J. Oral Diag. 2023;08:e20230227.

CASE REPORT

Hepatocellular carcinoma metastasis to the mandible: a challenging diagnosis

Rosana Mastrofrancisco [1]
Marcelo Marcucci [1]
Anderson Costa Lino Costa [2]
Luiz Felipe Palma [3]*

Abstract:

Introduction: Metastasis of hepatocellular carcinoma (HCC) to the mandible is an extremely rare condition with less than a hundred cases reported worldwide. Such lesions do not have any pathognomonic clinical, radiologic, or histologic features, and they can mimic many other conditions or diseases with orofacial involvement. **Case report:** We present an interesting but intriguing case of metastasis of HCC to the mandible, which presented as an orofacial swelling accompanied by intense pain and spontaneous bleeding following tooth removal. **Conclusion:** This paper highlights the importance of integration of the in-depth medical history of the patient, clinical findings, and microscopic examinations in cases of uncommon oral lesions of challenging diagnosis.

Keywords: Liver Neoplasms, Neoplasm Metastases, Jaw Neoplasms.

[1] Heliópolis Hospital, Stomatology and Oral and Maxillofacial Surgery Center - São Paulo - São Paulo - Brasil.
[2] Heliópolis Hospital, Pathological Anatomy Service - São Paulo - São Paulo - Brasil.
[3] Federal University of São Paulo, Department of Pathology - São Paulo - São Paulo - Brasil.

Correspondence to:
Luiz Felipe Palma.
E-mail: luizfelipep@hotmail.com

Article received on June 14, 2023.
Article accepted on August 21, 2023.

DOI: 10.5935/2525-5711.20230227

INTRODUCTION

Hepatocellular carcinoma (HCC) accounts for more than 90% of all primary liver tumors.[1] It is related to patients with cirrhosis in approximately 85% of the cases but viral hepatitis (hepatitis B and C), alcoholic liver disease, and other non-alcoholic conditions such as steatohepatitis and fatty liver disease are the most common etiological factors.[2] HCC is the fifth most prevalent cancer[3] worldwide and the five-year survival is estimated to be 18%.[4]

Metastasis of HCC to the mandible is an extremely rare condition, with less than a hundred cases reported so far.[5] However, approximately 50% of HCC patients experience extrahepatic metastasis, with the most frequent sites being the colon, kidneys, lungs, and bones. Considering only bone involvement, rates from 1.6% to 16% have been reported, with a higher prevalence in the rib, humerus, femur, iliac, and vertebra, consecutively.[6] When the oral cavity is affected, the mandible is the most commonly affected site, with a male predilection.[7]

In light of these facts, the current paper aims to report an interesting but intriguing case of metastasis of HCC to the mandible with a very unusual clinical presentation.

CASE REPORT

A 62-year-old Caucasian man was referred to the Stomatology and Oral and Maxillofacial Surgery Center of Heliópolis Hospital due to an orofacial swelling on the left side of his mandible, accompanied by intense pain and spontaneous bleeding. The patient's medical history revealed cirrhosis induced by hepatitis C, which had progressed to HCC approximately a year prior. At the time of admission, he reported that his disease was in an advanced stage and that he was undergoing chemotherapy, but further detailed information could not be obtained.

Also according to the patient, the swelling had developed 50 days earlier, following the extraction of two mandibular molar teeth. On extraoral examination, gross facial asymmetry and swelling were noted but no signs of inflammation were apparent (Figure 1A). Moreover, ipsilateral regional lymphadenopathy (palpable nodes) affecting the submandibular lymph nodes was present. Intraoral examination revealed a 3-cm submucosal mass of fibroelastic consistency on the left mandibular alveolar ridge. The overlying mucosa displayed areas of ecchymosis and superficial ulceration, with the center partially covered by a pseudomembrane (Figure 1B).

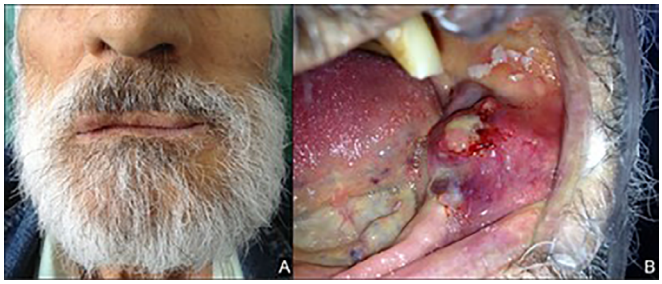

Figure 1. Initial clinical aspect.

A computerized tomography scan was obtained and revealed a radiolucent osteolytic expansile lesion in the left mandibular body, causing extensive and aggressive bone destruction in the medullary and cortical portions and resulting in a pathologic mandibular fracture. The mandibular canal could not be visualized, indicating the involvement of the inferior alveolar neurovascular bundle. Invasion of the buccal, sublingual, and submandibular spaces was also observed, with the implication of the neighboring muscles and soft tissues (Figure 2A-B).

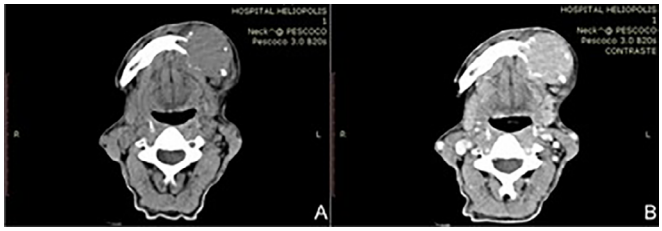

Figure 2. The initial aspect of the radiolucent osteolytic expansile lesion in the left mandibular body from a computed tomography scan.

Given the patient's medical history and the non-specific clinical and radiological features, the provisional diagnosis of distant metastasis of HCC was considered but other pathologic conditions such as multiple myeloma, non-Hodgkin lymphoma, and osteosarcoma were not ruled out. An incisional biopsy was then performed for conventional histopathological analysis and further immunohistochemistry staining. Invasion of lamina propria by atypical epithelial cells was observed, as well as tumor cell positivity for polyclonal carcinoembryonic antigen (Figure 3A-B).

Based on the patient's medical history, clinical features, and histopathologic findings, the diagnosis of metastasis of HCC to the mandible was confirmed. Only palliative care was provided (i.e., analgesia) because of the patient's medical status and extension and location of the lesion. He was referred to the Oncologist in charge of the HCC treatment for further investigation and appropriate management.

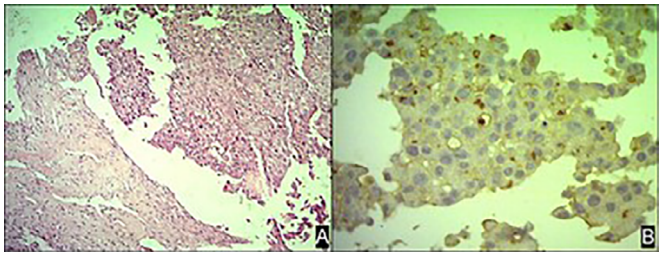

Figure 3. Histopathological analysis from the incisional biopsy.

The patient read and signed the informed consent for the clinical procedures and publication of this case report and related images.

DISCUSSION

The mechanisms and pathways by which primary malignant cells spread to the oral cavity are not yet fully understood. Although the portal hematogenous route is the main pathway for most oral metastasis, the lungs are not always affected concomitantly in metastasis of HCC. So, the vertebral venous system has been suggested as an alternative route of dissemination.[8]

No pathognomonic clinical, radiologic, or histologic features are related to mandibular lesions of metastasis of HCC. Clinically, these lesions may mimic either an odontogenic tumor in cases presenting a tumoral mass with swelling or an oral squamous cell carcinoma when surface ulcerations are present. Radiographic features are also non-specific and may reveal either radiolucent or radiopaque areas with ill-defined borders.[7]

Histopathological findings of a metastatic HCC lesion generally show cell strands or duct-like patterns resembling hepatocytes, surrounded by a highly vascular stroma. In addition to conventional histopathological analysis, immunohistochemical markers play an important role in confirming the diagnosis.[5] Although hepatocyte paraffin 1 and arginase-1 are the most frequently used marker of hepatocellular differentiation, polyclonal anti-carcinoembryonic antigen--antibody can be useful for experienced pathologists as it cross-reacts with biliary glycoprotein and shows a characteristic canalicular staining pattern in hepatic tissues.[9] However, there is currently no universally accepted immunohistochemical marker for all cases of metastatic liver tumors.

The management of metastatic HCC is controversial. While resection of oral metastatic neoplasms can have a positive impact on quality of life and survival, achieving a cure is not typically possible.[6] Palliative treatments (e.g., radiotherapy, chemotherapy, and immunotherapy)[6] may also enhance the prognosis and survival time of patients with HCC metastatic to bones.[5] Unfortunately, the appearance of oral metastasis often indicates widespread, advanced disease and, then, a poor prognosis. In these cases, death usually occurs within a few months.[10]

CONCLUSION

The current paper emphasizes the importance of combining a thorough patient health history, clinical observations, and microscopic analyses when dealing with unusual oral lesions that pose diagnostic challenges.

Acknowledgments: nothing to disclose.

Conflict of interest: the authors have not declared any conflicts of interest.

Consent for publication: written informed consent was obtained.

REFERENCES

1. Ioannou GN, Splan MF, Weiss NS, McDonald GB, Beretta L, Lee SP. Incidence and predictors of hepatocellular carcinoma in patients with cirrhosis. Clin Gastroenterol Hepatol. 2007 Aug;5(8):938-45.e4. DOI: https://doi.org/10.1016/j.cgh.2007.02.039
2. Asafo-Agyei KO, Samant H. Hepatocellular carcinoma [Internet]. Treasure Island: StatPearls Publishing; 2023; [access in ANO Mês dia]. Available from: https://pubmed.ncbi.nlm.nih.gov/32644603/
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2014;136(5):E359-E86. DOI: https://doi.org/10.1002/ijc.29210
4. Jemal A, Ward EM, Johnson CJ, Cronin KA, Ma J, Ryerson AB, et al. Annual report to the nation on the status of cancer, 1975-2014, featuring survival. J Natl Cancer Inst. 2017 Sep;109(9):djx030. DOI: https://doi.org/10.1093/jnci/djx030
5. Radzi AB, Tan SS. A case report of metastatic hepatocellular carcinoma in the mandible and coracoid process. Medicine (Baltimore). 2018;97(4):e8884. DOI: https://doi.org/10.1097/MD.0000000000008884
6. Liu H, Xu Q, Lin F, Ma J. Hepatocellular carcinoma metastasis to the mandibular ramus: a case report. Int J Clin Exp Pathol. 2019;12(3):1047-51.
7. Misra S, Shankar Yu, Rastogi V, Maragathavalli G. Metastatic hepatocellular carcinoma in the maxilla and mandible, an extremely rare presentation. Contemp Clin Dent. 2015 Mar;6(Suppl 1):S117-S21. DOI: https://doi.org/10.4103/0976--237X.152966
8. Klasser GD, Echandi L, Shannon M. Hepatocellular carcinoma metastasis to the condyle. J Am Dent Assoc. 2014 Oct;145(10):1063-7. DOI: https://doi.org/10.14219/jada.2014.70

9. Takahashi Y, Dungubat E, Kusano H, Ganbat D, Tomita Y, Odgerel S, et al. Application of immunohistochemistry in the pathological diagnosis of liver tumors. Int J Mol Sci. 2021;22(11):5780. DOI: https://doi.org/10.3390/ijms22115780

10. Lee YH, Lee JI. Metastatic carcinoma of the oral region: an analysis of 21 cases. Med Oral Patol Oral Cir Bucal. 2017 May;22(3):e359-e65. DOI: https://doi.org/10.4317/medoral.21566