is found in this study.

Habits

Patients from lower socioeconomic strata are largely ignorant about the significance of early diagnosis. Their financial problems make them adopt habits, such as smoking, alcohol which is a predisposing factor toward oral cancer. Poor oral hygiene significantly adds to the problem. Most of the patients in this study were from lower socioeconomic strata. In the present study, only a small number of patients had habits thus, suggesting that salivary tumors are perhaps independent of habits.

Histopathological Variants

The two most common histopathological variants in minor salivary glands are: Mucoepidermoid carcinoma and adenoid cystic carcinoma. Mucoepidermoid carcinoma is the most common variant followed by adenoid cystic carcinoma in this study. Auclair PL et al found mucoepidermoid carcinoma to be the most common malignant lesion of major and minor salivary glands.¹⁰ As each histopathological variant has its own pattern of growth, spread and invasion, and hence independent histological behavior, this highly influences the prognosis. Adenoid cystic carcinoma accounts for 21 to 42% of minor salivary gland carcinoma and occurs most commonly on the hard palate. This carcinoma is characterized by its infiltrative growth and perineural invasion. Spread to regional lymphatics is relatively uncommon, but hematogenous spread occurs in 25 to 50% of cases which directly affects the prognosis. Systemic involvement is said to occur in the presence of uncontrolled disease at the primary site.⁹ The three major subtypes of adenoid cystic carcinoma are cribriform, tubular, basaloid or solid variant.¹¹

Adenocarcinomas are characterized by small clusters of neoplastic cells surrounding nerve fibers in a concentric laminated fashion, forming multifocal perineural whorls.¹² They may also be arranged in solid nests, strands or trabeculae, and in acini or tubular structures. This tumor is rarely encountered in minor salivary glands and in this study only 14 cases were seen over a period of 24 years.

According to Huang MX et al the histological type of tumor is an important factor influencing prognosis.¹³ In contradiction to this, Parsons JT et al stated that the histological type did not influence survival in their review of 95 patients with minor salivary gland cancer.¹⁴ Hyam DM et al reviewed 30 cases of malignant minor salivary gland tumors and concluded adenoid cystic carcinoma as the most common histological variant.⁷ Jansisyanont P et al in their retrospective study over a period of 10 years included 80 cases of minor salivary gland tumors and reported mucoepidermoid carcinoma as the most common malignant tumor.¹⁵ In the present study, mucoepidermoid carcinoma had a significantly better survival at the end of 5 years compared to adenoid cystic carcinoma and adenocarcinoma. Similar to literature, this study too showed an influence of histopathological variant on survival.

CONCLUSION

- Mean age of the patients was 46.7 years.
- Only a small number of patients had habits suggesting that salivary gland tumors are perhaps independent of habits.

- c. Mucoepidermoid carcinoma was the most common histopathological variant followed by adenoid cystic carcinoma. Adenocarcinoma was the third common histological type and only one case of epidermoid carcinoma was found.
- d. The histological type of minor salivary gland tumor was found to significantly influence survival.
- e. Gender and habits had no significant influence on survival.

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