Mandibular Metastasis from Undiagnosed Hepatocellular Carcinoma - A Case Report

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Abstract

Rationale: Cancer metastatic to the oral cavity accounts for 1%–4% of all oral malignancies, spreading from a distant primary site. Nevertheless, oral metastasis is often the first presentation of primary cancer. **Patient Concerns:** A 53-year-old male was referred to our institution because of painful swelling of the left parotid region that did not respond to medications. A firm mass extending towards the mandbular angle had caused trismus; furthermore, the patient complained about hypoesthesia in the V3 area. No noticeable findings could be seen intraorally. **Diagnosis:** Computed tomography imaging showed non-homogeneous post-contrast enhancement of the left vertical mandible branch; moreover, there were clear signs of bone erosion and swelling of the contiguous soft tissues. **Treatment:** Biopsy was performed under general anaesthesia, through a transoral approach. **Outcomes:** Histology and immunohistochemical analysis revealed hepatocellular carcinoma metastatis. **Take-away Lessons:** In the differential diagnosis of oral neoplasms, metastasis coming from a distant site should always be taken into consideration.

Keywords: Cancer, diagnosis, hepatocellular carcinoma, mandibular metastasis, oral cavity

Introduction

According to the latest poster published by the Dana Farber/ Harvard Cancer Centre, liver cancer represents the 5th most frequent cancer worldwide and the 3rd cause of death by cancer. Amongst liver cancers, hepatocellular carcinoma (HCC) is the most common one and accounts for almost 90% of cases.[1] The most prominent risk factor for HCC is hepatitis B virus (HBV) infection, whereas the risk related to hepatitis C virus (HCV) infection has decreased due to the valid response to antiviral drugs. Both infections can lead to liver cirrhosis, which can progress to HCC.[1]

The main sites of HCC metastasis are represented by lungs (55%), lymph nodes (53%), bone (28%) and adrenal glands (11%),[2] although some cases of unusual metastatic sites as the jaws have been reported. The first mandibular metastasis of HCC was described in 1957. Since then, <70 cases of mandibular metastasis have been documented,[3] and even if we take into account maxillary metastasis and other metastatic sites and 17 reports of metastatic HCC to the sinonasal region, the total amount of metastases from HCC to the oral and maxillo-facial area described in the literature barely exceeds 100 cases.[4] In this paper, we describe the case of a 53-year-old male who presented a growing mass in the left parotid region that was initially undiagnosed and later found to be a metastasis from unknown HCC.

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Case Report

This case report was written in accordance with CARE guidelines.[5] A 53-year-old male [Figure 1] with a history of hepatic cirrhosis of mixed origin (HCV and alcohol)

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presented at the emergency room at Santa Chiara Hospital in Trento, Northern Italy and was referred to the Maxillofacial Surgery Unit for the evaluation of a progressively growing facial mass of the left parotid region associated with pain and paraesthesia. The patient had been evaluated by a neurologist 15 days earlier and had undergone computed tomography (CT) and magnetic resonance imaging (MRI) to better investigate the case. Based on imaging findings, the consultant had not recognised any neurological causes, and therefore, had prescribed pregabalin to treat the pain. Physical examination revealed a firm mass in the left posterior mandibular region; moreover, the patient presented trismus and hypoesthesia in the left V3 area, denoting a possible involvement of the inferior alveolar nerve. No noticeable findings were present in the oral cavity.

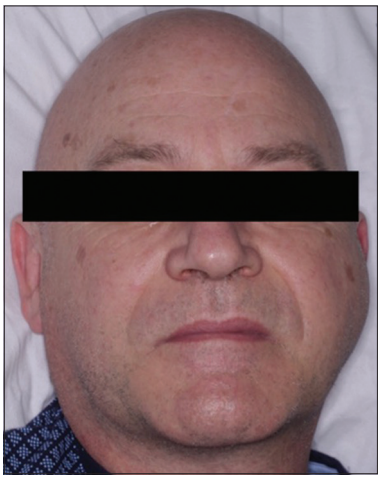

Figure 1: Clinical picture of patient's face

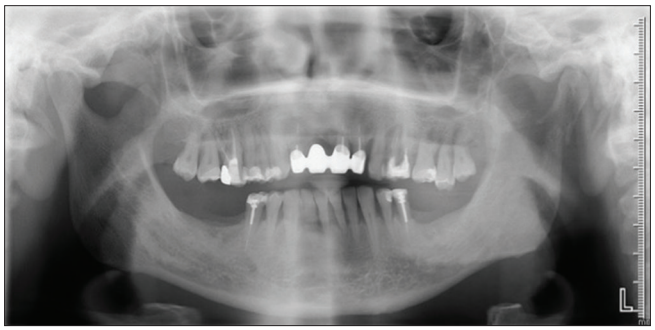

Figure 2: Orthopantomograph showing fracture of the left mandibular ramus

Orthopantomography [Figure 2] showed a fracture of the left mandibular ramus; however, the patient had no history of recent trauma. More accurate analysis of the CT scan and MRI [Figure 3] revealed a mass in the left mandibular ramus associated with bony destruction. A parotid ultrasound was then performed and showed a 3 cm × 1 cm × 3 cm mass with no significant alterations of the parotid gland [Figure 4].

CT with medium contrast was repeated: Non-homogeneous post-contrast enhancement of the left vertical mandibular branch, accompanied by evident bone erosion and swelling of the contiguous soft tissues, was noted. Dimensions were approximately 35 mm × 31 mm × 32 mm, and there were concomitant millimetric submandibular lymph nodes. MRI was repeated, too, without detecting any parotid involvement.

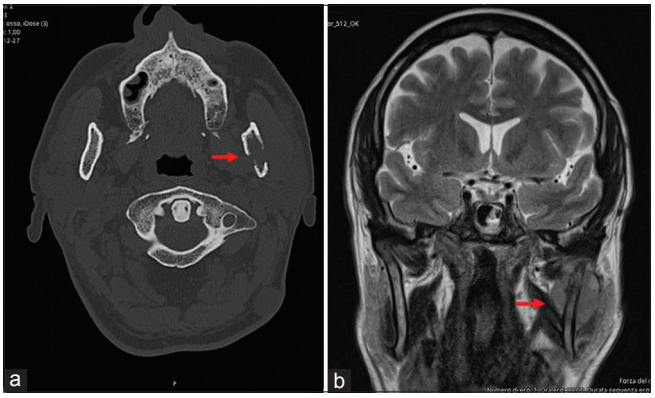

Figure 3: Computed tomography and magnetic resonance imaging: axial view and coronal view (a and b); the red arrow indicates the mandibular tumour

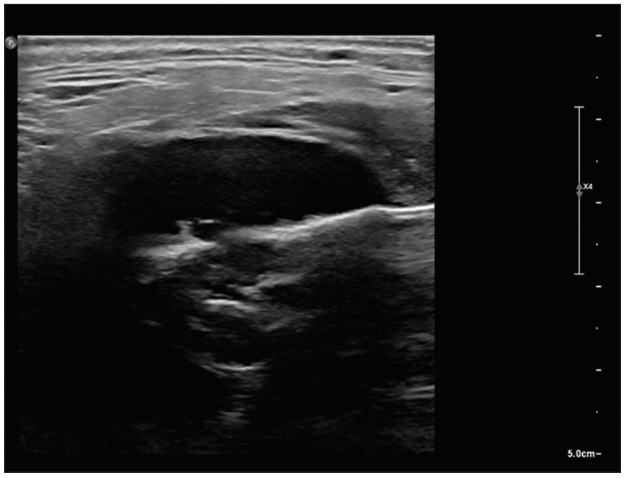

Figure 4: Ultrasonography revealing left parotid mass

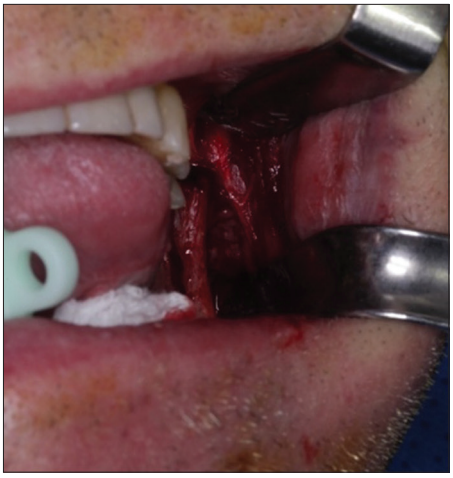

Figure 5: Mandibular biopsy: Intraoperative view

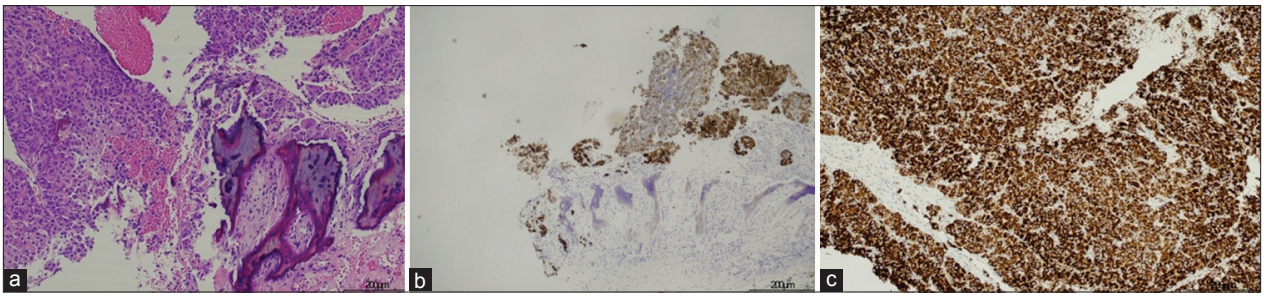

Figure 6: (a) Haematoxylin and eosin ×10; (b) Broad spectrum keratin x 10; (c) Heppar-1 positive stain ×10

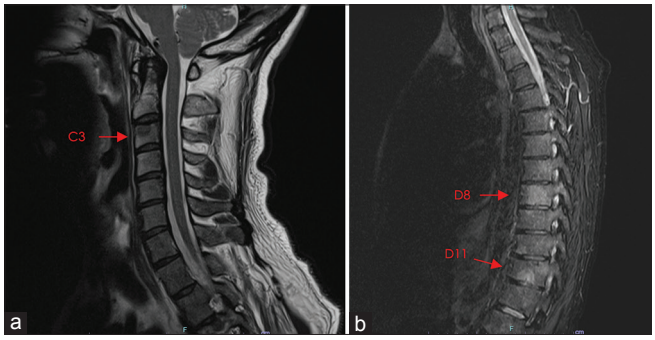

Figure 7: (a) Magnetic resonance imaging (MRI) T2 – weighted cervical spine, in red the metastasis to C3; (b) MRI T2 – weighted with contrast medium dorsal spine, in red the metastasis to D8 and D11

The patient underwent surgical biopsy [Figure 5] under general anaesthesia, through intraoral approach. Neither intraoperative nor post-operative complications arose. Histological analysis revealed medium-sized cells with abundant eosinophilic cytoplasm and irregular nuclei [Figure 6]; immunohistochemical stain was positive for CD138, CK8/18, CD10 and hepatocyte antigen (HepPar-1). Focal positivity for CEA, as well as negativity for PAX8, SATB2, HMB45, MUM1, TTF-1, CDX2, CD20, CK7, CK20, CALP63, kappa and lambda chains, CD30, EMA, myc, SOX10, S110 and EBER were detected. Proliferative index was valued by Ki67 resulting in 30% of growth. Overall, these findings were suggestive for metastatic HCC. A total body CT revealed multiple hepatic lesions as well as bone metastasis to the spine that were confirmed by MRI [Figure 7]. The patient was then referred to the Oncology Unit and underwent systemic therapy with atezolizumab and bevacizumab, mandibular mass localised radiotherapy and bisphosphonates for other bone localisations.

Discussion

According to Park and Yoon, mandibular metastasis from HCC has been estimated to occur in 0,6% of cases[6] confirming the rarity of such a clinical presentation. Generally, HCC has two possible metastatic pathways: the haematogenous pathway (through the hepatic artery or the portal venous branches) and the paravertebral anastomotic network. This second route is thought to be responsible for vertebral bodies metastases, which are in fact the HCC preferred bony metastatic site.[4,7,8] Furthermore, HCC cells demonstrated mandibular tropism because of the abundance of hemopoietic tissue and the favourable environment for tumour emboli implantation. In our case, cancer metastasis was localised to the mandibular angle; in addition, CT imaging showed cancer metastases to the spine [Figure 7], strengthening the hypothesis of the spreading following the Batson's pathway.

Cancer metastases to the oral and maxillofacial area are often detected before the discovering primary malignancy. This happens in 73% of cases, and therefore cancer suspicion in oral neoplasms of unknown nature should never be underestimated. Hence, it is important to take into consideration the possibility of HCC metastasis in presence of a tumour mass in the maxilla or mandibular region associated with pain and hypoesthesia, especially when the patient's anamnesis reports HBV or HCV infections or history of cirrhosis. Radiographic imaging may report a typical aspect of a malignant lesion such as a destructive and radiolucent appearance with ill-defined borders, lacking sclerotic limits.[3]

In this case, incisional biopsy was performed to better investigate the neoplasm; however, some authors cautiously prefer FNAB, as severe haemorrhage during or after an open surgical procedure has been reported, likely due to the rich tumour vascularisation.

The pathological analysis might show strands, hepatic plate-like or duct-like patterns of cells that resemble hepatocytes in a highly vascular stroma.[9] Usually, immunohistochemical analysis is useful to distinguish HCC from other malignant tumours: Glypican-3 and HepPar-1 are the main markers used to confirm the diagnosis.[3] Glypican-3 has high sensitivity and specificity for HCC and results positive in more than 80% of HCC; HepPar-1 is negative in hepatic metastasis stemming from lung or breast and is highly specific for HCC cells. In this case, immunohistochemistry tested responsiveness for CD138, CK8/18 and CD10, which are, respectively, non-specific markers for epithelial carcinomas (CD138) and solid non-squamous epithelial carcinomas (CK8/18) and highly specific markers for hepatocytic differentiation (CD10).[10]

Once the hepatic origin was confirmed, a total body CT scan was used to search for the primary tumour and better investigate its extension. A comprehensive evaluation

of the patient is essential to correctly stage the cancer and to choose the best treatment option: considering that prognosis in patients affected by malignancies is influenced more by systemic control of the disease than by local treatment of metastasis, the treatment for metastasis from HCC is frequently palliative, and radiotherapy is a viable option; moreover, targeted drugs such as the association of atezolizumab and bevacizumab are now used as main treatment: An increasing overall survival has been shown thanks to this association.[3] In our case, the patient started radiotherapy, chemotherapy and antiresorptive treatment simultaneously. The survival rate of patients affected by HCC with bony localisations is tremendously poor: 1-year survival ranges from 15% to 20%, 2-year survival is around 4%. The patient died 2 years after receiving a cancer diagnosis.

Conclusions

In the differential diagnosis of oral neoplasms, metastasis coming from a distant site should be always taken into consideration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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