

# Hepatocellular carcinoma first presenting as a tumor of the oral cavity



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Hepatocellular carcinoma (HCC) is the sixth most common neoplasm worldwide; HCC metastasis is common affecting 50% of cases. However, metastasis to the oral cavity is extremely infrequent. We present a case of hepatocellular cancer first presenting as a mass lesion at the upper alveolus and review metastatic hepatocellular carcinoma to the oral cavity in 73-year-old male patient.

**KEYWORDS:** Oral cavity; Hepatocellular carcinoma

**H**epatocellular carcinoma (HCC) is the sixth most common neoplasm worldwide, with 748,000 new cases each year. Its very poor prognosis makes it now the third leading cause of cancer mortality, responsible for 695,000 deaths annually.<sup>1</sup> It has been recognized that HCC develops within an established background of chronic liver disease in most cases. Hepatitis C (HCV), hepatitis B (HBV), aflatoxin B1, and alcohol use are the major etiological agents that lead to the development of HCC.<sup>2</sup> HCC metastasis is common and present in 50% of cases. The lungs, diaphragm, abdominal lymph nodes, and bones are the most frequently affected extrahepatic sites.<sup>3,4</sup> However, metastasis to the oral cavity is extremely infrequent and rarely encountered.<sup>5</sup> We report a case of hepatocellular carcinoma that first presented as an oral cavity mass lesion of the upper alveolar process of a 73-year-old male patient. We also present a review of metastatic hepatocellular carcinoma to the oral cavity.

## REPORT

A 73-year-old male patient with a past medical history of diabetes mellitus was referred to our hospital

with a two-month history of an upper gingival, painless mass lesion which gradually increased in size until it protruded through the mouth opening and bled occasionally, especially after eating. Almost simultaneously, the patient also experienced a significant decrease of appetite. The patient denied any history of smoking, alcohol consumption or use of chewable recreational material.

Examination of the oral cavity confirmed the presence of a 4 × 5 cm exophytic non-tender mass lesion in the upper middle alveolus extending posteriorly to the hard palate and covered with blood clots (Figure 1). His airway was clear and no other oral cavity or head and neck abnormalities were identified. No lymph nodes or other mass lesions were present during his neck examination. The abdomen was somewhat distended but no palpable mass lesions were detected and a mild pitting edema of both legs was present.

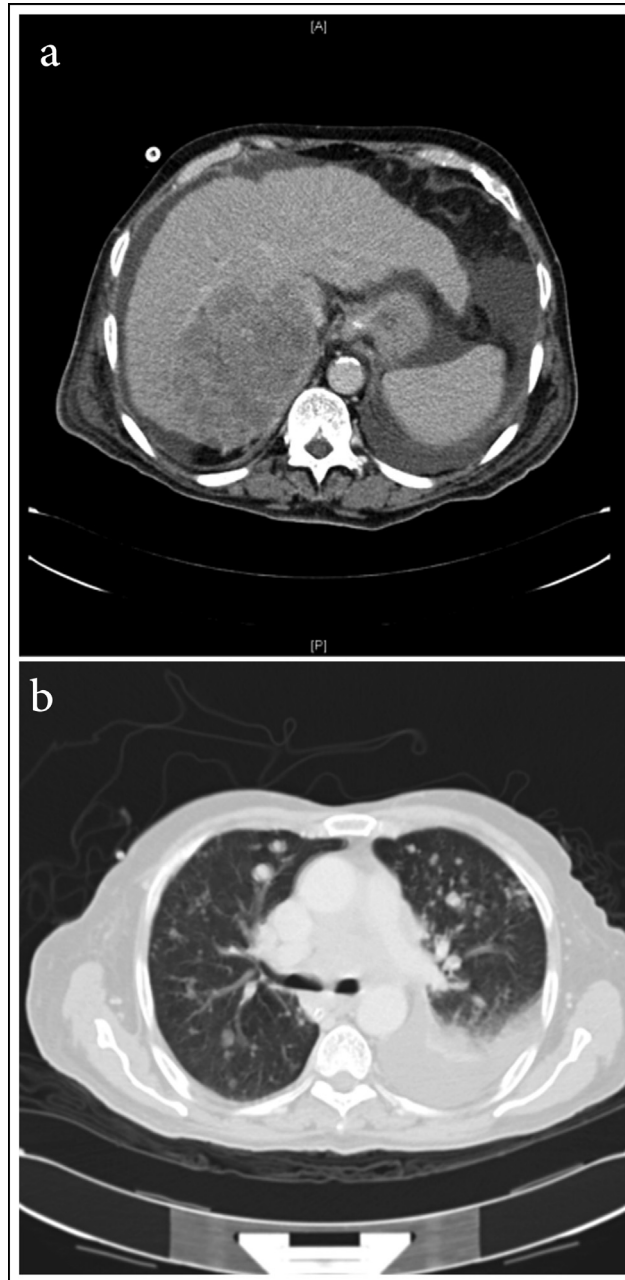
The patient was admitted to our institution for further management where he immediately received nutritional support. His iodinated contrast computed tomography (CT) scan of the head and neck confirmed the presence of a 2.7 × 5.1 × 4.3 cm soft tissue mass lesion of the maxillary alveolar process that bulged into the lingual and buccal surfaces of the



**Figure 1.** Photograph of the lesion demonstrating exophytic mass, covered with blood clots, in the upper alveolus protruding through the mouth opening and extending backward to involve the hard palate.



**Figure 2.** CT head and neck (sagittal view) showing the alveolar mass.



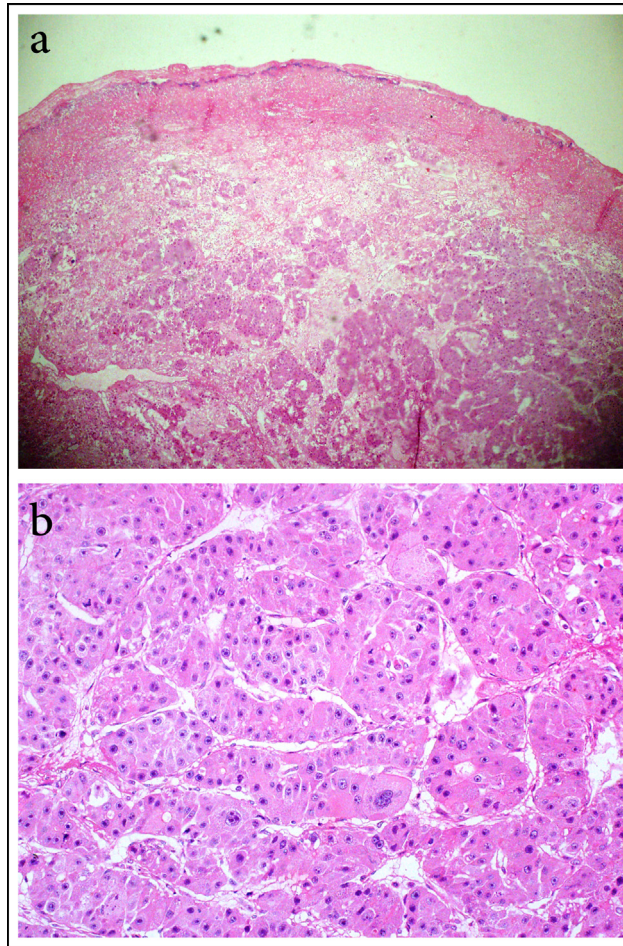
**Figure 3.** (a) CT abdomen demonstrating moderate ascites and large tumor mass in the right lobe of the liver ( $9.6 \times 9.8 \times 11$  cm). (b) CT chest showing right pleural effusion and multiple bilateral metastatic lung nodules.

process itself (Figure 2). Two left side occipital and cerebellar enhancing lesions consistent with brain metastasis were also identified with his CT scan.

The patient's CT scan of the chest revealed a right pleural effusion, a pronounced mediastinal lymphadenopathy and a large number of lung metastases (Figure 3). CT scan of the abdomen also demonstrated moderate ascites and a large tumor mass in the right lobe of the liver measuring  $9.6 \times 9.8 \times 11$  cm.

(Figure 3). In addition, a malignant-appearing mass lesion of the left kidney was identified.

Histopathological assessment of the oral lesion was initially reported by the referring hospital as a "high grade tumor". Further histopathological review performed at our hospital demonstrated findings compatible with metastatic high grade hepatocellular carcinoma as the tumor cells were large with hepatoid appearance, forming cords and trabeculae with



**Figure 4.** Hematoxylin and eosin section showing ulcerated surface above the tumor (a) and the trabecular sinusoidal growth pattern of the lesion under high power field (b).

sinusoidal pattern, and surrounded in some areas by endothelial cells, as noticed on CD34 staining. Tumor cells were negative for vimentin and AE1/AE3 cytokeratin but strongly positive for alpha fetoprotein and low molecular weight cytokeratin 8/18. CD10 also highlighted some of the canalicular patterns seen in hepatocellular carcinoma (Figures 4 and 5). Hep-Par 1 immunostain demonstrated multifocal positivity (Figure 6).

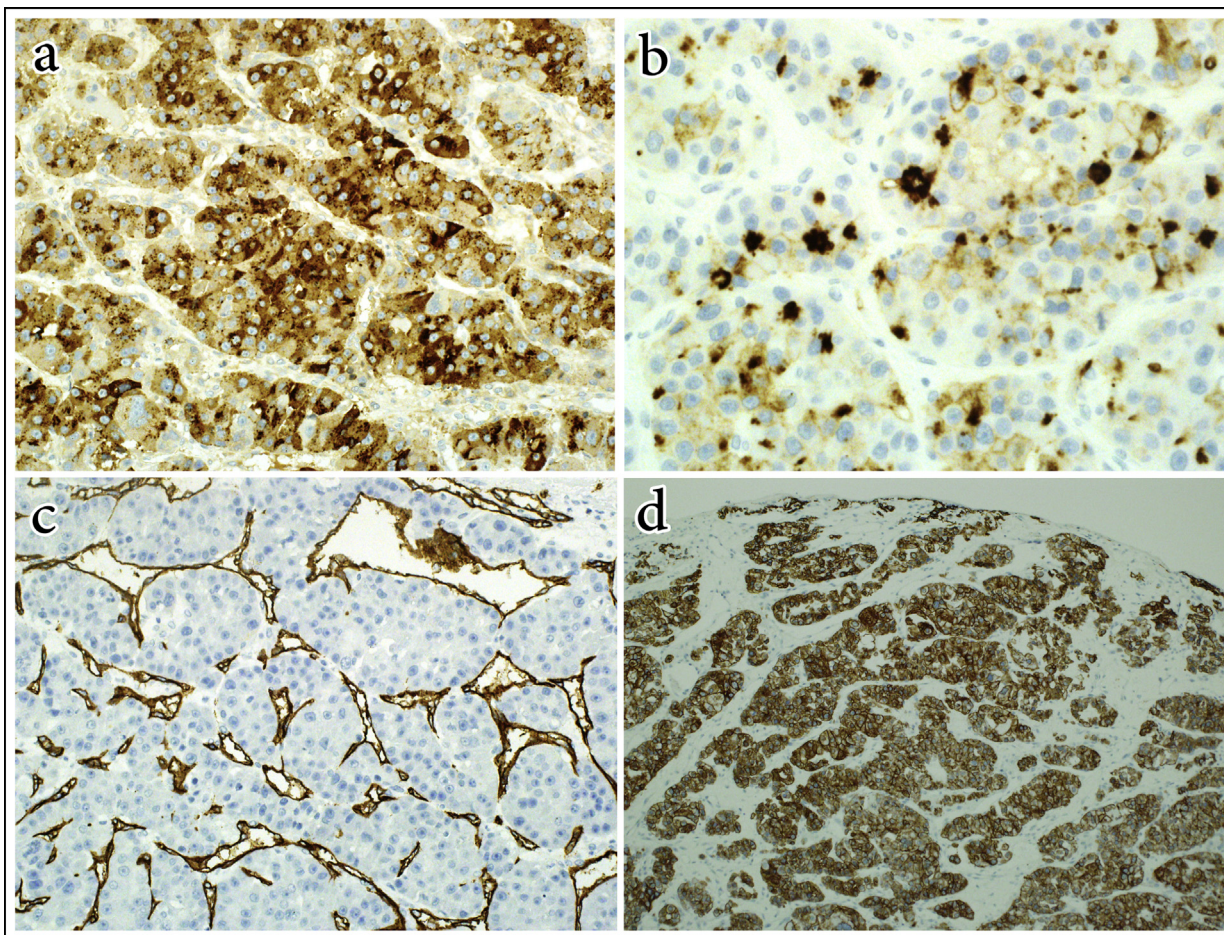
Based on the above findings, serum alpha fetoprotein was measured and found to be abnormally high (16,901  $\mu\text{g/L}$ ). Hepatitis profile showed a picture of chronic hepatitis B infection. In light of these findings, the diagnosis of hepatocellular carcinoma secondary to chronic hepatitis B infection with multiple metastases to the oral cavity, brain, lung, and kidney was established.

At some point during his hospitalization, the patient experienced severe bleeding from the oral lesion, which was controlled by angioembolization. According to the assessment by the medical oncology team, the patient

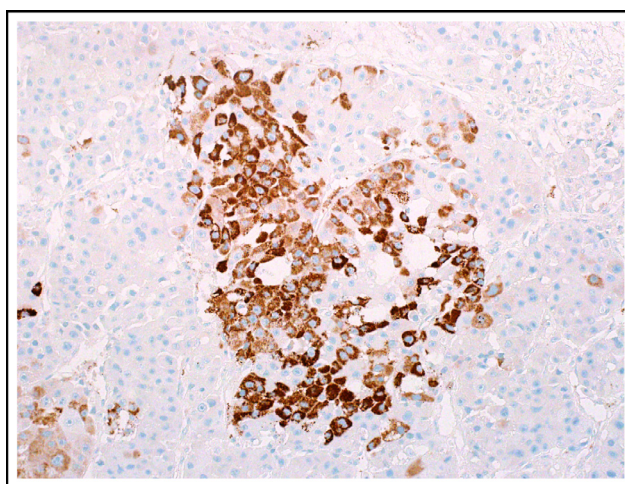
was unfit for chemotherapy and was therefore referred back to the local hospital for palliative care.

## DISCUSSION

This case is of special interest as the patient was referred to our combined head and neck clinic with an oral mass lesion from a region where squamous cell carcinoma of the oral cavity is highly prevalent. The initial biopsy report was suspicious for high grade tumor and the patient was admitted with an impression of high grade oral cancer to be managed by our Head and Neck Multidisciplinary Team. The radiological workup revealed multiple malignant masses involving the maxillary alveolus, the brain, the lung, the liver, and the kidney, giving the impression of an advanced oral cavity malignant tumor. Later on, a further review of the biopsy at our histopathology department led to the diagnosis of metastatic hepatocellular carcinoma to the oral cavity.



**Figure 5.** Sections showing positive alpha-fetoprotein staining (a). CD10 stain highlighting some canalicular pattern (b). CD34 staining highlighting the endothelial cells (sinusoidal pattern) (c). Low molecular weight CK8/18 positive staining (d).



**Figure 6.** Hep-Par 1 immunostain which demonstrates multifocal positivity.

Extrahepatic metastasis of hepatocellular carcinoma is relatively common. The lungs, abdominal lymph nodes and bones are, in decreasing order of incidence, the common sites of metastasis.<sup>3,4</sup> Metastasis to the oral cavity and jaws is rare, but in the event, the most common oral sites are the mandible and the gingiva.<sup>5</sup>

A review of the PubMed literature through to December 2012 using the search keys “metastasis”, “gingiva”, “mandible”, and “hepatocellular carcinoma” yielded 80 reported cases of metastatic hepatocellular carcinoma to the oral cavity and the jaw region. Of these 80 cases, 17 involved the gingiva.

Pires et al. reported a case of hepatocellular carcinoma metastasis to the anterior mandibular gingiva. In their review, 61 cases of hepatocellular carcinoma metastasis to the oral cavity region were found. Of these 61 cases, seven were in the maxillary gingiva, one in the anterior maxilla, two in maxillary sinus, and three involved both mandible and maxilla.<sup>5</sup>

Ramirez et al. reported a case of isolated gingival metastasis from hepatocellular carcinoma. In their review, they found 10 reported cases of gingival metastasis in the literature through to 2003.<sup>6</sup>

However, up to 8% of all oral malignancies and about 1% of jaw tumors represent metastatic cancer.<sup>8</sup> For men, the most commonly reported primary sites are the lung, kidney, liver, and prostate; while for females, breast, genital organs, kidney, and colorectum are the most commonly reported primary sites.<sup>7</sup>

A retrospective study by Seoane et al. on 39 patients with oral metastatic tumors between 1978 and 2007 found gingival metastases in 63% of oral soft tissue metastasis and the primary tumors were located in the lung, liver, and breast. The mean age was 65.2 years. In this series, two out of seven patients

presented with gingival metastasis from primary hepatocellular carcinoma and both of them were in the upper gingiva.<sup>8</sup>

Analysis of 673 cases of metastatic tumors to the oral cavity by Hirshberg et al. demonstrates that 23% of the cases were the first indication of undiscovered primary neoplasms. Jaw bones, particularly the mandible, were affected more frequently than oral soft tissues. The gingiva was the most frequently affected oral soft tissue. Lung, kidney, liver, and prostate were the most common primary sites for men while in women breast, female genital organs, kidney, and colorectum were the most common primary sites.<sup>9</sup>

The prognosis of patients with metastatic hepatocellular carcinoma is poor. The cumulative survival rates at one year, two years, three years, and five years after the diagnosis of extrahepatic in a cohort of 342 by Uchino et al. were 39.3%, 15.3%, 7.4%, and 4%, respectively. With treatment of extrahepatic metastasis, the rates at one year, two years, and three years were 48.9%, 21.2%, and 10.6%, respectively. These rates fell to 19%, 2.3%, and 0%, respectively, when no treatment was administered.<sup>10</sup>

## CONCLUSIONS

Malignant lesions of the oral cavity are not always primary lesions originating in the cavity itself but could sometimes be metastatic lesions of a distant undisclosed primary site. Thorough clinical, radiological and histopathological evaluations are key factors in determining the diagnosis and management of such lesions.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

## REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127(12):2893–917.
2. Forner A, Llovet JM, Bruix J. Hepatocellular carcinoma. *Lancet* 2012;379(9822):1245–55.
3. Katyal S, Oliver 3rd JH, Peterson MS, Ferris JV, Carr BS, Baron RL. Extrahepatic metastases of hepatocellular carcinoma. *Radiology* 2000;216(3): 698–703.
4. Anthony PP. Hepatocellular carcinoma: an overview. *Histopathology* 2001;39(2):109–18.
5. Pires FR, Sagarra R, Corrêa ME, Pereira CM, Vargas PA, Lopes MA. Oral metastasis of a hepatocellular carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;97(3):359–68.
6. Ramón Ramirez J, Seoane J, Montero J, Esparza Gómez GC, Cerero R. Isolated gingival metastasis from hepatocellular carcinoma mimicking a pyogenic granuloma. *J Clin Periodontol* 2003;30(10):926–9.
7. Katyal S, Oliver 3rd JH, Peterson MS, Ferris JV, Carr BS, Baron RL. Extrahepatic metastases of hepatocellular carcinoma. *Radiology* 2000;216(3): 698–703.
8. Seoane J, Van der Waal I, Van der Waal RI, Cameselle-Teijeiro J, Antón I, Tardío A, et al. Metastatic tumours to the oral cavity: a survival study with a special focus on gingival metastases. *J Clin Periodontol* 2009;36(6):488–92.
9. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumours to the oral cavity - pathogenesis and analysis of 673 cases. *Oral Oncol* 2008;44(8):743–52.
10. Uchino K, Tateishi R, Shiina S, Kanda M, Masuzaki R, Kondo Y, et al. Hepatocellular carcinoma with extrahepatic metastasis: clinical features and prognostic factors. *Cancer* 2011;117(19): 4475–83.