



Neck dissection for oral mucosal melanoma: Caution of nodular lesion



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ARTICLE INFO

Article history:

Received 31 December 2013

Accepted 20 January 2014

Available online 16 February 2014

Keywords:

Oral
Melanoma
Neck dissection
Nodular
Prognosis

SUMMARY

Background: Oral mucosal melanoma (OMM) often metastasizes to cervical nodes. A great number of studies have been conducted to evaluate the efficacy of neck dissection in the treatment of OMM, but considerable controversy remains in this field.

Patients and methods: The clinical features, treatments, and outcomes of 254 OMM patients were retrospectively analyzed from Jan. 1998 to Jul. 2012. Multivariate analysis was performed to identify the variables related to overall survival (OS).

Results: Tumor size greater than 4 cm ($p = 0.01$) and nodular types ($p < 0.0001$) were independent prognostic factors for OS. Patients with nodular melanomas were more likely to have distant metastases than those with macular melanomas ($p < 0.0001$). 164 Patients (65%) had CLN metastases. The multivariate analysis revealed that prophylactic neck dissection was an independent favorable factor for OS ($p = 0.0016$) in patients with cN0 nodular melanomas; whereas radical neck dissection ($p = 0.03$) in patients with positive CLN. Patients undergoing functional neck dissection were more likely to have neck recurrence ($p < 0.001$).

Conclusion(s): Nodular type is a dangerous signal to OMM. It is advisable for patients with cN0 nodular melanomas to have prophylactic neck dissection, close observation is recommended for patients with cN0 macular melanomas, and patients with positive CLN should undergo radical neck resection.

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Introduction

Melanoma is a highly aggressive tumor arising from melanocytes that are found predominantly in epidermis and seldom in oral mucosal epithelium [1]. Oral mucosal melanoma (OMM) is extremely rare, accounting for less than 1% of all melanomas in the United State and about 7.5% in Asians [2,3]. The prognosis of OMM is poor in general, and reported 5-year overall survival (OS) varies between 12.3% and 35.3% [4–6]. Metastasis of cervical lymph nodes (CLN) is known to be a poor prognostic factor in OMM, and the rate of CLN involvement at diagnosis could reach more than 50% [7–9]. However, considerable controversy remains as to the necessity of prophylactic neck dissection and choice of neck dissection for CLN positive patients. There are only few studies on the OMM, most of which are case reports with only a few cases, and long term follow-up and multivariate analyses are lacking.

In this study, we retrospectively analyzed the clinical features, treatments, and outcomes of 254 OMM patients between 1998 and 2012 in the 9th Hospital of Shanghai Jiaotong University, a leading center for the treatment of OMMs in China that admits about 40 patients with primary OMMs per year. Specifically, we aim to (1) define the clinical features of OMM, (2) evaluate the efficacy of prophylactic neck dissection in cN0 patients, (3) compare the efficacy of radical and functional neck dissection in CLN positive patients, and (4) identify new prognostic factors for OMM.

Patients and methods

Patient selection

A total of 254 OMM patients (155 males and 99 females aged from 24 to 79 years at diagnosis, including 177 patients of <60 years and 77 patients of ≥ 60 years; mean age, 52 years) hospitalized in the 9th Hospital of Shanghai Jiaotong University from Jan. 1998 to Jul. 2012 were eligible for this study. The data collected included gender, age, primary site, tumor size, tumor type, CLN, therapy mode, and survival time. Patients were excluded if they were above 80 years of age, had tumors originating from lip,

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amelanotic melanomas, distant metastasis at diagnosis, unresectable tumors, or prior radiotherapy.

The primary disease was diagnosed by biopsy, and the immunohistochemical staining of HMB-45, Melan-A, and S-100 protein was used as markers for diagnosis. All histological stainings were reviewed by pathologists in our hospital. CLN was evaluated by clinical examination, ultrasound or radiological examination, including the magnetic resonance imaging (MRI), computed tomography (CT). The final diagnosis was confirmed by the pathological examination after neck dissection.

Once the diagnosis was confirmed, a radical resection was performed in all patients for primary lesions with at least 1.5 cm of healthy tissue. Prophylactic, functional, or radical neck dissection was performed for different patients. Postoperative chemotherapy with DTIC (dacarbazine injection, Nanjing Pharmaceutical Factory Co. Ltd., Jiangsu, China) and CDDP (cisplatin injection, Qilu Pharmaceutical Co. Ltd., Shandong, China) was repeated every 3 weeks for 2 circles for cN0 patients and 4 circles for CLN positive patients. DTIC was administered on day 2–5 at a dose of 250 mg/m², and CDDP on day 1 at a dose of 75 mg/m² (with hydration).

Statistical analysis

Survival was measured from the date of pathologic diagnosis. Patients still alive in Jul. 2012 or lost to follow-up were censored. Outcome was defined by overall survival (OS).

Statistical analysis was performed using SAS 9.13. The survival rate was calculated by the Kaplan–Meier method. The prognostic variables included gender, age, primary site, tumor size, tumor type, CLN, and therapy mode. The statistical significance of differences between survival curves was established by the log-rank test, and multivariate analysis was performed with the Cox proportional hazard model.

Results

Table 1 shows the tumor characteristics of the 254 patients. The median follow-up for survivors was 80 months (range, 6–153 months), and the five-year OS was 30.5% (Fig. 1a). The log-rank test showed that age did not correlate with prognosis ($p = 0.78$). Lesions occurred on hard palate in 124 patients (48.8%; Fig. 2a),

Table 1
5-Year OS of all patients by prognostic variables.

Variable	No. of patients	5-Year OS %	P	
			Univariate	Multivariate
Sex			0.14	–
Men	155	27		
Women	99	35		
Age			0.78	–
<60 y	177	31		
≥60 y	77	29		
Primary site			0.61	–
Palate	124	30		
Maxillary gum	77	26		
Mandible gum	39	25		
Tumor size			<0.001	0.01
<4 cm	99	48		
≥4 cm	155	18		
Tumor type			<0.0001	<0.0001
Macular	108	62		
Nodular	146	6		
CLN			<0.001	<0.0001
Positive	164	25		
Negative	90	39		
Neck dissection			0.002	0.46
Yes	216	21		
No	38	48		

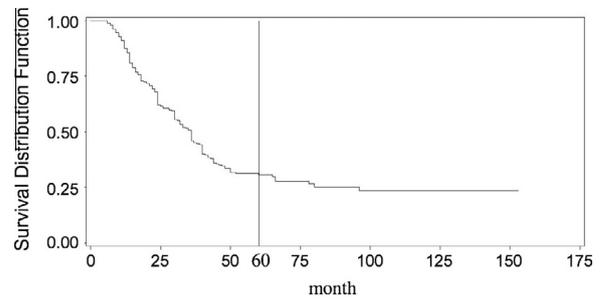


Figure 1a. The overall survival of all patients.

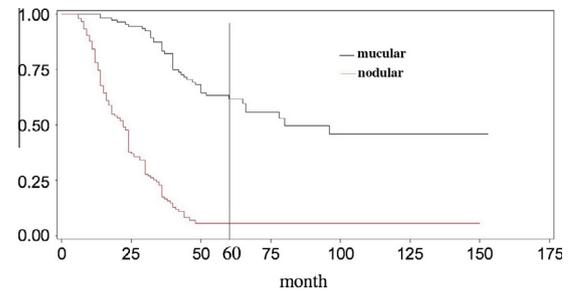


Figure 1b. The overall survival by tumor types.

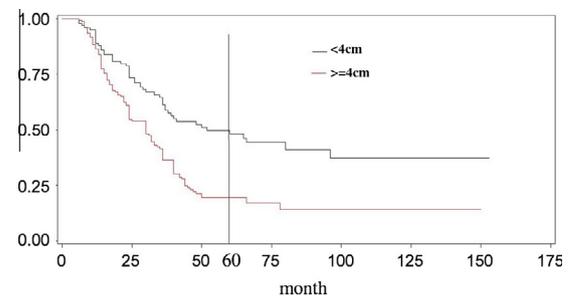


Figure 1c. The overall survival by tumor size.

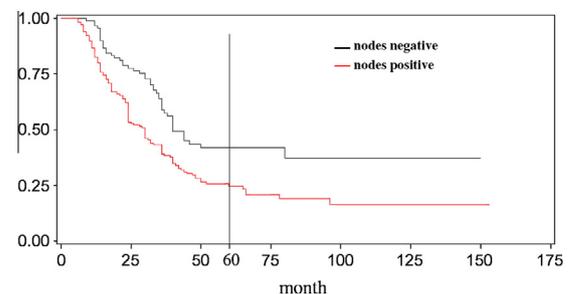


Figure 1d. The overall survival by cervical lymph nodes.

maxillary gum in 77 patients (30.3%; Fig. 2b), mandible gum in 39 patients (15.4%; Fig. 2c), buccal in 12 patients (4.7%; Fig. 2d), and tongue in 2 patients (0.8%; Fig. 2e). The log-rank test showed that primary site did not correlate with prognosis ($p = 0.61$).

Tumor type and tumor size were critical prognostic factors in OMM

Clinically, pigmented OMM lesions can be macular or nodular [10]. The surface of the macular melanoma was smooth and flat with an overlying mucosa (Fig. 3). Patients with macular mucosal melanomas generally have a long history of oral melanin

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