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Case Report

Treatment modality of malignant melanoma that metastasized to the mandible and multiple organs: A rare case report and the literature review

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ABSTRACT

Malignant melanoma is a neoplasm that arises from melanocytes or melanocytic lesion. It occurs on oral mucosa as a primary lesion or as a metastatic lesion from other organs. It usually metastasizes to the lymph node, lung, and brain. Metastatic melanoma primarily arising from other organs and spreading to the mandible is very rare so its treatment modality is not established yet. Surgery, chemotherapy, radiotherapy, and immunotherapy are applied in various ways but survival rate is still low. General condition of the patient, age, site and number of metastasis, and patient's will to treat must be considered when treating complicated patients.

We report a case of metastatic malignant melanoma which primarily arose from the left great toe and metastasized to mandible and a review of previous reports and recent treatment modalities of metastatic melanoma.

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1. Introduction

Melanoma is a malignant neoplasm that arises from benign melanocytic lesion or *de novo* from melanocytes within the tissue that melanocytes exist. Acute sun damage, especially UV radiation, affects the development of malignant melanoma. Mutations in the tumor suppressor gene CDKN2A and the oncogene *N-ras* and *H-ras* are known to be associated with the development of melanoma. [1] According to recent studies in molecular biology, the mutation of BRAF-gene kinase also plays a role in its development. [2]

Metastatic melanoma to mandible is very rare. Lymph nodes and lung are the most frequently involved metastasis sites, while oral cavity and esophagus occupy only 9.3 percent [3]. To the best of our knowledge, since 1941, there were only 17 reported cases of

malignant melanoma metastasized to mandible region [4]. Herein we present a case of metastatic malignant melanoma that primarily arose from the left great toe and spread to mandible and multiple organs later.

2. Report of a case

A 39-year-old man visited the Department of Oral and Maxillofacial Surgery of Yonsei University Dental Hospital. He was referred for gingival swelling and ulceration on the left retromolar trigone. At the time of visit, surface ulceration, necrosis, and irregular surface with black pigmentation were observed on the left retromolar trigone. Bleeding tendency and tenderness to palpation were not present (Fig. 1). Jaw cone-beam computed tomography and magnetic resonance imaging were taken (Fig. 2) and incisional biopsy was done. The pathology was reported as metastatic malignant melanoma.

In November 2009, he went to the Department of Orthopedic Surgery for a small skin lesion on the left great toe and was diagnosed with malignant melanoma. He had no specific medical history and drug allergy. He had smoked half a pack a day for 20 years. Left great toe amputation and inguinal lymph node dissection followed by 4 weeks of high dose interferon adjuvant chemotherapy were done. One year after the toe surgery, a small nodule was

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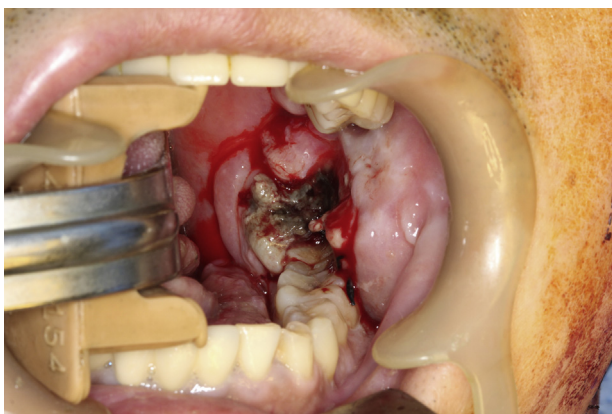


Fig. 1. Preoperative clinical photograph showing ulcerative lesion on retro-mandibular trigone with black pigmentation.

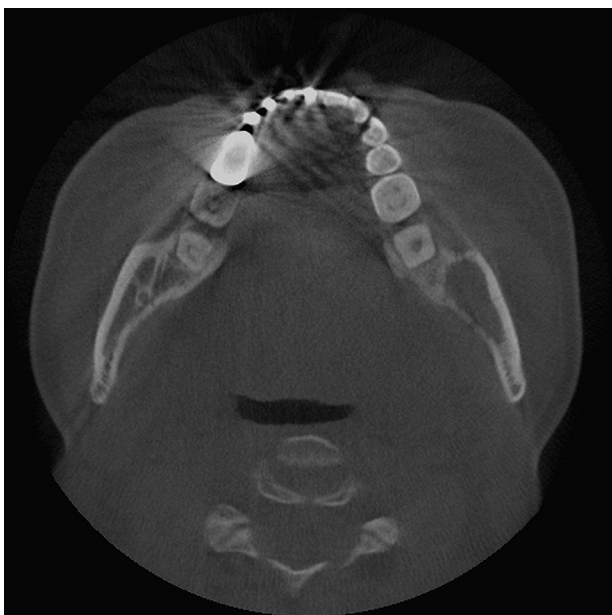


Fig. 2. Cone-beam CT image showing radiolucency on the left mandibular angle area.

detected on chest computed tomography suggesting lung metastasis and left upper lobe wedge resection was done. Eighteen months after the initial diagnosis, sigmoid colon thickening was newly detected on positron emission tomography-computed tomography (PET-CT). The colonoscopic biopsy result was also metastatic malignant melanoma so he underwent chemotherapy with dacarbazine. During chemotherapy, metastasis on descending colon and small bowel was detected. Laparoscopic segmental bowel resection was done and the pathology was read as metastatic malignant melanoma. Two weeks after laparoscopic surgery, he complained of symptoms of gingival swelling and was referred to the Department of Oral and Maxillofacial Surgery. After we confirmed the pathology report of incisional biopsy, we did an operation under general anesthesia to perform the following: extraction of #36 and 37, wide excision with segmental mandibulectomy, selective neck dissection (level I to II), hard tissue reconstruction with reconstruction plate, soft tissue reconstruction with radial forearm free flap, repair of donor site defect with split thickness skin graft from thigh. The pathologic diagnosis was metastatic malignant melanoma from the left great toe (Fig. 3). The neck node was positive on level II. The patient was discharged 12 days after the surgery without complication. He was referred to the Department of Oncology for

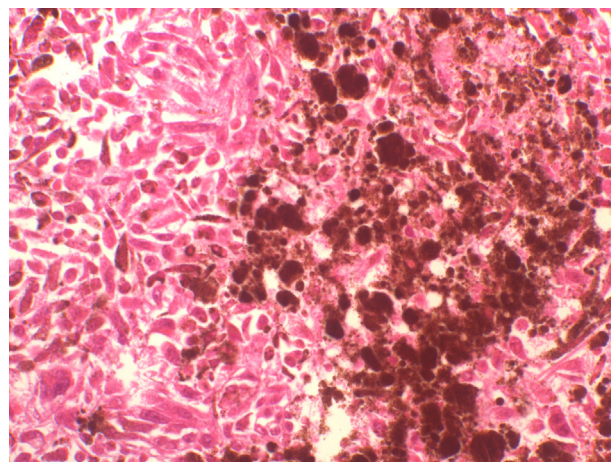


Fig. 3. Histopathology at 400× magnification (H–E stain). Microscopic features revealed atypical spindle-shaped or epithelioid melanocytes with nuclear pleomorphism and hyperchromatism. Abundant deposits of melanin granules were also identified.

additional chemotherapy. Although there has been no newly developed lesion on follow-up brain magnetic resonance imaging, there showed an abnormal uptake by the lung, colon and femur on PET-CT. Regardless of supplemental chemotherapy with carboplatin and paclitaxel, lung mass observed in follow-up chest CT was growing progressively. After 8 months of our operation, the patient was transferred for hospice care. We presume the patient expired as his medical insurance was invalid since February 2014.

3. Discussion

Malignant melanoma is one of the most aggressive skin cancers which develop from benign melanocytic lesion or *de novo*. The incidence has been increasing during the last 20 years. [18] There has been only 17 English-translated case reports that malignant melanoma metastasized to the mandible since De Chonoky first reported it in 1941 [4]. We investigated the past 17 case reports from the literatures and analyzed them with our case (Table 1).

Age and sex were identified in 15 cases. The age was distributed broadly from 16 to 68 years. However, most patients were middle-aged. There was no sex predominance; male and female were in same proportion. There were 12 cases that metastasized to posterior mandible and 2 cases that metastasized to anterior mandible. Four cases did not specify anterior or posterior. There was no difference between right side and left side of mandible. There were 6 cases that metastasized to contralateral side. Various treatment methods including surgical resection, immunotherapy, chemotherapy and radiotherapy were applied to treat mandibular metastatic lesions. Although the survival period has been extended compared to earlier days, the prognosis of metastatic malignant melanoma is still poor. The reported median survival period was only 8 months and a 3-year survival rate was estimated as less than 15 percent. [19]

The malignant melanoma cannot occur on bone primarily, because the melanocyte originates from the neural crest [14]. Our patient had already been diagnosed with malignant melanoma of the great toe with multiple metastases and our pathology report also confirmed metastatic malignant melanoma.

A recent report suggests surgical resection, chemotherapy and immunotherapy for treating distant metastatic disease without brain metastasis [20]. Thus, he underwent palliative surgery followed by chemotherapy with carboplatin and paclitaxel.

Atallah et al. [21] reported that resection of solitary metastatic melanoma contributes to prolonged survival and has palliative

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