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Lymph node involvement predicts poor prognosis in primary tongue adenoid cystic carcinoma: A preliminary study of 54 cases

Nannan Han [a], Huishan Ong [a, 1], Zhihui Liu [b, **], Min Ruan [a, *], Wenjun Yang [a], Chenping Zhang [a]

[a] Department of Oral Maxillofacial-Head Neck Oncology, Faculty of Oral and Maxillofacial Surgery, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Key Laboratory of Stomatology (Head: Pro. Chenping Zhang), 639 Zhizaoju Road, Luwan District, Shanghai 200011, PR China
[b] Department of Stomatology, Taizhou Municipal Hospital Affiliated with Taizhou University (Head: Pro. Zhihui Liu), 381 East Road of Zhongshan, Taizhou, Zhejiang 318000, PR China

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ABSTRACT

Purpose: Primary tongue adenoid cystic carcinoma (ACC) is extremely rare. The relationship between the patient's prognosis and the tumor's clinicopathological characteristics is uncertain. The aim of this study was to identify the prognostic factors and analyze the overall outcomes for patients with tongue ACC.
Patients and methods: A retrospective analysis of the medical records of patients diagnosed with primary tongue ACC between 1998 and 2008 was conducted. The study comprised 54 patients, with a median age of 53.4 years. The incidence of ACC in the base of the tongue was almost 3.5 times in comparison to that in the mobile portion of the tongue. The 3-year and 5-year overall survival rates were 87.4% and 65.3%, respectively, whereas the 3-year and 5-year disease-free survival rates were 54.3% and 32.8%, respectively. Significant prognostic factors regarding overall survival in univariate analyses included tumor size and lymph node status.
Results: A multivariate model identified lymph node status as the only significant independent predictor of overall survival. Further analysis showed that tumor size ($P = 0.034$), histological grade ($P = 0.021$), and perineural invasion (PNI, $P = 0.023$) were three important factors affecting lymph node metastasis. Patients with lymph node metastasis have a higher tendency of developing distant metastasis ($P < 0.01$).
Conclusions: Lymph node status was a significant determinant of prognosis in primary tongue ACC and could be used for a rational design of treatment strategies in future.

1. Introduction

Adenoid cystic carcinoma (ACC) is a malignant neoplasm originating from both the minor and major salivary glands, with only 1–2% of all malignant neoplasms involving the head and neck (Kim et al., 1994). Histologically, ACC manifests three histological patterns, including the solid, cribriform, and tubular forms, in variable combinations and dominance. The palate is the most common site for minor salivary gland ACC. Primary tongue ACC is extremely rare and accounts for less than 5% of all minor salivary gland ACC (Soares et al., 2008).

Primary tongue ACC is usually asymptomatic as it grows gradually within the submucosal layer, thus hindering early diagnosis (Luna-Ortiz et al., 2009). Kokemueller et al. reported that prolonged tumor burden might contribute to potential regional lymph node or distant metastases, predominately in the lungs and bones (Kokemueller et al., 2004; Spiro, 1997). The rarity of this lesion, together with its high unpredictability, makes this group of lesions one of the most difficult diseases to manage in the head and neck region (Khan et al., 2001; Fordice et al., 1999). New insights regarding these rare tumors might help in designing comprehensive treatment strategies for clinical application. Thereby, we chose a retrospective study to thoroughly investigate primary tongue ACC.

* Corresponding author. Fax: +86 21 23271699.
** Corresponding author. Fax: +86 576 88858235.
E-mail addresses: liuzhihui1209@sina.com (Z. Liu), doctorruanmin78@hotmail.com (M. Ruan).
[1] Co-first author.

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2. Material and methods

A retrospective study was conducted on patients who were diagnosed with primary tongue ACC between January, 1998 and December, 2008 at the Department of Oral and Maxillofacial–Head and Neck Oncology, Shanghai Ninth People's Hospital. This study was approved by the Shanghai Ninth People's Hospital Institutional Review Board (2014–2016). Before inclusion in the study, all patients were informed of the purpose, protocols, and consent forms for participation in the study. Our inclusion criteria were (1) primary tongue ACC confirmed by postoperative histopathology; (2) did not receive pre-operative radiotherapy or chemotherapy; (3) radical surgical resection was primarily performed. Patients with a large lesion that was suspected to develop from the posterior floor of the mouth and invade to the adjacent tongue muscle were excluded.

Medical records were systemically retrieved to evaluate clinical parameters, treatment factors, and clinical outcomes. Two pathologist consultants reviewed the histological slides for tumor grading, surgical resection margin, and the presence of peritumoral lymphatic, vascular and neural invasion individually; only similar results were taken into account. A third pathologist consultant was consulted when disagreements occurred. The histological grade was determined according to the following criteria: Grade 1: a tubular and cribriform pattern without solid component; Grade 2: tubular, cribriform and solid pattern with less than 30% of solid component; and Grade 3: tubular, cribriform and solid pattern with more than 30% of solid component (Dardick, 1996).

Statistical analyses were performed using the SPSS (version 13.0; SPSS, Chicago, IL, USA). Paired sample *t*-tests and X^2 analyses were performed to determine the correlation between the clinicopathological features and lymph node metastasis. Postoperative survival was estimated using the Kaplan–Meier method, and logistic regression analysis was used to determine any correlation between clinicopathological parameters and patient outcomes.

3. Results

3.1. Patient characteristics

A total of 1263 salivary gland carcinoma cases were evaluated, of which only 54 patients were eligible for our inclusion criteria (Fig. 1A and B). The median age of patients in our study was 53.4 years (range: 30 to 82) and consisted of 30 male and 24 female patients. The incidence of ACC in the base of tongue (42 cases, 77.8%) was almost 3.5 times greater than those arising in the mobile portion of the tongue (12 cases, 22.2%). Twenty-four (44%) patients had tumors ranging between 3 and 4 cm, whereas 10 (18.5%) patients had primary lesions larger than 4 cm. Histological analysis demonstrated that 49 patients (90.7%) had tumors classified as Grade 1 (without solid), while 5 patients (9.3%) had tumors that were Grades 2 or 3 (with solid). Positive surgical margin, perineural invasion (PNI), and lymph node metastases (Fig. 1C and D) were confirmed in 9 (16.7%), 33 (61.1%), and 11 (20.4%) patients, respectively. However, among these features, no difference was found between the Low/Intermediate and High grade tongue ACC.

3.2. Treatment and outcome

All 54 patients were treated with surgery as the mainstay treatment option. Twenty-nine (53.7%) patients were treated with local resection only, while 25 (46.3%) patients were treated with local resection and neck dissection. Our department's treatment protocols for neck dissection were those with either cN^+ status, size >4 cm lesions, or intraoperative frozen section reported as having a positive margin. Ultrasound and computed tomography (CT) were routinely performed for postoperative follow-up and neck status evaluation.

Postoperative radiotherapy was performed in 36 patients. Our department's treatment protocol indicated adjuvant radiotherapy if

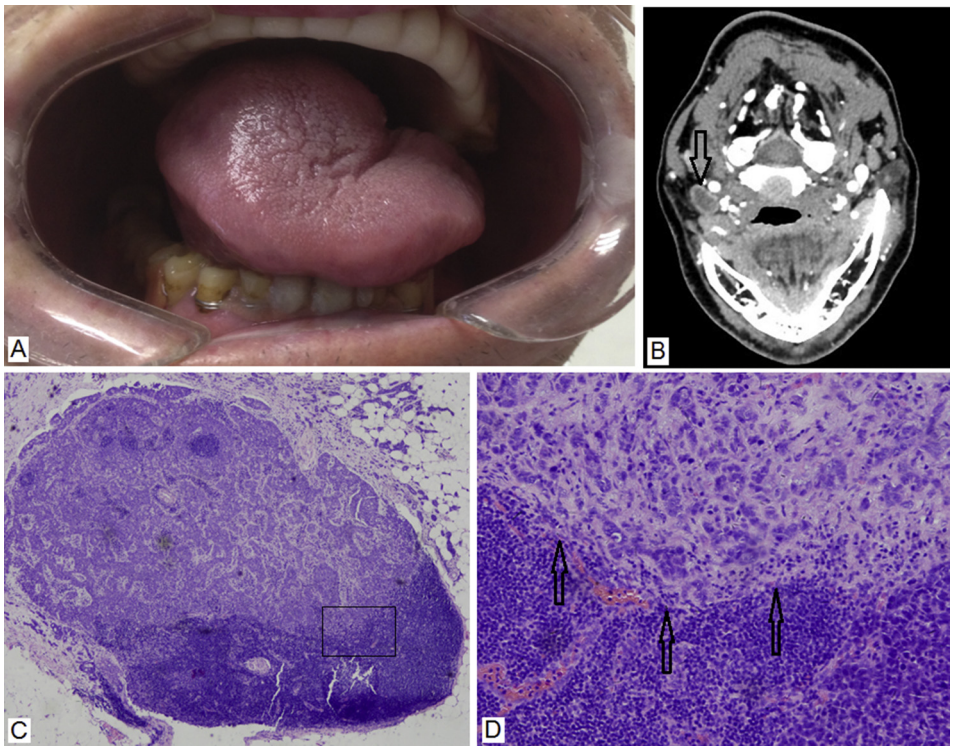

Fig. 1. A: A 62-year-old male with a lateral mobile tongue ACC. **B:** CT scan shows ring-like enhancement of Level II lymph node in this patient. **C:** Confirmed cervical lymph node metastases by HE stain (HE × 100). **D:** Boundary of normal lymph cells and ACC cells in metastatic cervical lymph node (HE × 400).