

## Case Report

# En block resection of a giant gingival malignant melanoma with mandible invasion - a case report

Xiaoshan Wu, Bailan Huang, Qingping Gao, Xinchun Jian, Feng Guo

Department of Stomatology, Xiangya Hospital, Central South University, Xiangya Road 87#, Changsha 410008, Hunan Province, China

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**Abstract:** Oral malignant melanoma (OMM) is a rare tumor of the oral cavity with very poor prognosis. This paper aims to present a rare case and a comprehensive review of clinical feature and treating methods. We report a case of a giant gingival malignant melanoma with mandible invasion and regional lymph node metastases. The tumor was dissected 1.5 cm beyond the tumor margins and hemimandibulectomy with disarticulation was performed. Incontinuity dissection of primary tumor and cervical lymph nodes was completed. Anterolateral thigh flap was used to reconstruct the defect of mouth floor. Immunotherapy (Interleukin-2) was carried out after surgery. An inclined bite plane was placed to maintain the normal occlusion. There was a satisfactory result and no symptoms of recurrence 18 months after surgery. Early diagnosis and aggressive surgical treatment combined with immunotherapy may provide better outcome to patients.

**Keywords:** Oral, melanoma, surgery

## Introduction

Oral mucosal melanoma (OMM) is a rare neoplasm arising from melanocytes with the incidence ranging from 0.2% to 8.0% of all melanoma cases [1]. Sex, age, race and other factors are found to be correlated with the incidence of the disease. Men are affected more frequently than women and have a worse prognosis [2, 3]. The fifth decade of life is the peak age for the diagnosis [4]. Besides, the incidence of OMM is found more frequent in white population [5, 6].

OMM is more frequently seen on the hard palate and maxillary gingiva. Surface pigmentation and painless swelling are the main primary symptoms [2, 7]. OMM is thought to be distinct from cutaneous melanomas because of its different growth pattern and very poor prognosis [8]. The clinical staging is regarded to be the most important prognostic factor. Other prognostic factors include the thickness and size of the tumor, lymph node metastases, age, anatomic site, and presence or absence of ulceration [8]. The 3-year and 5-year overall survival (OS) rates of 51 cases of OMM are 35.0% and

20.7%, respectively. Patients of age  $\geq 55$  years and size  $\geq 4$  cm have a lower survival rate than those of aged  $< 55$  years and size  $< 4$  cm [9]. Despite good regional control, most of patients die owing to distant metastases to lungs, brain, liver, and bones.

To date, there is still much controversy regarding the classification, prognosis and treatment plan of OMM. Since mucosal melanoma carries a bad prognosis, it is necessary to discuss the treatment plan before the treatment is applied on OMM patients. Here we present a case of a giant gingival malignant melanoma with mandible invasion and regional metastasis. En block resection including primary tumor, surrounding mandible, and cervical lymph nodes was done on the patient. Anterolateral thigh flap was used to reconstruct the defect of mouth floor. Immunotherapy (Interleukin-2) was carried out after surgery. Satisfactory result was obtained 18 months after surgery.

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A 50-year-old male patient reported to the Department of Oral and Maxillofacial Surgery



**Figure 1.** Presurgical intra-oral view.

with complaint of a pigmented mass in the mandibular gingiva for 3 months (**Figure 1**). Three months ago, he went to a dental clinic because of constant “toothache” and then he was informed there was a pigmented mass in the mandibular gingiva. The mass grew bigger significantly in the 3 months, but was not associated with any ulceration, bleeding or numbness of lower lip.

Extraoral examination revealed an enlargement left submandibular lymphnode, which was oval in shape, immovable and nontender on palpation. Intraoral examination showed an elevated pigmented lesion, measuring about 4 cm on the buccal aspect of the left mandibular region, extending from the third molar to the first premolar, and about 7 cm on the lingual aspect of the left mandibular region, extending from the third molar to the lateral incisor. From the buccal to lingual side, the maximum thickness of the tumor was about 3.5 cm. The degree of pigmentation of the lesion mucosa was not homogeneous. The obvious dark region ranged from the third molar to the first molar on the lingual side, however, the light pigmented region extended to the lateral incisor. The satellite lesions were small pigmented dots found 0.5 cm beyond the frontier edge of the lingual side (**Figure 1**). A presumptive diagnosis of OMM was made by medical history and clinical examination.

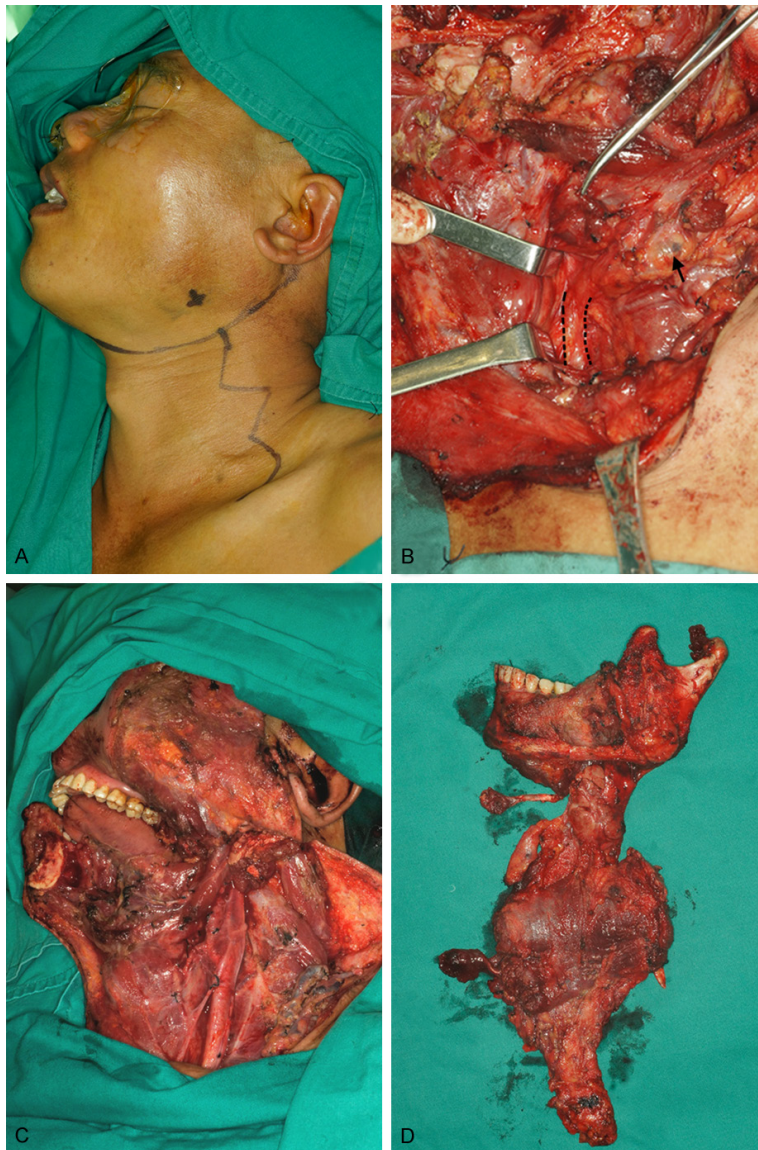
In detecting mandibular invasion, cone-beam computed tomography (CBCT) was performed and alveolar bone encroaching was found beneath the first, second, and third molars. The

hemimandibulectomy with disarticulation was planned due to the bone invasion. To choose whether or not to do neck dissection, and the method of neck dissection, the frozen biopsy of the suspicious metastatic submandibular lymph node was completed first before the tumor excision. The result confirmed the diagnosis of OMM and therefore the radical neck dissection was selected.

During the radical neck dissection, the frozen biopsies of another two suspicious lymph nodes from two regions (a superior deep cervical lymphatic node and a superior clavicular lymphatic node) were completed and the results were also positive. Since some lymph nodes were often found in the floor of mouth, the intermediate tissue of the floor of mouth was also resected, to assure en bloc excision of the tumor together with cervical lymph nodes. The tumor was dissected about 1.5 cm beyond the tumor margins and hemimandibulectomy was performed (**Figure 2A-D**). The jugular lymphatic trunk of left side was found obvious, in hard texture and wide in diameter, probably because of the dominated lymphatic drainage pathway for the metastases (**Figure 2B**). Anterolateral thigh flap was used to reconstruct the defect of mouth floor. Regarding the bad outcome of this tumor, hard tissue reconstruction was not performed this time. Reconstruction plate was not placed either. Biotherapy of hypodermic injection of Interleukin 2 (3,000,000 U) 16 times was carried out after surgery.

There was a satisfactory result and no symptoms of recurrence 18 months after surgery. An inclined bite plane was designed to prevent the displacement of the mandible after the resection of the affected side. It was placed inside to maintain the normal occlusion one week after surgery (**Figure 3A-C**).

Histopathological study (hematoxylin and eosin staining) revealed numerous atypical melanocytes existing both primary tumor (**Figure 4A, 4B**) and metastatic lymph node (**Figure 4C, 4D**). These cells were distributed into sheets and groups and were found in spindle and epithelioid shapes. In the mucosa of primary tumor, they were mainly located in the lamina propria. Epidermal infiltrating and migration were observed in the dermoepidermal junction (**Figure 4A, 4B**). The nuclei were hyper-



**Figure 2.** A. Presurgical incision marking line; B. Cervical lymphadenectomy: the arrow points to a black lymph node; the broken line shows the obvious jugular lymphatic trunk of left side; C. The view of head and neck after cervical lymphadenectomy; D. In-continuity of the mandible tumor and the cervical lymph nodes.

chromatic, prominent and with vesicular (Figure 4A-D).

## Discussion

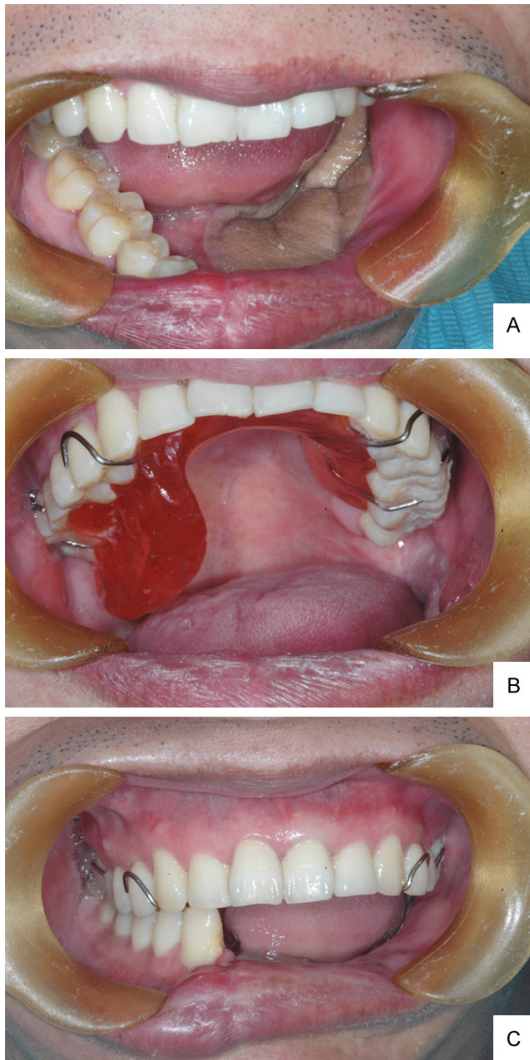
Clinical types of malignant melanoma include amelanotic, mucosal, subungual, ulcerated, and verrucous phenotypes [10]. The coloration of OMM has a wide range, which can appear as black, gray, purple, or even reddish. About 10% of oral melanomas are amelanotic. These amelanotic malignant melanomas have a worse

prognosis than other kinds [2]. It is believed that traditional staging system for cutaneous malignant melanoma, including Breslow's depth of penetration and Clark's level of invasion, was not suitable for the classification of OMM [8]. To provide specific guidelines, Prasad proposed a clinical staging system with histopathologic micro staging [11]. Recently, AJCC-TMN cancer staging is applied to classify mucosal melanoma of the head and neck. There is no tumor size T1 and T2 and no clinical stage I and II under this new classification, because of the bad prognosis of this disease. T3 is defined as the tumor located in the epithelium or submucosa. T4a is moderately advanced and is defined as the deep tissues like bone, cartilage or skin are encroached. T4b is very advanced and is defined as the important artery, nerve or other organs are encroached. Regarding stage grouping, stage III is T3N0M0, stage IVA is T4aN0M0 and T3-4aN1M0, stage IVB is T4bAnyN and stage IVC is AnyTAnyNM1 [7, 12]. In this classification, the current OMM case was in stage IVA (T4aN1M0).

Histologically, junctional activity and epidermal migration of atypical melanocytes can be observed in primary melanomas [13]. Atypical melanocytes are often found in the dermoepidermal junction of OMM. These cells are in sheets and nests separated by scant fibrous stroma. They are usually larger than the normal ones and have varying degrees of nuclear pleomorphism and hyperchromatism [4]. Prominent nucleoli and high mitotic activity are also prominent features of the tumor cells. In some cases, tumor was seen infiltrating into the superficial squamous epithelium in a pagetoid fashion [14]. Immunohistochemical studies



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**Figure 3.** A. Intra-oral view 18 months after surgery; B. Intra-oral view with the inclined bite plane; C. The satisfactory occlusion with the inclined bite plane.

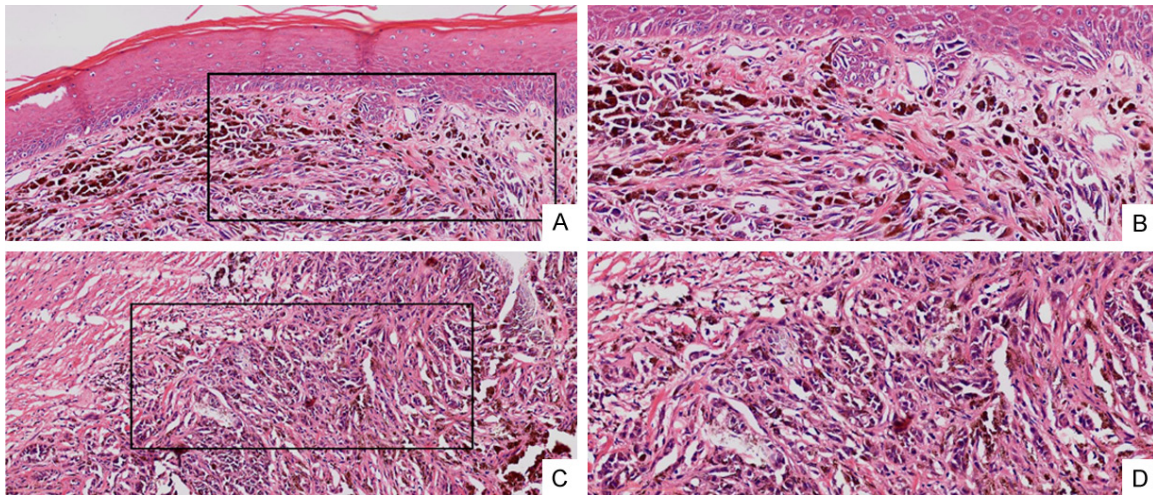
show the positive expressions of S-100 protein, MART-1, and HMB-45 in the lesional cells. Immunohistochemical staining is beneficial to distinguish OMM from other malignancies [3, 4].

The radical resection with negative margin is regarded as the main therapy for OMM, and radiotherapy and chemotherapy are only adjuvant to surgery [8]. Post-operative chemotherapy with/without radiotherapy is suggested for the OMM patients with advanced nearby invasion [7]. One study shows that only 53% cases of radiotherapy group without surgery have controlled primary lesion, compared with 92.3% cases of surgery group [15].

Negative margins are sought during the surgery. It is reported that positive surgical margins are found in about 43% OMM patients and patients with positive margins had a 21-fold increase in dying risk [16, 17]. However, negative margins may be difficult to achieve because of the microscopic spread and the proximity of vital structures [8, 18]. In this case, satellite lesions were observed 0.5 cm beyond the extending margin in the lingual gingival of the mandible, and it caused difficulty to define the real tumor margin. Compared with cutaneous malignant melanoma, OMM does not need to invade deeply before reaching the bone. Most OMM cases present at a more advanced stage with nearby organs being involved. To achieve the negative margins, some researchers choose to make the extended resection with subtotal maxillectomy for lesions of the hard palate and maxillary gingival, and make marginal mandibulectomy for lesions of the mandibular gingiva regardless of the size. If the lower cranial nerves, masticator space and other important tissues are involved, the more aggressive method of segmental mandibulectomy is selected [7, 8].

Another argument area is whether or not to do neck dissection. Various authors have reported about 25-50% of patients with OMM had regional lymph node metastases [15, 19, 20]. Recently, most authors agree that neck dissection is recommended in OMM patients with clinically positive lymph node metastasis (LNM), and the choice of the neck dissection modality should be guided by the extent and the level of nodes [21]. However, there are still some debates on the issue of neck dissection in the clinically LNM negative patients. Some research shows that regional metastases and prophylactic neck dissection does not affect the prognosis and survival [15, 22, 23], but other studies shows LNM is significantly correlated with survival rate in the OMM patients [24, 25]. Krengli et al. reported that the regional recurrence rate was 77% for OMMs, suggesting the potential advantage for prophylactic neck dissection in these patients [26]. Another important issue is that clinically negative LNM is not equal with pathological negative LNM. One study found that about 44.4% of the clinically LNM negative patients were confirmed with pathological positive LNM. As a result, it is proposed that radical neck dissec-

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**Figure 4.** Histopathological pictures (the black rectangle region in (A) ( $\times 20$ ) is magnified as (B) ( $\times 100$ ); the black rectangle region in (C) ( $\times 20$ ) is magnified as (D) ( $\times 100$ )). (A, B) Histopathological section of mucosa of primary tumor; (C, D) Histopathological section of the metastatic lymph node.

tion should be planned in patients with clinically positive LNM while functional neck dissection should be planned in patients with clinically negative LNM [7]. Besides, sentinel lymph node biopsy (SLNB) may provide an alternative to identify patients who could benefit from a standard neck dissection [27]. In this case, we only found one clinically positive lymph node in the submandibular area before surgery, but by frozen biopsy, three lymph nodes of different regions were all pathological positive during the radical neck dissection.

There is a debate on whether cutting into an OMM for incisional biopsy would lead to seeding of tumor cells into bloodstream or lymphatics or not. Martin et al studied the differences among complete surgical excision, incisional biopsy, and shave biopsy, and found there was no evidence that biopsy type adversely affected locoregional or distant recurrence [28]. However, some other scholars believe that cutting into an OMM for incisional biopsy may lead to seeding of tumor cells into bloodstream or lymphatics [8]. Furthermore, some scholars believe that all surgical procedures including biopsy have negative effect on the prognosis and survival rate. One research showed that the 5-year survival rates of patients who underwent surgical procedures including biopsy were lower than those who did not undergo such procedures [29]. Another research showed that the distant metastasis rate of the patients who underwent surgical procedure was higher than those who did not undergo such procedures

[15]. In this case, the frozen biopsies of the cervical lymph nodes during surgery were performed instead of preoperative incisional biopsy. This step may help to prove the clinical diagnosis before the tumor excision.

Traditional neck dissection completed below the lower border of the mandible and the lingual nerve is generally considered adequate for removal of lymph nodes at risk for metastases from oral cavity cancer. However, deep biopsy of floor of mouth revealed lymph nodes located in the superficial floor of mouth associated with the sublingual gland above the lingual nerve. In the oral squamous cell carcinoma, positive metastasis is often found in the superficial floor of mouth lymph node and it is often missed during traditional practice of discontinuous neck dissection [30, 31]. Compared to the discontinuous neck dissection, in-continuity dissection of primary tumor and neck nodes in squamous cell carcinoma of the oral cavity proves a lower neck recurrence rate and a higher 5-year survival rate. Since lymphatic drainage is the main pathway for the metastases of OMMs and oral malignant tumors share one lymphatic drainage pathway [32], it may be useful to complete in-continuity dissection of primary tumor and neck nodes on the OMM patients.

### Conclusion

Primary OMM is a rare tumor with very poor prognosis. Because of the proximity of mandi-



ble bone, aggressive mandible resection can be performed for the cases of the giant mandibular gingiva malignant melanomas. En block resection of primary tumor and cervical lymph nodes may have positive effect on reducing regional recurrence of OMM. An inclined bite plane can help to maintain the occlusion temporarily before the hard tissue reconstruction.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Feng Guo, Department of Stomatology, Xiangya Hospital, Central South University, Xiangya Road 87#, Changsha 410008, Hunan Province, China. Tel: 86-731-89753046; E-mail: dentguofeng@163.com

## References

- [1] Rapini RP, Golitz LE, Greer RO Jr, Krekorian EA and Poulson T. Primary malignant melanoma of the oral cavity. A review of 177 cases. *Cancer* 1985; 55: 1543-1551.
- [2] Kruse AL, Riener MO, Graetz KW and Luebbbers HT. Mucosal malignant melanomas in head and neck surgery: a retrospective study of six patients and review of the literature. *Oral Maxillofac Surg* 2010; 14: 143-147.
- [3] Santos RS, Andrade MF, Alves Fde A, Kowalski LP and Perez DE. Metastases of Melanoma to Head and Neck Mucosa: A Report of Short Series. *Clin Exp Otorhinolaryngol* 2016; 9: 80-84.
- [4] Hashemi Pour MS. Malignant melanoma of the oral cavity: a review of literature. *Indian J Dent Res* 2008; 19: 47-51.
- [5] Moreno MA and Hanna EY. Management of mucosal melanomas of the head and neck: did we make any progress? *Curr Opin Otolaryngol Head Neck Surg* 2010; 18: 101-106.
- [6] Manolidis S and Donald PJ. Malignant mucosal melanoma of the head and neck: review of the literature and report of 14 patients. *Cancer* 1997; 80: 1373-1386.
- [7] Yang X, Ren GX, Zhang CP, Zhou GY, Hu YJ, Yang WJ, Guo W, Li J and Zhong LP. Neck dissection and post-operative chemotherapy with dimethyl triazeno imidazole carboxamide and cisplatin protocol are useful for oral mucosal melanoma. *BMC Cancer* 2010; 10: 623.
- [8] Mohan M, Sukhadia VY, Pai D and Bhat S. Oral malignant melanoma: systematic review of literature and report of two cases. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013; 116: e247-254.
- [9] Sun CZ, Chen YF, Jiang YE, Hu ZD, Yang AK and Song M. Treatment and prognosis of oral mucosal melanoma. *Oral Oncol* 2012; 48: 647-652.
- [10] De Vries E BF, Coebergh JW. Malignant melanoma: Introduction. In: LeBoit PE BG, Weedon D, editors. *World Health Organization Classification of Tumors. Pathology and Genetics of Skin Tumors*. Lyon: IARC Press; 2006. pp. 56.
- [11] Prasad ML, Patel SG, Huvos AG, Shah JP and Busam KJ. Primary mucosal melanoma of the head and neck: a proposal for microstaging localized, Stage I (lymph node-negative) tumors. *Cancer* 2004; 100: 1657-1664.
- [12] Edge SB BD, Compton CC, Fritz AG, Greene FI, Trotti A. Mucosal melanoma of the head and neck. In: Edge SB BD, Compton CC, Fritz AG, Greene FI, Trotti A, editors. *AJCC cancer staging manual*. New York: Springer; 2010. pp. 97-100.
- [13] Billings KR, Wang MB, Sercarz JA and Fu YS. Clinical and pathologic distinction between primary and metastatic mucosal melanoma of the head and neck. *Otolaryngol Head Neck Surg* 1995; 112: 700-706.
- [14] Venugopal M, Renuka I, Bala GS and Sessaiah N. Amelanotic melanoma of the tongue. *J Oral Maxillofac Pathol* 2013; 17: 113-115.
- [15] Tanaka N, Mimura M, Ogi K and Amagasa T. Primary malignant melanoma of the oral cavity: assessment of outcome from the clinical records of 35 patients. *Int J Oral Maxillofac Surg* 2004; 33: 761-765.
- [16] McLean N, Tighiouart M and Muller S. Primary mucosal melanoma of the head and neck. Comparison of clinical presentation and histopathologic features of oral and sinonasal melanoma. *Oral Oncol* 2008; 44: 1039-1046.
- [17] Penel N, Mallet Y, Mirabel X, Van JT and Lefebvre JL. Primary mucosal melanoma of head and neck: prognostic value of clear margins. *Laryngoscope* 2006; 116: 993-995.
- [18] Bachar G, Loh KS, O'Sullivan B, Goldstein D, Wood S, Brown D and Irish J. Mucosal melanomas of the head and neck: experience of the Princess Margaret Hospital. *Head Neck* 2008; 30: 1325-1331.
- [19] Rogers RS 3rd and Gibson LE. Mucosal, genital, and unusual clinical variants of melanoma. *Mayo Clin Proc* 1997; 72: 362-366.
- [20] Meleti M, Leemans CR, Mooi WJ, Vescovi P and van der Waal I. Oral malignant melanoma: a review of the literature. *Oral Oncol* 2007; 43: 116-121.
- [21] White N, Yap LH and Srivastava S. Lymphadenectomy for melanoma in the clinically N1 neck: radical, modified radical, or selective? *J Craniofac Surg* 2009; 20: 385-388.
- [22] Snow GB, van der Esch EP and van Slooten EA. Mucosal melanomas of the head and neck. *Head Neck Surg* 1978; 1: 24-30.

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- [23] Lens MB, Nathan P and Bataille V. Excision margins for primary cutaneous melanoma: updated pooled analysis of randomized controlled trials. *Arch Surg* 2007; 142: 885-891; discussion 891-883.
- [24] Umeda M and Shimada K. Primary malignant melanoma of the oral cavity—its histological classification and treatment. *Br J Oral Maxillofac Surg* 1994; 32: 39-47.
- [25] Temam S, Mamelle G, Marandas P, Wibault P, Avril MF, Janot F, Julieron M, Schwaab G and Luboinski B. Postoperative radiotherapy for primary mucosal melanoma of the head and neck. *Cancer* 2005; 103: 313-319.
- [26] Krengli M, Masini L, Kaanders JH, Maingon P, Oei SB, Zouhair A, Ozyar E, Roelandts M, Amichetti M, Bosset M and Mirimanoff RO. Radiotherapy in the treatment of mucosal melanoma of the upper aerodigestive tract: analysis of 74 cases. A Rare Cancer Network study. *Int J Radiat Oncol Biol Phys* 2006; 65: 751-759.
- [27] Sugiyama VE, Chan JK and Kapp DS. Management of melanomas of the female genital tract. *Curr Opin Oncol* 2008; 20: 565-569.
- [28] Martin RC 2nd, Scoggins CR, Ross MI, Reintgen DS, Noyes RD, Edwards MJ and McMasters KM. Is incisional biopsy of melanoma harmful? *Am J Surg* 2005; 190: 913-917.
- [29] Umeda M, Komatsubara H, Shigeta T, Ojima Y, Minamikawa T, Shibuya Y, Yokoo S and Komori T. Treatment and prognosis of malignant melanoma of the oral cavity: preoperative surgical procedure increases risk of distant metastasis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; 106: 51-57.
- [30] Dutton JM, Graham SM and Hoffman HT. Metastatic cancer to the floor of mouth: the lingual lymph nodes. *Head Neck* 2002; 24: 401-405.
- [31] Leemans CR, Tiwari R, Nauta JJ and Snow GB. Discontinuous vs in-continuity neck dissection in carcinoma of the oral cavity. *Arch Otolaryngol Head Neck Surg* 1991; 117: 1003-1006.
- [32] Starek I, Koranda P and Benes P. Sentinel lymph node biopsy: A new perspective in head and neck mucosal melanoma? *Melanoma Res* 2006; 16: 423-427.