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ORIGINAL RESEARCH

Clinicopathological characteristics, treatment, and survival outcomes of cystadenocarcinoma of the salivary gland: a population-based study

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Background: The aim of this study was to investigate the clinicopathological characteristics, treatment, and survival of cystadenocarcinoma of the salivary gland.

Patients and methods: Cases in the Surveillance, Epidemiology, and End Results database from 1991 to 2012 were identified. Factors significantly associated with survival were identified using Kaplan–Meier survival analysis and Cox proportional hazard regression.

Results: A total of 65 patients were identified; of these patients, 64 received surgical treatment, 25 underwent lymphadenectomy, and four (16.0%) patients had nodal metastasis and only one (2.1%) patient had poorly differentiated disease. The most common tumor location was the parotid gland (87.7%). The median follow-up was 55 months. None of the patients died of salivary gland malignant-tumor-related disease. The 5- and 10-year cause-specific survival rates were 97.0% and 81.4%, respectively. The 5- and 10-year overall survival rates were 84.6% and 60.7%, respectively. Surgical procedures, lymphadenectomy, and adjuvant radiotherapy did not affect survival.

Conclusion: Salivary gland cystadenocarcinoma is extremely rare but has an excellent prognosis, and surgery is the mainstay of treatment.

Keywords: cystadenocarcinoma, salivary gland, SEER, treatment, survival

Introduction

Cystadenocarcinoma of the salivary gland is an extremely rare malignant tumor that was first described by the World Health Organization in 1991.[1] The estimated incidence of cystadenocarcinoma is ~2–5% of all salivary gland malignancies.[1–3] Diagnosis is based on pathologic findings, in which there is a predominantly cystic growth pattern that often exhibits intraluminal papillary proliferation.[4] Currently, there are few reported cases related to cystadenocarcinoma of the salivary gland in the literature,[5–10] and the related clinicopathological characteristics, treatment, and outcome results are limited.[3] In this study, we used a population-based national registry (Surveillance, Epidemiology, and End Results, SEER) to investigate the clinicopathological characteristics, treatment, and survival outcomes of patients with cystadenocarcinoma of the salivary gland.

Patients and methods

Patients and clinicopathological characteristics

Patients with a pathologic diagnosis of cystadenocarcinoma of the salivary gland were identified using the SEER database from 1991 to 2012.[11] Pathologic diagnosis was based on the primary site using the International Classification of Disease for Oncology,

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Third Edition. This study was approved by the ethics committee of the Affiliated First Hospital, Medical College, Xiamen University, who did not require that informed consent be obtained, as the study used SEER database data.

The following clinicopathological characteristics were obtained from the SEER database: year of diagnosis, race, age, tumor location, grade, SEER stage, and nodal status. Local treatment modalities including surgery, lymphadenectomy, and radiotherapy were also identified. Survival status, including cause of death, and the duration of follow-up were recorded.

Statistical analysis

Univariate and multivariate Cox regression analyses were used to analyze the risk factors for cause-specific survival (CSS) and overall survival (OS). Calculation of survival rates was plotted using the Kaplan–Meier method and compared using the log-rank testing. All data were analyzed using the SPSS software package, version 21.0 (IBM Corporation, Armonk, NY, USA). A *P*-value of <0.05 was considered statistically significant.

Results

Clinicopathological characteristics

A total of 16,923 patients were diagnosed with salivary gland malignant tumors from 1991 to 2012, including 65 (0.4%) patients with cystadenocarcinoma (Table 1). The median age was 62.0 years (range, 10–95 years); 90.8% of patients were diagnosed after 2000, and there was equal disease incidence in male and female patients. The most common tumor location was the parotid gland (57 patients, 87.7%), followed by the submandibular gland (four patients, 6.2%); four patients (6.2%) had no specific site records. Most of the patients (98.5%) were at localized and regional SEER stage, and only one patient (1.5%) was unstaged. Of the 47 patients with histological grade available, 42.6%, 55.3%, and 2.1% had Grade 1, Grade 2, and Grade 3 disease, respectively.

Table 1 Clinicopathological characteristics of patients (n=65)

Characteristics	
Age (years)	
Median (range)	62.0 (10–95)
<50	7
≥50	58
Year of study	
1991–1995	2
1996–2000	8
2001–2005	15
2006–2012	40
Race	
White	52
Black	5
Other	8
Sex	
Male	34
Female	31
Tumor location	
Parotid gland	57
Submandibular gland	4
Others	4
Grade (n=47)	
1	20
2	26
3	1
SEER stage	
Localized	56
Regional	8
Unstaged	1
Surgery	
No	1
Yes	64
Surgical procedures (n=61)	
Partial parotidectomy	43
Total parotidectomy	18
Radiotherapy	
No	49
Yes	16
Lymphadenectomy (n=64)	
No	39
Yes	25
Nodal status (n=25)	
Negative	21
Positive	4

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.

Treatment

Of the 65 patients, 64 (98.5%) received surgical treatment. Of the 61 patients with surgical procedure information available, 43 (70.5%) underwent local tumor excision or less than total parotidectomy, and 18 (29.5%) underwent total parotidectomy or radical parotidectomy. A total of 25 patients underwent lymphadenectomy, and only four patients (16.0%) had nodal metastasis. A total of 16 patients underwent adjuvant radiotherapy.

Outcomes

The median follow-up was 55 months (range, 1–204 months). A total of 13 patients died; ten patients died of noncancer disease, and three patients died of other malignant tumors; none of the patients died of salivary gland malignant-tumor-related disease. The 5- and 10-year CSS rates were 97.0% and 81.4%, respectively (Figure 1A). The 5- and 10-year OS rates were 84.6% and 60.7%, respectively (Figure 1B).

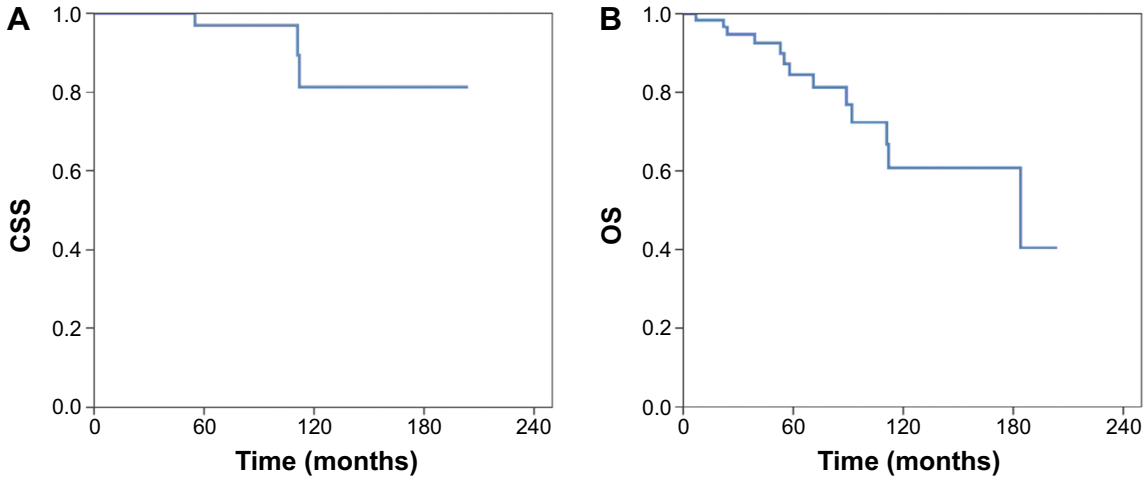

Figure 1 CSS (**A**) and OS (**B**) of cystadenocarcinoma of the salivary gland.
Abbreviations: CSS, cause-specific survival; OS, overall survival.

Influence of local treatment on survival

The effects of local treatment for cystadenocarcinoma of the salivary gland on CSS and OS were further analyzed, and the results showed that surgical procedures, lymphadenectomy, and adjuvant radiotherapy did not affect the CSS and OS (all, $P>0.05$).

Discussion

Cystadenocarcinoma of the salivary gland had an excellent prognosis, but most studies currently have few patients.[5–10] The study with the most patients in the literature was by Foss et al,[3] which involved 57 patients; the median age was 58.8 years, and the main disease site was the parotid gland (61.4%). In our study, we used the SEER database to assess the clinicopathological characteristics, treatment, and survival outcomes of cystadenocarcinoma of the salivary gland, and our findings are similar to those of Foss et al.[3] Regarding cystadenocarcinoma of the salivary gland, a high-grade malignant tumor usually leads to a relatively high risk of disease recurrence with rapid progression.[12,13] However, in our study, only one patient was pathologically diagnosed with poorly differentiated disease.

Currently, the main treatment for cystadenocarcinoma of the salivary gland is radical surgery. Lymphadenectomy is recommended for patients with lymph node enlargement.[14] The main site of recurrence following radical resection is the cervical lymph nodes, and there is less recurrence in the primary tumor bed.[3,15] Mills et al[16] reported that three of five patients (60%) with cystadenocarcinoma of the salivary gland had cervical lymph node metastases after 2–21 years. Similarly, Mukaigawa et al[15] reported on four patients with cystadenocarcinoma of the salivary gland who underwent radical resection, where two patients underwent lymph node dissection, and three patients had cervical lymph node recurrence after 7, 17, and 24 months (with parotid lymph node recurrence after 43 months), respectively. Foss et al reported that one patient had regional lymph node metastasis after 55 months and three patients had lymphatic metastasis at initial diagnosis.[3] In our study, 25 patients underwent lymphadenectomy, and 16.0% of patients were node positive. Due to the limitations of the SEER data, we could not clarify the lymph node status of the patients. However, based on the results of the abovementioned studies, the clinical course of follow-up for patients should also pay close attention to lymph node metastasis.

Radiotherapy is usually recommended for high-grade, recurrent disease, or for inoperable patients.[14] Foss et al[3] also recommended postoperative radiotherapy for patients with cervical lymph node metastasis. Our results also show that surgery is the main therapeutic method for cystadenocarcinoma of the salivary gland; other local treatment modalities such as lymphadenectomy and adjuvant radiotherapy had no effect on survival, which may be related to the excellent control rate of surgical resection.

In this study, none of the patients with cystadenocarcinoma of the salivary gland died of salivary gland malignant-tumor-related disease. Although mortality in cystadenocarcinoma of the salivary gland tends to be from other causes, long-term follow-up is essential, as some patients might relapse after a very long time, which may be associated with the slow growth and low-grade destructive features of cystadenocarcinoma of the salivary gland.[16]

The current study has several limitations that need to be considered. The main limitation is the inherent biases that

exist in any retrospective study. Second, the SEER database does not record data such as systemic therapy regimen and dose, margin status, and local and regional recurrence. In addition, there is little information to guide the analysis of why lymphadenectomy and postoperative radiotherapy were or were not completed in certain patients. Furthermore, some adenocarcinomas recorded in the SEER database such as cystadenocarcinomas may be other entities that have been only recently recognized, ie, cribriform adenocarcinoma of tongue, mammary analog secretory carcinoma, and acinic cell carcinoma, which may be difficult to discriminate from cystadenocarcinoma and may require advanced techniques (immunohistochemistry and molecular pathology).

Conclusion

Cystadenocarcinoma is an extremely rare type of salivary gland malignant tumor with excellent prognosis, and surgery is the mainstay of treatment.

Disclosure

The authors report no conflicts of interest in this work.

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