Auris Nasus Larynx xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Auris Nasus Larynx

journal homepage: www.elsevier.com/locate/anl

Adenoid cystic carcinoma of head and neck: A retrospective clinical analysis of a single institution

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ARTICLE INFO

Article history:
Received 15 July 2017
Accepted 16 October 2017
Available online xxx

1. Introduction

Adenoid cystic carcinoma (ACC), first described by Billroth in 1856, was originally called cylindroma because of its histologic appearance [1]. ACC is a rare tumor, accounting for about 1% of head and neck tumors, but it is the most common malignancy of the minor salivary glands [2]. Characteristically, ACC progresses slowly, with wide perineural invasion; lymphatic spread to the neck is rare. Histologically, adenoid cystic carcinomas also arise in other sites in the head and neck field, such as the major salivary glands, the tracheobronchial tree, the esophagus, the lacrimal gland, and even sites outside the head and neck.

Previous studies have attempted to determine the factors that predict outcome variables, especially the rates of local control and long term survival. The possible predictive factors include histological grade, perineural invasion, and safe margin of tumor resection. Tumor grade is generally considered an indicator of poor prognosis, although some reports have shown that tumor stage is also significant. Tumor stage has proved to be a reliable and reproducible determinant of tumor control and survival. Perineural invasion and a positive tumor margin are predictors of adverse outcomes in patients with ACC. Tumor site is also significant, independent of the patient's age or sex, and patients with tumors of the nasal cavities and sinuses are usually associated with poorer outcomes [2–4].

An optimum treatment for ACC has not yet been established, probably because of the neurotropic and infiltrative nature of the disease and its protracted course. Surgical excision is the mainstay of adequate therapy, although combined therapy with radiation has led to superior results in many studies. The radiosensitivity of these tumors has now been established, but the intervention value of radiation therapy (RT) still remains controversial [5,6].

The purpose of this retrospective analysis was to report our experience with ACC in our hospital. We discuss the relevant clinicopathological prognostic factors of this rare malignancy, and we also attempted to determine the best treatment concepts according to the local-regional recurrence and long term survival, using different treatment strategies.

2. Materials and methods

A total of 33 patients with ACC of the head and neck were treated at the Department of Otorhinolaryngology, Head and

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https://doi.org/10.1016/j.anl.2017.10.009
0385-8146/© 2018 Published by Elsevier Ireland Ltd.

Please cite this article in press as: Chang C-F, et al. Adenoid cystic carcinoma of head and neck: A retrospective clinical analysis of a single institution. Auris Nasus Larynx (2018), https://doi.org/10.1016/j.anl.2017.10.009

Neck Surgery in Changhua Christian Hospital between January 1995 and December 2010. All patients registered with ACC were identified by pathologists. Data concerning patient characteristics, including primary tumor site, clinical and pathologic tumor characteristics, and treatment modalities, as well as the results of management, were obtained by a retrospective review of medical records. Specific information was obtained by a comprehensive chart review of all patients. Four patients were lost of follow up due to rejection of treatment or managed in other hospitals, and were excluded from further analysis. This study was initiated after being approved by the Institutional Review Board of Jen-Ai Hospital, Taiwan. Because the identification numbers and personal information of the individuals included in the study were not included in the secondary files, the review board stated that written consent from patients was not required.

The distribution of tumors according to site of origin is shown in Table 1. Based on the obtained information, major salivary gland tumors were staged retrospectively according to the American Joint Committee for Cancer's (AJCC) staging protocols [7]. Minor gland tumors were staged using the AJCC criteria for squamous cell carcinomas in identical sites, which have been shown to be prognostically useful in ACC. A total of 29 patients had adequate information in their charts for stage assignment. The extent of disease, according to T stage, AJCC stage, and grade of tumor, is shown in Table 2. Histopathologic variables, retrieved from patient charts when available, included the grade of the tumor, margin status, and perineural invasion. Margin status was recorded as either positive, negative, or close (<5 mm). Tumor grade was reviewed when pathology reports were available and was assigned as well differentiated, moderately differentiated, poorly differentiated or undifferentiated (grades 1–3). The terms tubular, cribriform, and solid were roughly assigned grades 1, 2, and 3, respectively. Because of the inherent difficulties of this method and the variability in the semantics used by pathologists, the grades of tumors are all recorded in Table 2. A total of 14 (48.3%) patients had positive margins reported in their pathology reports and 15 (51.7%) had documented perineural invasion.

All patients underwent surgical resection, while some of them received combined therapy (radiation or chemotherapy plus radiation). Facial nerve monitoring system was routinely used in parotid surgery in our hospital. We always identified and preserved the facial nerve before tumor excision. The facial nerve was sacrificed only when the nerve was obviously invaded by malignancy. Indications for adjuvant radiotherapy include lymph node metastasis, high tumor grade, positive surgical margin and advanced tumor stage [43]. The radiation dose was 60–66 Gy. The field of radiotherapy involved skull base and paranasal sinus for patients with paranasal sinus ACC.

Table 1
Distribution by tumor site.

Site	Number
Major salivary glands	11
Parotid	6
Submandibular	5
Minor salivary glands	3
Oral cavity	2
Lower lip	1
Oropharynx	5
Tongue base	1
Palate	4
Nasal cavity and sinus	5
Nasopharynx	3
Ear	2

Table 2
Distribution by stage and grade.

Stage	T stage (n)	AJCC stage (n)	Grade (n)
I	5	5	2 (tubular)
II	10	10	23 (cribriform)
III	8	8	4 (solid)
IV	6	6	

The distribution of patients according to primary therapy is shown in Table 3. All patient data, including demographics, staging, treatment, and outcome variables, are tabulated in Table 4. The recurrence status of the primary tumor sites is documented in Table 5. Overall survival and Disease-specific survival were calculated using the Kaplan–Meier method, and the log-rank test was used to calculate the differences between the actuarial curves (Figs. 1 and 2). Follow-up data were obtained until December 2010. All patients who survived until this date were evaluated for survival analysis, and all patients without local, regional, and distant recurrence until this date or death were censored for local, regional, and distant control analysis. Fisher's Exact test was used to verify categorical associations. A value of $P < 0.05$ was considered statistically significant.

3. Results

During a 16-year period, a total of 33 patients with ACC of the head and neck were treated at our institution. Patients not receiving primary surgical treatment (n = 1) and patients with incomplete medical documentation (n = 3) were excluded from the study. Of the remaining 29 patients, 16 (55.2%) were men and 13 (44.8%) were women. The average age at diagnosis was 54.7 years (range from 32 to 79 years), and the mean follow-up was 63.3 months. At the time of diagnosis, 15 patients were known to have early (T1–T2) lesions and 14 had late-stage (T3–T4) lesions. The results of a detailed analysis of different tumor sites by stage are given in Tables 1 and 2. Eleven (37.9%) ACCs originated from the major salivary glands, sixteen (55.2%) from the minor salivary glands, and two (6.9%) from the secretory gland in the ear. The most commonly affected site was the parotid, presenting in 6 (20.6%) patients.

Table 3
Distribution by primary therapy.

Therapy	Total patients (N)	Total patients (%)
Surgery	4	13.8
Surgery + radiotherapy	21	72.4
Surgery + radiotherapy + chemotherapy	4	13.8

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