

# Gingival metastasis from primary hepatocellular carcinoma: a case report

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Yuan Huang<sup>1</sup>, Yanqiu Bao<sup>2</sup>, Dongyuan Xu<sup>2</sup> and Lan Liu<sup>2</sup> 

## Abstract

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide; however, cases with metastasis to the oral cavity are extremely rare. Herein, we report a 68-year-old man who was diagnosed with HCC. Ten months after surgical removal of the right half of his liver, the patient developed gingival metastasis. Unfortunately, the patient died 4 months after the diagnosis. We discuss treatment options, pathological results, and disease prognosis. When a mandibular gingival mass is found, metastatic tumors should be considered in the differential diagnosis. In this regard, the patient's medical history and physical examination are valuable indicators for the diagnosis of mandibular gingival metastasis. This case provides a basis for the clinical diagnosis of metastatic HCC involving the oral cavity.

## Keywords

Hepatocellular carcinoma, mandibular metastasis, gingival metastasis, case report, hepatitis C virus, segmental mandibulectomy

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## Introduction

Worldwide, hepatocellular carcinoma (HCC) is one of the most common malignant tumors, and its mortality is lower only to lung cancer and gastric cancer.<sup>1</sup> According to recent statistics, HCC accounts for more than 700,000 new cancer diagnoses annually.<sup>2</sup> When HCC is diagnosed, it may already be advanced due

<sup>1</sup>Department of Gastroenterology, Yanbian University Hospital, Jilin, China

<sup>2</sup>Department of Pathology, Yanbian University Hospital, Jilin, China

### Corresponding author:

Lan Liu, Department of Pathology, Yanbian University Hospital, No. 1327 Juzi Street, Yanji 133000, China.  
Email: [lliu@ybu.edu.cn](mailto:lliu@ybu.edu.cn)



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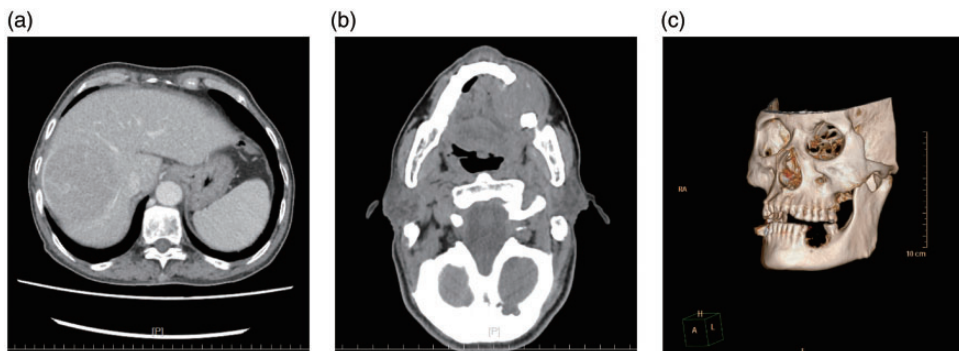
to its insidious onset, lack of obvious symptoms, and rapid progression. Advanced HCC is prone to distant metastasis, which is also the main cause of death in HCC patients. Generally, HCC can show both intrahepatic and extrahepatic spread. The lung is the most common site of extrahepatic metastasis, accounting for 53.8% of all extrahepatic metastases.<sup>3</sup> Other extrahepatic metastases can occur in the adrenal gland, bone, kidney, brain, and gingiva.<sup>4</sup> According to the literature, only 1% of extrahepatic metastases occur in the oral cavity and maxillofacial region.<sup>5</sup> Additionally, the degree of gingival metastasis from liver cancer has a greater impact on male patients, with invasion into the upper gingiva being most common.<sup>6</sup> Herein, we report a rare case of HCC with mandibular gingival metastases.

## Case report

The reporting of this study conforms to the CARE guidelines.<sup>7</sup> A 68-year-old man with a liver lesion was admitted to our hospital. The patient had no known comorbidities and no history of smoking or any personal or family history of other diseases. Upper abdominal computed tomography revealed

a circular mass in the liver S8 segment with clear borders and a diameter of approximately 7.2 cm (Figure 1a). Laboratory test results were as follows: aspartate aminotransferase, 68 U/L (normal range: 15–40 U/L); alanine aminotransferase, 63 U/L (normal range: 9–50 U/L); albumin, 31 g/L (normal range: 40–55 g/L); and alpha-fetoprotein, 36.4 ng/mL (normal range: 0–8 ng/mL). The test for hepatitis C virus (HCV) was positive. A pathological section of the liver tumor showed primary liver cancer (Figure S1). Thus, the surgeon diagnosed the patient as having primary liver cancer and performed right partial hepatectomy.

Ten months later, an examination of the patient's oral cavity revealed an erythematous soft tissue mass measuring 2 × 2 × 3 cm and involving the left mandible. Three-dimensional computed tomography revealed destruction of the left mandibular and alveolar bones (Figure 1b, c). The affected area was approximately 2.5 cm long, the edge was blurred, and a soft tissue mass had formed locally. The patient underwent left mandibular mass resection, segmental mandibulectomy, and titanium plate reconstruction. Histopathological examination revealed evidence of metastatic hepatic carcinoma with



**Figure 1.** Radiographic findings of the patient. (a) Upper abdominal enhancement computed tomography showed liver cancer in the right lobe. (b, c) Three-dimensional computed tomography revealed the bone of the left jaw and alveolar bone were destroyed. The region was approximately 2.5 cm long, edges were blurred, and a soft tissue mass was formed locally.

infiltration and obvious vascular thrombus (Figure 2a). Immunohistochemical analysis revealed that the tumor cells were positive for Heppar-1 (Figure 2b) and Ki-67 (Figure 2c) and negative for p63 (Figure 2d). The final diagnosis was a left mandibular gingival metastasis from HCC.

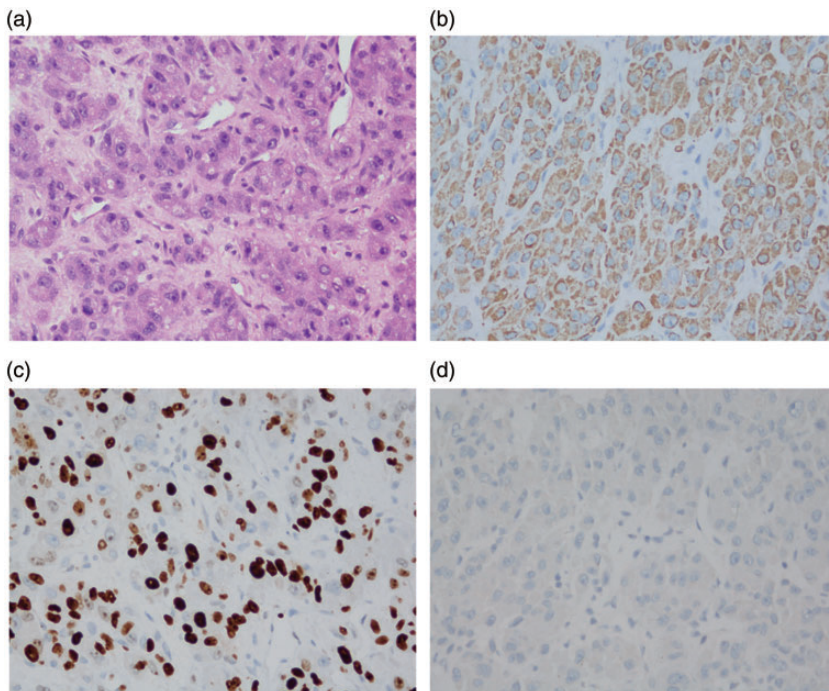
The patient was subsequently treated with traditional Chinese medicine. Unfortunately, the patient's condition deteriorated, and he died of multiple organ failure 4 months later.

## Discussion

According to global cancer statistics, hepatic cancer is the sixth most common malignancy and has the third highest mortality rate.<sup>8</sup> This high mortality rate is primarily attributed to recurrence and metastasis.

In early stages, HCC mainly spreads through the portal vein. Additionally, the lungs, abdominal lymph nodes, and bone are the most common sites of extrahepatic metastatic disease.<sup>9</sup> Among these organs, the lung is the most common site for distant HCC metastatic spread.<sup>10</sup> Metastasis of HCC to the gums and mandible is rare. Although a few studies have reported cases of gingival metastasis of HCC, this case has educational significance for diagnosing and treating oral metastatic cancer.

Oral metastatic carcinomas are uncommon and primarily involve the jaw and gingiva.<sup>11</sup> They account for approximately 1% of all malignant oral tumors.<sup>12</sup> In metastatic carcinoma of the jaw, the mandible is more commonly involved than the maxilla. The most frequently involved sites are the molar area, premolar area, angle, and



**Figure 2.** Histological findings of the tumor. (a) Microscopic view of the gingival neoplasm stained with hematoxylin and eosin (magnification: 400 $\times$ ). (b–d) Immunohistochemical staining showed tumor cells were positive for Heppar-1 (magnification: 400 $\times$ ) (b) and Ki-67 (magnification: 400 $\times$ ) (c) and negative for p63 (magnification: 400 $\times$ ) (d).

ramus.<sup>11,13,14</sup> Metastatic lesions of the jaw and gingiva can originate from many primary tumors. In male patients, lung cancer is the most frequent metastatic tumor of the oral cavity, while in female patients, breast cancer is the most common primary tumor.<sup>15</sup> The primary treatment is surgical resection combined with radiotherapy and chemotherapy. However, because of its poor prognosis, most patients die of multiple organ failure, with an average survival time of less than 7 months.<sup>15</sup>

Currently, the mechanism of HCC metastasis to the gingiva and jaw is unclear. Blood-borne transmission is considered the primary mechanism. The first route is through the portal hematopoietic pathway, whereby the main blood vessels, hepatic arteries, and portal veins of the liver are easily invaded, which then leaves the lungs particularly vulnerable. The second pathway occurs through the paraspinal venous plexus. The lack of valves allows other venous systems, such as the vena cava, portal vein, and pulmonary veins to be bypassed, providing a route for oral transfer.<sup>16–18</sup> Others believe that the sudden change in direction of blood vessels in the mandibular angle slows down the local blood flow, which is conducive to the shedding of malignant tumors and leads to metastasis to the gums.<sup>19,20</sup> Some studies have suggested that chronic oral inflammation is associated with oral tumors;<sup>21</sup> however, there is no direct evidence of a relationship between chronic periodontitis and cancer, so this needs to be further elucidated.

In this manuscript, we report a male patient with HCC gingival metastasis. Combined with previously reported cases and the relevant literature, it is considered that hematogenous metastasis to the oral cavity is the main route of dissemination. Because the oral health of the patient was poor during physical examination, an effect

of chronic oral inflammation cannot be ruled out. Laboratory examination of the patient was positive for HCV infection. Hepatitis B virus and HCV are independent factors for HCC. HCV can affect the progression of liver cancer through a variety of mechanisms, including inflammation, fibrosis, and angiogenesis.<sup>22</sup> However, there is no clear evidence that HCV infection is related to HCC gingival metastasis, but this needs to be further studied. Additionally, the latest systematic review showed that approximately 33% of oral and maxillofacial metastases were the first manifestation of primary tumors.<sup>23</sup> However, when diagnosing the primary lesion, imaging examinations could not determine whether there were oral lesions. Therefore, the possibility of oral lesions at the time of the initial diagnosis of primary lesions cannot be ruled out. This also suggests the importance of systemic examinations during the diagnosis of primary lesions. Early and timely detection of metastases may improve patient prognosis.

Although oral metastatic tumors are rare, they should be considered in the differential diagnosis when mandibular gingival masses occur. In this regard, the patient's medical history and physical examination may provide valuable clues for the correct diagnosis.

### Author contributions

Conceptualization: Lan Liu

Data curation: Yuan Huang

Investigation: Yanqiu Bao

Methodology: Yanqiu Bao

Project administration: Dongyuan Xu

Supervision: Lan Liu and Dongyuan Xu

Writing – original draft: Yuan Huang

Writing – review and editing: Lan Liu

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.


## Ethics statement

This study was approved by the ethical review board of Yanbian University Hospital. Written informed consent was obtained from this patient's son for publication of this case.

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## ORCID iD

Lan Liu  <https://orcid.org/0000-0002-3566-9666>

## Supplemental material

Supplemental material for this article is available online.

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