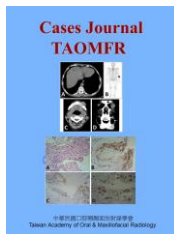


## Metastasis of Hepatocellular Carcinoma into the Mandible: A Case Report

Weng-Chen Wang<sup>1,2,3</sup>, Ching-Yi Chen<sup>1,2</sup>, Yuk-Kwan Chen<sup>1,2,4\*</sup>

<sup>1</sup>School of Dentistry, College of Dental Medicine, and <sup>2</sup>Oral & Maxillofacial Imaging Center, Kaohsiung Medical University, Kaohsiung, Taiwan; <sup>3</sup>Department of Dentistry, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan; <sup>4</sup>Division of Oral Pathology & Maxillofacial Radiology, Department of Dentistry, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan



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\*Corresponding author. Address: School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, 100, Shih-Chuan 1st Road, Kaohsiung, Taiwan

Tel.: +886 7 3121101~7107; fax: +886 7 3210637. E-mail: yukkwa@kmu.edu.tw (Y.-K. Chen)

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**H**epatocellular carcinoma (HCC) is uncommon in Europe and United States [1] but this disease has a relatively higher prevalence in Southeast East Asian countries including Taiwan where hepatitis B and C viral infections are the usual predisposing etiological factors [2]. Extrahepatic metastasis of HCC into oral and maxillofacial (OMF) region is infrequent. We hereby reported an uncommon case of HCC metastasis into the mandible.

### CASE PRESENTATION

A 57-year-old Taiwanese man had a diagnosis of HCC caused by hepatitis B viral infection as well as liver cirrhosis. Computed tomography (CT) of the abdomen revealed HCC in the bilateral hepatic lobes (Fig. 1A) and bone scan revealed no bony lesions at that time (Fig. 1B). The patient had received treatment with transcatheter arterial embolization and radiofrequency ablation with partial response.

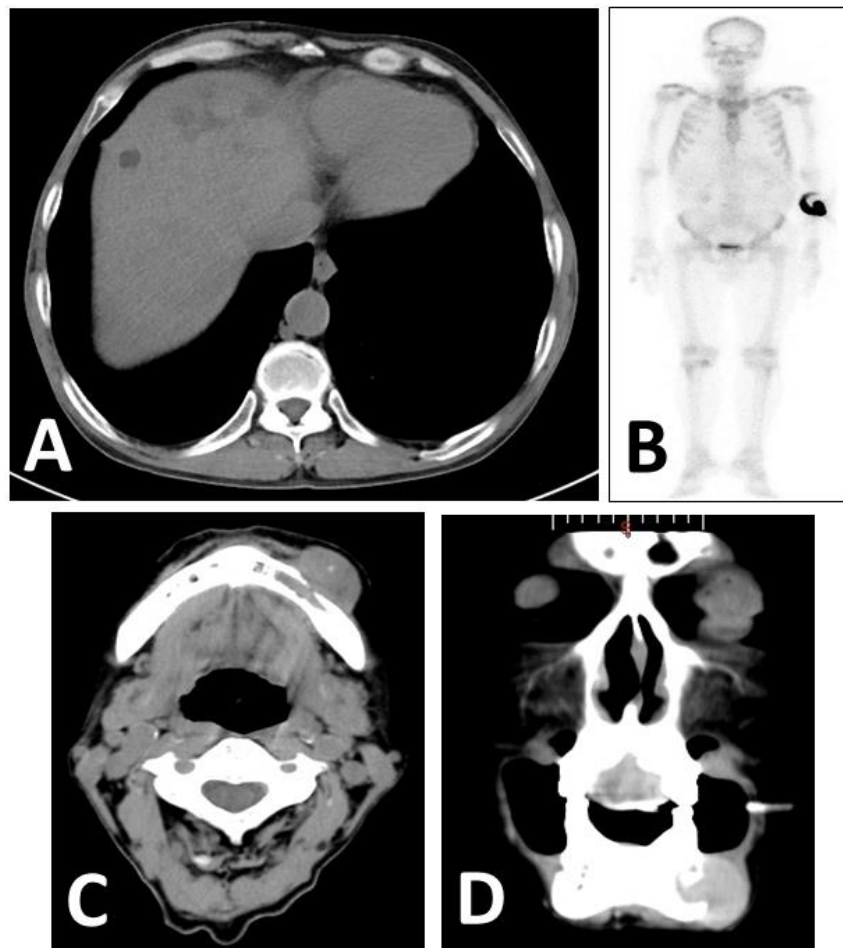
About three months later, the patient visited the out-patient dental clinic of the institution with a chief complaint of swelling and discomfort of the left mandible. Extraoral examination

revealed a diffuse, firm, painless, non-tender swelling, measured about 2.5 cm in diameter, over the left mandible. Left facial numbness was noted but trismus was not complained. Intraoral examination showed poor oral hygiene and a non-ulcerated swelling over the left lower vestibule of the molar area. Laboratory data revealed highly elevated GOT (555IU/l), GPT (189IU/l), and total bilirubin (1.65mg/dl), normal creatine (1.10mg/dl).

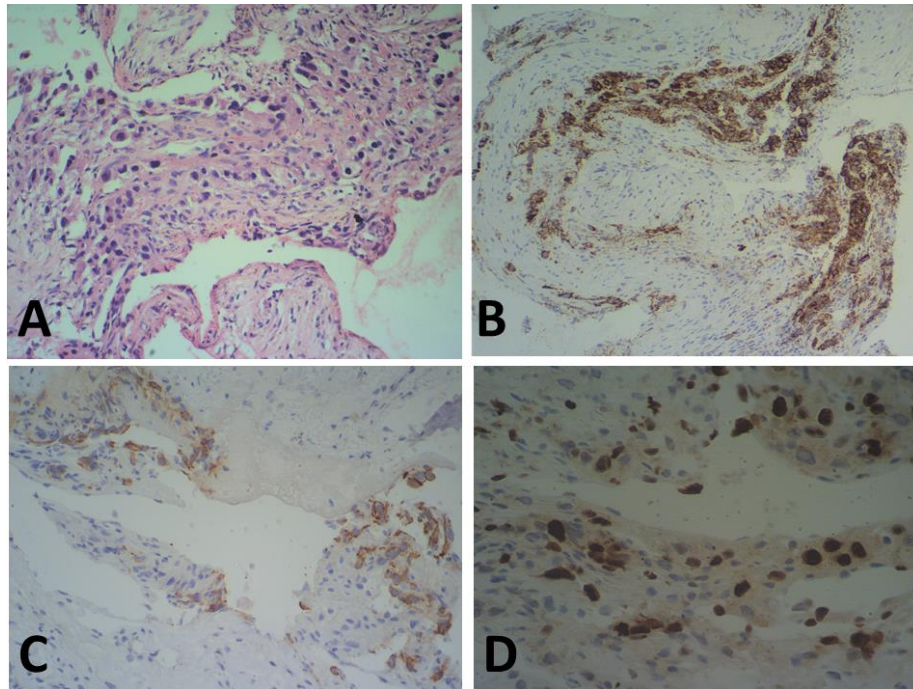
Computed tomography of the oral cavity revealed a swelling mass, measured about 2.7 × 1.3 × 2.7 cm in size, invading into the medullary and

buccal cortical portions of the left mandibular body producing an ill-defined radiolucent destructive lesion (Fig. 1C & D). Based on the clinical and radiological findings, a metastatic HCC was considered for this mandibular lesion. Hence, an incisional biopsy was implemented under local anesthesia. The specimen was sent for histological examination. Hematoxylin-eosin staining showed the lesion composed of anaplastic carcinoma cells with hyperchromatic nuclei and abnormal mitotic figures within a fibrovascular stroma (Fig. 2A). Immunohistochemical examinations revealed that the tumor cells were strongly positive for hepatocyte specific antigen (HepPar)-1 (Fig. 2B), and cytokeratin (CAM 5.2)

(Fig. 2C) but negative for alpha-fetoprotein (AFP); a high labeling index (>50%) of Ki-67 was also detected (Fig. 2D). Considering these pathological findings, a diagnosis of HCC metastasis to the left mandible was rendered. Upon the histological diagnosis of the mandibular metastatic lesion, the patient was subsequently referred to the oncologist of the Hepatitis and Hepatobiliary Unit of the institution for further evaluation and no other sites of metastasis were confirmed. The patient was then received palliative target chemotherapy (sorafenib), and radiation treatment (6000cGy with 30 fractions) for the metastatic mandibular lesion showing a partial response after the completion of the treatment.



**Figure 1** (A) Computed tomography (CT) of the abdomen revealed hepatocellular carcinoma (HCC) in the bilateral hepatic lobes; (B) Bone scan revealed no bony lesions at that time; Axial (C) and coronal (D) of CT showed a swelling mass invading into the medullary and buccal cortical portions of the left mandibular body producing an ill-defined radiolucent destructive lesion.



**Figure 5** (A, Hematoxylin-eosin stain) The lesion composed of anaplastic carcinoma cells with hyperchromatic nuclei and abnormal mitotic figures within a fibrovascular stroma ( $\times 200$ ); Immunohistochemical examinations revealed that the tumor cells were positive for hepatocyte specific antigen-1 (B,  $\times 100$ ), cytokeratin (C,  $\times 100$ ), and a high labeling index of Ki-67 (D,  $\times 200$ ).

**COMMENTS**

HCC is the most frequent malignant hepatic tumor with about 30-50% of HCC cases develops extrahepatic metastasis with the favored sites to be lung, regional lymph node, and bone [3, 4]. The favored location of bone metastasis is the vertebrae, followed by the ribs, sternum, and pelvis in decreasing order [5]. HCC metastasis to the mandible is rare, but if occurred, mandible is the most commonly affected site in OMF area as supported by a complete literature review by Yu et al [6] who demonstrated 98 reported cases of metastatic HCC in the OMF area in which 67 cases affected the mandible. Additionally, in the review [6], there were 68 cases of mandibular metastatic HCC with the mean age of the patients to be 63.3 years (range: 16-88 years); and a majority of males (only 9 female patients). The clinical data of the patient in this report was compatible to those reported in the literatures [6]. Metastasis

to the oral region was detected prior to the primary lesion in almost one-half of the reported cases [6]. A history of HCC has been found earlier than the occurrence of mandibular metastasis of the patient in this report, which would be helpful to ponder the differential diagnosis of the current lesion.

Radiologically, almost all reported cases of HCC metastasis to the mandible showed findings of tumor formation within the jawbones [7], or destructive lesions with ill-defined borders [8]. The radiological presentation of the current lesion was also consistent to the documented cases [6-11] from the literatures. Noteworthy, Fujihara et al [9] reported a metastatic HCC in the apex of the left mandibular third molar.

The confirmation of the diagnosis of metastatic HCC in OMF region may not be easy, especially when the primary tumor has not yet been detected. Immunohistochemical examination would be a useful aid to identify

metastatic HCC from other oral metastatic tumors: AFP has been found to be positive in about 30% of metastatic HCC [12]. On the other hand, HepPar-1 is a relatively specific marker of hepatocytes and HCC, and has also been useful for histological diagnosis [13]. In the current case, the anaplastic carcinoma cells revealed positivity for HepPar-1, and cytokeratin, but negative for AFP negative, as it has also been described in other studies [12, 14].


Treatment of choices available for the management of the patients' metastatic and primary lesions include excision of the oral lesion with and without reconstruction, palliative radiation, radiofrequency ablation, complete resection of the primary lesion, partial hepatic resection, liver transplantation, chemoradiation, percutaneous ethanol injection, transcatheter arterial chemoembolization, and spheres microspheres radio embolization [6]. In the present case, radical resection of metastatic HCC is controversial as the prognosis of patients with extrahepatic metastases is usually poor [15-17]. So, the patient received palliative chemoradiotherapy to control the metastatic lesion and prolong life.

Survival of patients with HCC is relatively good, with a 5-year survival rate of higher than 50% as surgery is implemented [18]; however, when bone metastasis occurs, the prognosis becomes worsen, with the survival rate declined harshly (1-year survival rate: 5-20%, 2-year survival rate: 4%), due to the fact that episode of an oral metastasis implicates a relatively late stage of the cancer [15-17]. Our patient was still alive after the diagnosis of mandibular metastasis receiving palliative chemoradiotherapy.

Review of literatures, there are two possible routes that HCC can disseminate from the liver into the OMF area [19]. When the hepatic artery and

the portal vein are affected, metastatic dissemination needs to initially attain the lung, and it may later reach the OMF area [19]; therefore, most of the reported cases of HCC with mandibular metastasis incline to be together with pulmonary metastasis [20, 21]. On the other hand, it has also been hypothesized that the metastatic dissemination may reach the OMF region via Batson's plexus (a connection between the azygos/hemiazygos veins and the vertebral venous plexus) [22, 23]. In the current case, no lung metastasis was identified; hence, this solitary mandibular metastasis may favor the second hypothesis.

### CONCLUSION

This report described a case of metastatic HCC affecting the mandible. Correct diagnosis of such a lesion relies on careful clinical, radiographic and histologic assessments. The current case indicated that dental practitioners should consider prudently the possible occurrence of a metastatic lesion in the jawbones. 

### THE AUTHORS



*Dr. Wen-Chen Wang is assistant professor of Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan*



*Dr. Ching-Yi Chen is visiting staff in Division of Oral Pathology, Department of Dentistry, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*



*Dr. Yuk-Kwan Chen is associate professor & head of Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan*

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