Case Report

Gingival metastasis of hepatocellular carcinoma: a rare case report

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Abstract: Hepatocellular carcinoma (HCC) is one of the most common malignancies and the third leading cause of cancer mortality in China. HCC frequently metastasizes to the lungs, abdominal lymph nodes, and skeletal system, but rarely to the gingiva. Here we reported a case of HCC that metastasized to the gingiva. A 60-year-old man with HCC came to our hospital complaining of abdominal distension, jaundice and a gingival mass. The gingival mass was adjacent to the upper incisors and had been bleeding for more than 24 hours. To stop the bleeding, the mass was surgically excised, and an incisional biopsy was performed. Immunohistochemical staining revealed that the tumor cells were positive for hepatocyte paraffin-1, cytokeratins, and glypican-3 and negative for antibody HMB-45, antibody Melan-A, S-100 protein, and α-fetoprotein. Approximately half (51%) of the tumor cells were positive for Ki-67. These observations suggested a histological diagnosis of gingival metastasis of HCC. Two months after surgery, new gingival lesions were observed. The patient refused treatment and died 2 months later. This case indicated that immunohistochemical staining of tumor cells from the gingival mass was necessary to confirm a diagnosis of gingival metastasis of HCC and that this type of HCC metastasis had a very poor prognosis.

Keywords: Hepatocellular carcinoma, metastasis, gingiva

Introduction

Hepatocellular carcinoma (HCC) is a common malignancy with a high mortality rate and an estimated annual incidence of one million people. The aggressiveness of HCC is demonstrated by intrahepatic and extrahepatic metastases, the latter are observed in approximately 50% of HCC cases. The common sites of extrahepatic metastasis are lung, abdominal lymphatics, skeletal system adrenal glands, great veins adjacent to the liver, diaphragm, and oral and perioral regions [1-3]. Malignant metastasis to the oral cavity is extremely rare (only 1-2% of oral malignancies are in situ). The rare metastatic malignancies in the oral cavity typically originate from cancerous cells from the lung, breast, and kidney [4]. Metastasis of liver cancer cells to the oral cavity is extremely rare. In this report, we described one such case of gingival metastasis in a patient with HCC.

Case report

A 60-year-old man who had been diagnosed with HCC 6 years previously and undergone seven sessions of transcatheter arterial embolization for the primary lesions presented to our hospital with complaints of abdominal distension, jaundice, and a gingival mass adjacent to the upper incisors which had been bleeding for more than 24 hours. The mass was surgically excised, and an incisional biopsy was performed. Immunohistochemical staining revealed the tumor cells were positive for hepatocyte paraffin-1, cytokeratins, and glypican-3 and negative for antibody HMB-45, antibody Melan-A, S-100 protein, and α-fetoprotein. Approximately half (51%) of the tumor cells were positive for Ki-67. These observations suggested a histological diagnosis of gingival metastasis of HCC. Two months after surgery, new gingival lesions were observed. The patient refused treatment and died 2 months later. This case indicated that immunohistochemical staining of tumor cells from the gingival mass was necessary to confirm a diagnosis of gingival metastasis of HCC and that this type of HCC metastasis had a very poor prognosis.
HCC metastasis to the gingiva

Findings supported a histological diagnosis of gingival metastasis of HCC.

Two months after surgery, the patient again presented to our hospital with abdominal distension and other complaints. Upon examination, new gingival lesions that extended from the mandibular right central incisor to the right
HCC metastasis to the gingiva

Figure 7. A lesion in the left posterior mandibular gingiva after surgery.

lateral incisor on the labial aspect were observed (Figures 6 and 7), suggesting that the HCC metastasis in the gingiva was still active. Unfortunately, the patient declined any further treatment and died 2 months later.

Discussion

HCC is one of the most common malignant cancers, and its aggressiveness is manifested by frequent extrahepatic metastasis in approximately 50% of HCC cases [5-7]. Nonetheless, the metastasis of HCC to oral and perioral regions is extremely rare, and very few cases of recurrent metastatic gingival tumors have been reported in the literature. Only about 50 cases of HCC metastasis to oral regions have been reported in the past 58 years since the first case of HCC metastasis to the mandible was reported in 1957 [8].

The pathway of HCC metastasis to the maxillofacial area is not well established [9, 10]. It is thought to be primarily mediated via a hematologic route [11] in which cancer cells, once out of the tumor mass, travel from the hepatic vein and Batson’s venous plexus [12]. The very low frequency of gingival hepatocellular metastasis could be attributed to the relatively long distance between the liver and the gingiva.

Although metastatic HCC spreads more rapidly than benign gingival tumors, it is difficult to distinguish a HCC metastatic lesion from an epulis caused by an exophytic mass because both have similar gross appearance and imaging findings. Because HCC gingival metastases can sometimes be confused with nonmalignant reactive gingival tumors, immunohistochemical analysis to detect the hepatic origin of cancer cells is necessary to confirm a definite diagnosis of gingival metastasis of HCC. Relatively specific cellular markers that can confirm the presence of HCC cells include HepPar-1 and alpha-fetoprotein. In addition, Ki-67 labeling can determine the extent of cell proliferation. In the present case study, though there was no metastasis in other extrahepatic locations and the gross appearance of mass was similar with epulis, we cautioned the possibility of HCC metastatic lesion and taken immunohistochemical analysis, the result revealed that the gingival tissue contained hepatocyte-like cells that were positive for HepPar-1, cytokeratins, GPC-3, and Ki-67, supporting the diagnosis of HCC gingival metastasis [3, 13, 14].

The prognosis of patients with HCC gingival metastasis is primarily determined by the aggressiveness of the primary HCC and whether the metastasis recurs. The mean survival period of patients with hepatitis B virus-related HCC accompanied by oral metastases has been reported to be 21 weeks (range, 2 weeks to 2 years) [15, 16]. In the case presented here, the gingival tumor recurred 2 months after surgery of the first metastasis, and the survival period of the patient was only 4 months. Very few cases of recurrent metastatic gingival tumor have been reported in the literature, and the general tendency underlying the prognosis of this disease is still unclear. The results of our case corroborate the prediction of a very poor prognosis for patients with aggressive HCC and recurring gingival metastases. In this case, the patient’s survival period may also have been impacted by the initial surgery for the gingival tumor. In our opinion, a surgical approach might not be the best way to treat patients with gingival metastasis of HCC because of the risk of concurrent transmission of cancer cells from the tumor mass to the oral region.

In summary, we presented a very rare case of an oral metastasis of HCC that resembled a granulation tissue-like gingival tumor. The morphology of tumor cells shown with hematoxylin and eosin staining and the positive HepPar-1 staining confirmed the diagnosis of HCC gingival metastasis. We caution that a patient with gingival metastasis of HCC likely has a very poor prognosis and that a surgical approach might not be the best way to treat patients with this condition.
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Disclosure of conflict of interest

None.

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