Available online at www.sciencedirect.com

SciVerse ScienceDirect

British Journal of Oral and Maxillofacial Surgery 52 (2014) 715–720

BRITISH Journal of Oral and Maxillofacial Surgery

www.bjoms.com

Clinical and prognostic analysis of second primary squamous cell carcinoma of the tongue after radiotherapy for nasopharyngeal carcinoma

Chuanzheng Sun [a,1], Zedong Hu [a,1], Zhaoming Zhong [a], Yue Jiang [a], Ruimei Sun [a], Jimin Fei [a], Yan Xi [a], Xiaojiang Li [a], Ming Song [b,c], Wenhui Li [d,*], Qiuli Li [b,c,*]

[a] *Department of Head and Neck Surgery, The Third Affiliated Hospital of Kunming Medical University, 519 Kunzhou Road, Kunming, China*
[b] *Department of Head and Neck Surgery, Sun Yat-sen University Cancer Center, 651 Dongfeng Road East, Guangzhou, China*
[c] *State Key Laboratory of Oncology in South China, 651 Dongfeng Road East, Guangzhou, China*
[d] *Department of Radiotherapy, The Third Affiliated Hospital of Kunming Medical University, 519 Kunzhou Road, Kunming, China*

Accepted 24 June 2014
Available online 30 July 2014

Abstract

We have investigated the clinical characteristics and prognostic factors of squamous cell carcinoma (SCC) of the tongue after definitive radiotherapy for nasopharyngeal carcinoma, and evaluated the effect of common therapeutic regimens for these patients. We retrospectively reviewed follow-up data for patients whose nasopharyngeal carcinoma had been treated by radiotherapy, and selected the 68 who had then developed SCC of the tongue, in the border of the tongue in half, and in the dorsum in 25 (37%). Eight of the 68 patients had clinical lymph node metastasis (12%), and 45 presented with stage I-II disease at the time of the diagnosis of the SCC (66%). Resection or radiotherapy alone was an effective treatment for patients with stage I-II SCC of the tongue, but patients with stage III-IV disease had a poor prognosis, despite being given multidisciplinary treatment. Multivariate analysis showed that the risk factors that independently influenced the survival of these patients were use of alcohol, recurrence of their nasopharyngeal carcinoma, the latency period, and the clinical TNM stage. Tongue SCC after radiotherapy was generally at an early stage and commonly occurred on the border or the dorsum of the tongue, with few lymph node metastases. Resection or radiotherapy is an effective treatment, and the risk factors that independently influenced the survival of patients indicate that improving the technique of radiotherapy and close follow-up after nasopharyngeal cancer are vitally important.

Keywords: Nasopharyngeal carcinoma; Radiotherapy; Second primary tumour; Tongue squamous cell carcinoma; Latency period

Introduction

Although ionising radiotherapy is an effective treatment for malignant tumours, its use has been associated with the development of second primary tumours,[1–5] the occurrence and treatment of which is a topic of interest.[5]

Nasopharyngeal carcinoma is common in Southeast Asia, particularly in south China, and it affects 15-80/100,000 people in these regions. It is highly radiosensitive, and many patients survive for a long time.[3,4,6–8] The second primary

* Corresponding authors: Department of Head and Neck Surgery, Sun Yat-sen University Cancer Center, 651 Dongfeng Road East, Guangzhou 510060, China. Tel.: +86-20-87343767; fax: +86-20-87343392 (Q. Li), Department of Radiotherapy, The Third Affiliated Hospital of Kunming Medical University, 519 Kunzhou Road, Kunming 650118, China. Tel.: +86-871-68185656; fax: +86-871-68181942 (W. Li).
E-mail addresses: liql@sysucc.org.cn, lql2206@126.com (Q. Li), wenhuili64@aliyun.com (W. Li).
[1] C.S. and Z.H. contributed equally to the work and share first authorship.

http://dx.doi.org/10.1016/j.bjoms.2014.06.015

tumours that develop in these patients after radiotherapy include soft tissue sarcoma, osteosarcoma, squamous cell carcinoma (SCC), leukaemia, and neuroendocrine carcinomas, which may develop in the head and neck, oesophagus, lung, or stomach.[1,3,4,6,8–10] However, no studies of them (histologically limited to SCC) in a particular organ after radiotherapy for nasopharyngeal carcinoma have been reported. We have therefore collected the clinical and survival data of 68 patients with SCC of the tongue after treatment of a nasopharyngeal carcinoma at our hospital between January 1965 and December 2007. Their clinicopathological characteristics, treatment, and survival data were then analysed retrospectively.

Materials and Methods

Patients studied

This study was approved by the Ethics Committee of the Sun Yat-sen University Cancer Centre, and informed consent was obtained from all of the participants or their guardians before enrolment. The criteria used for the diagnosis of SCC of the tongue after radiotherapy were modified from those originally described by Cahan et al.[12] and Arlen et al.[13] and included the following: a previous history of irradiation for nasopharyngeal carcinoma, the development of a new cancer of the tongue, a latency period (from the end of the radiation treatment to the diagnosis of the SCC of the tongue) of no less than 6 months, and histological confirmation of the new diagnosis as SCC. The exclusion criteria were: the use of radiotherapy for a previous malignancy before the nasopharyngeal carcinoma, and development of the new cancer of the tongue as a result of a metastasis from, or recurrence of, the nasopharyngeal cancer.

Among 55,620 patients given definitive radiotherapy for nasopharyngeal carcinoma between January 1965 and December 2007, 68 patients met the criteria and were enrolled. All patients had been treated with definitive radiotherapy in median doses of 68 (range 56-87) Gy to the nasopharynx and 56 (range 48-76) Gy to the neck, which were delivered by 2-dimensional radiotherapy, three-dimensional conformal radiotherapy, or intensity-modulated radiotherapy. The size of fraction given daily was 2.0 Gy.[11]

Clinical data

The clinicopathological data and therapeutic regimens of the 68 patients are shown in Table 1. The median age at diagnosis of the SCC of the tongue was 52 years (range 31-72). Twelve patients had recurrences of their nasopharyngeal carcinoma, which were treated with further radiotherapy before the diagnosis of tongue SCC. The median size of the primary SCC of the tongue was 2.5 cm, range 0.2 -6.0, at diagnosis. Eight patients had clinical lymph node metastases (level I, n=5, and level II, n=3). Distant metastases (to the lung) developed in 1 patient. The stage of the tongue SCC was reclassified according to the 2010 criteria of the American Joint Committee on Cancer (AJCC),[14] and the chemotherapy regimens included bleomycin, cisplatin, and 5-fluorouracil, and paclitaxel and cisplatin. The external beam radiotherapy was given in a dose of 2 Gy/session (5/week), and the overall dose ranged from 56 to 68 Gy. When possible, patients were treated by operation with the goal of obtaining microscopically clear margins. We did 1 of 2 operations, either resection of the primary lesion alone (n = 25), or resection combined with neck dissection (n = 12).

Follow-up and statistical analysis

The patients were followed up until December 2012, and 20 patients developed recurrences: local recurrence (n=13), regional recurrence (n=3), locoregional recurrence (n=2), or distant metastases (n=2). One patient died during the perioperative period, and 56 patients died during the follow-up period. All data were analysed using PASW SPSS (version 18.0 SPSS, Chicago, IL, USA). Survival curves were generated using the Kaplan–Meier method, and the log-rank test was used for univariate analysis. For multivariate survival analysis we used a Cox proportional hazards model, and probabilities of less than 0.05 were accepted as significant difference.

Results

Survival analysis

The 3-year and 5-year overall survival were 56% and 43%, respectively, and the median survival was 39 (range 4-321) months. On univariate analysis smoking, drinking alcohol, T classification, N classification, clinical TNM stage, recurrence of the nasopharyngeal carcinoma, and the latency period significantly influenced the prognosis (Table 1). Multivariate analysis indicated that drinking alcohol, recurrence of the nasopharyngeal carcinoma, the latency period, and the clinical TNM stage were independent prognostic factors (Table 1, Figs. 1–3).

Evaluation of the therapeutic regimens according to clinical TNM stage

Among the patients with stage I-II disease, patients treated by resection or radiotherapy had a significantly better prognosis than those given chemotherapy, but there was no significant difference between the patients whose tumours were resected and those given radiotherapy (p=0.59) (Fig. 4). However, no significant differences were found among any of the therapeutic regimens for patients with stages III-IV disease (p=0.46) (Table 2).