

Metastatic hepatocellular carcinoma in the maxilla and mandible, an extremely rare presentation

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Abstract

Malignancy is characterized by anaplasia, invasiveness, and metastasis. Primary oral squamous cell carcinoma is the most prevalent oral malignancy, but secondary malignancy from distant sites have also been reported. Hepatocellular carcinoma (HCC) is a common primary liver malignancy that frequently metastasizes during the course of the disease, but < 1% of cases show oral involvement. Such secondary neoplasms do not have any pathognomonic clinical or radiologic findings, and therefore they pose a diagnostic challenge. Hence, in the differential diagnosis of malignant tumors of the oral cavity, it is essential to consider the occurrence of both primary as well as metastatic tumors despite the low incidence of the latter. A rare case of HCC metastasizing to both the maxilla and mandible is presented, in which the patient succumbed to the disease as a result of the delay in diagnosis.

Keywords: Hepatocellular carcinoma, jaw metastasis, secondary malignancies

Introduction

Metastatic malignancies of the oral cavity are rare lesions, accounting for only 1–4% of all oral malignancies and can occur in the jaw bones, the oral soft tissues or even both.^[1] The primary tumors that metastasize to the oral cavity are usually from the lungs, breast, kidney and bone.^[2] The valve less Batson's paravertebral plexus (BPP) is the pathway for distant metastasis into the oral cavity.^[3] Hepatocellular carcinoma (HCC) is the most common hepatic malignancy, and about one-thirds of HCC metastasize, usually to the lungs and regional lymph nodes.^[4] Very rarely, HCCs metastasize to the oral cavity, and such cases have a poor prognosis due to delay

in diagnosis. We report an extremely rare case of metastatic HCC in a 50-year old female patient with concomitant involvement of the right maxilla and the left mandible, which is the second case to be reported in the English literature within our best knowledge for documentation.^[5]

Case Report

A 50-year-old female reported to the dental hospital with the complaint of swelling in the left lower jaw and the right side of the face for the past 3 months [Figure 1a-c].

History revealed that the swelling in the left mandible was present since 3 months and swelling in the right side of the face was present since 1 month. Both the swellings were rapidly increasing in size. Patient was asymptomatic initially but experienced pain 10 days back with the rapid increase in size of the swellings. The patient took analgesics, but there was no relief. Further, the patient also developed a growth in the gingiva 1 month back which was also rapidly increasing in size causing a gradual reduction in mouth opening. Patient was on treatment for gastritis and abdominal pain since 1 year.

On clinical examination, a diffuse swelling was seen in the left side of the body of the mandible, ovoid in shape and another diffuse swelling present in the right side of the face. Depressions were seen in the superior part of the swelling in the zygomatic region. On palpation, both the swellings were firm with mild tenderness on palpation. Mouth opening was limited to 20 mm. Intra-oral examination revealed a localized growth present on gingiva and alveolar mucosa extending both buccally and lingually from 33 to 37 region. The growth was irregular in shape; surface was irregular covered by slough. Margins were everted with the obliteration of buccal sulcus, and the growth was firm in consistency, fixed to the

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underlying bone [Figure 2]. Another swelling was seen in the right buccal mucosa that was spherical in shape, slightly ulcerated in the centre, firm in consistency and nontender on palpation.

Since the swellings and growth were sudden in onset, irregular in shape, rapidly increasing in size and destroying the surrounding structures, a provisional diagnosis of malignant growth was made.

Squamous cell carcinoma, primary intra-osseous carcinoma and metastatic carcinoma were considered in the differential diagnosis.

Investigations

Conventional radiography

Panoramic radiograph revealed ill-defined mixed radiopaque-radiolucent lesion with irregular bone destruction in 33–35 region. Hyperostosis was seen in the periapical region of 36, 37 which appeared to be separated from the surrounding bone [Figure 3].



Figure 1: Frontal picture (a) showing swelling on the right maxilla and left mandible, right profile picture (b) with maxillary swelling and left profile picture (c) with mandibular swelling



Figure 3: Panoramic radiograph showing a localized, ill-defined mixed radiolucent-radiopaque lesion in the left body of the mandible

Computed tomography

Computed tomography scan showed a lytic destructive lesion involving left anterior mandibular region with external soft tissue component. An irregular cortical defect in the anterior margin of right mandibular angle/ascending ramus was observed [Figure 4] with a large solid enhancing mass having few internal calcifications and regional pressure effect on the right masseteric and buccal spaces with scalloping and erosion of posterior wall of the right maxillary antrum [Figure 5a and b].

Histopathologic investigation

An incisional biopsy of the growth present in the right buccal mucosa region was made under local anesthesia. Under low power magnification ($\times 4$), Hematoxylin and Eosin stained section shows epithelium and connective tissue. Under higher



Figure 2: Intra-oral picture showing a restricted mouth opening with an ulcero-proliferative growth in the left mandibular alveolus

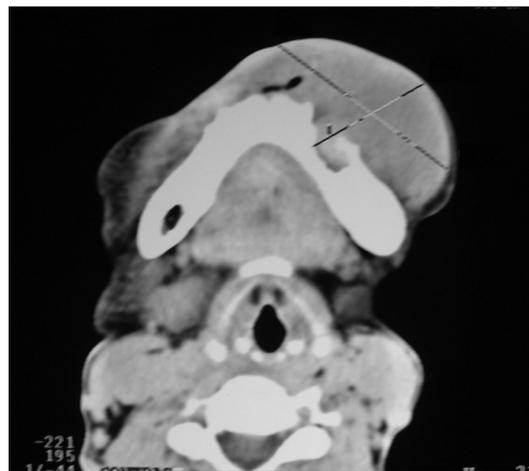


Figure 4: Contrast-enhanced axial computed tomography scan showing a lytic destructive lesion involving left anterior mandibular region with external soft tissue component measuring 4.1 cm \times 6.8 cm in size



Figure 5: (a) Contrast-enhanced coronal computed tomography scan showed a lytic destructive lesion involving left anterior mandibular region with external soft tissue component. (b) An irregular cortical defect in the anterior margin of right mandibular angle/ascending ramus was observed with a large solid enhancing mass having few internal calcifications and regional pressure effect on the right masseteric and buccal spaces with scalloping and erosion of posterior wall of the right maxillary antrum seen in axial section

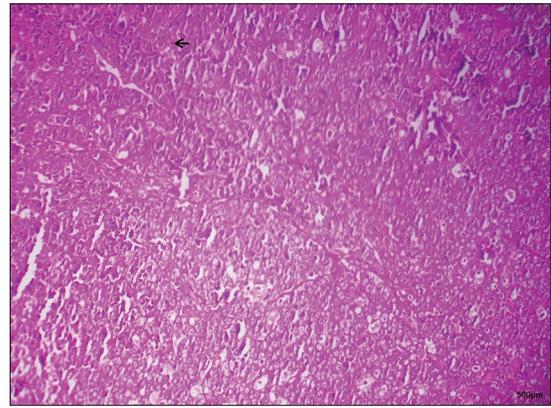


Figure 6: H and E stained section show epithelium and connective tissue. The lesion is composed of atypical cells similar to hepatocytes, having eosinophilic granules in the cytoplasm

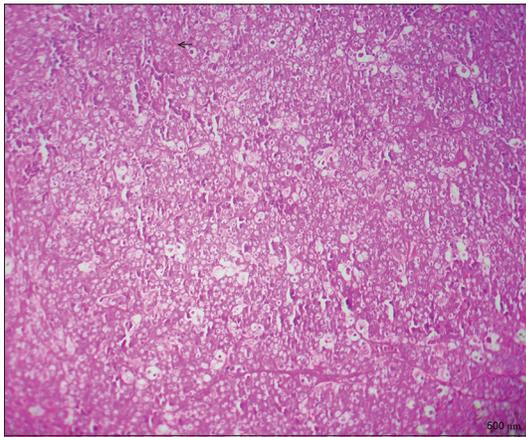


Figure 7: H and E stained section show proliferation of atypical malignant cells forming nests and cords of malignant appearing hepatocytes with a central lumen. The nuclei appear hyperchromatic with one or more prominent nucleoli. The malignant hepatocytes are separated by dense bundles of collagen

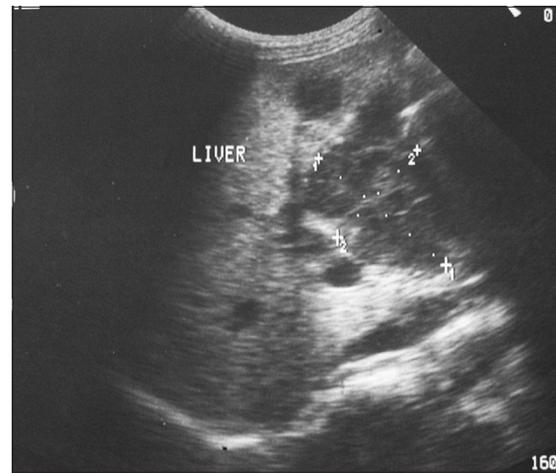


Figure 8: Ultrasonography of the abdomen revealed a large lesion in the left lobe of the liver and another lesion in the right lobe. Both lesions were irregular and hypoechoic with multiple septa within the lesion

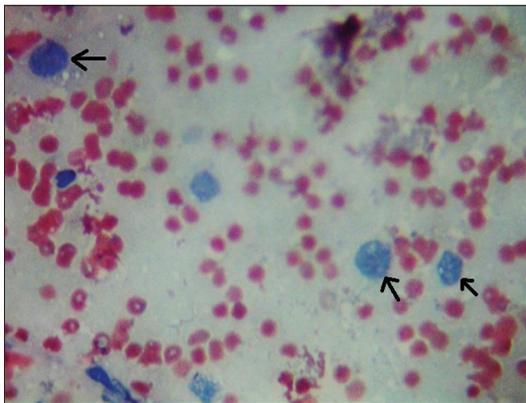


Figure 9: Ultrasound-guided fine needle aspiration cytology taken from the liver revealed pleomorphic malignant appearing hepatocytes (arrows)

magnification ($\times 10$), the lesion was composed of atypical cells similar to hepatocytes, having eosinophilic granules in the cytoplasm [Figure 6]. These cells proliferate forming nests and cords of malignant appearing hepatocytes with a central lumen. The nuclei appear hyperchromatic with one or more prominent nucleoli. The malignant hepatocytes are separated by dense bundles of collagen [Figure 7] and there is also evidence of hemorrhage. There is presence of overlying parakeratinized stratified squamous epithelium that is thinned out in many areas.

Correlating the histological features, suspecting oral metastatic HCC, the patient was subjected to further investigations to locate the primary malignancy.

Chest radiograph

Chest radiograph revealed no abnormality.

Hematological investigation

Hepatitis B surface antigen was positive, and the serum alfa-fetoprotein level was 413 ng/ml.

Ultrasonography of abdomen

Ultrasonography of the abdomen revealed a large lesion in the left lobe of the liver and another lesion in the right lobe. The lesions were irregular with multiple septa within. Two irregular, hypoechoic lesions in the left and right lobe of the liver were observed. Abdominal ultrasound examination revealed hypoechoic mass in the liver [Figure 8].

Ultrasound guided fine-needle aspiration cytology

Ultrasound-guided fine-needle aspiration cytology (FNAC) taken from the liver revealed the pleomorphic malignant appearing hepatocytes [Figure 9]. These features were consistent with that of HCC.

A final diagnosis of metastatic HCC to the jaws was made, and the patient was referred to the regional cancer hospital for treatment where she passed away within 3 months due to multiple metastatic lesions.

Discussion

Metastatic oral malignancies arise as a secondary from a distant primary site, like the breast, adrenal gland, colorectal system, genital organs and thyroid in females; and from lung, prostate, kidney, bone and adrenal gland in males.^[6] HCC is the most common hepatic malignancy and the third leading cause of cancer deaths worldwide. HCC predominantly occurs in male patients secondary to either a viral hepatitis infection (hepatitis B and C) or due to underlying chronic liver disease and cirrhosis.^[7]

This disease frequently metastasizes to extra hepatic sites like the lungs, regional lymph nodes and bone (vertebrae, ribs, and long bones).^[2,7] In the oro-facial region, the mandible is the commonly affected site and like the primary HCC, metastatic HCC also has a definite male predilection.^[8] HCC can spread through hematogenous route with a concomitant lung metastasis.^[9] Another route of spread is through BPP or the venous plexus of Batson. This is a system of valve less vein located in the epidural space between the spinal column bone and dura mater.^[3] Malignant cells entering the plexus get lodged in the venous and sinusoidal system of bones that are connected to BPP, thus bypassing the other venous system such as the pulmonary, caval and portal systems as in the present case, the spread of HCC from the liver to the jaw bones (mandible and maxilla) has occurred bypassing the lungs, via the Batson's plexus.^[9] HCC has been sometimes reported in the maxilla and only once in the maxilla and mandible simultaneously.^[5] According to Pires *et al.* in about two-thirds of oral metastatic HCC, the oral lesions were the initial presentation of the disease.^[10]

Hepatocellular carcinoma clinically appears as a tumor mass in the oral cavity that may mimic an odontogenic tumor when it occurs as a swelling and oral squamous cell carcinoma when associated with surface ulceration.^[11-13] Radiographic features are nonspecific which may vary from radiopaque to radiolucent lesions with ill-defined borders.^[14,15] The jaw lesions may be the initial manifestation of the metastatic disease in the majority of cases thereby mimicking an odontogenic lesion leading faulty diagnosis and subsequent delay in management.^[16]

Histologically, the lesion may comprise of strands or duct-like patterns composed of cells resembling hepatocytes, in a highly vascular stroma. It can mimic adenocarcinoma with a pseudo-glandular pattern or may be poorly differentiated, causing difficulty in detecting the cells of origin.^[17] Hence, immunohistochemical (IHC) markers are used for diagnosis. Glypican-3, HepPar1, CD34 are the markers that can be used to confirm the microscopic diagnosis of HCC.^[18,19] In the present case, IHC was not used but diagnosis was done correlating the histopathologic features of the oral lesions and the cytologic features of ultrasound-guided FNAC taken from the liver.

Since there is no pathognomonic clinical, radiologic or histologic features of metastatic hepatic malignancy, and the oro-facial manifestations may be the only signs of an otherwise occult disease.^[20] Early diagnosis of metastatic oral lesions is quite challenging because such patients report to the oral physician/dental surgeon first for treatment and require multiple investigations to detect the primary lesion.^[21]

Acknowledgments

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