**Bile Formation in Hepatocellular Carcinoma Metastatic to the Mandible: A Case Report**

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Abstract:

OBJECTIVE: To present a unique finding of bile formation in Hepatocellular Carcinoma (HCC) metastatic to the mandible, including histopathology, radiologic analysis, treatment recommendations and literature review.

STUDY DESIGN: A case report in the setting of the Greater Los Angeles Veterans Administration Tertiary Care Medical Center. METHODS: Presentation of a single patient report including history, physical findings, along with gross, histologic, and radiologic analyses.

RESULTS: A 55 year old patient with known multifocal hepatocellular carcinoma, hepatitis B and C and cirrhosis, presented with a painful mandibular mass after Sorafenib treatment. The patient underwent an FNA of the mandibular mass which showed bile canaliculi and bile formation along with immunoperoxidase staining consistent with hepatocellular carcinoma. Hepatocellular carcinoma rarely metastasizes to the mandible and with only 50 cases having been reported in the literature. We describe a unique histopathologic representation of hepatocellular carcinoma metastatic to the mandible showing bile formation. Radiologic findings in this case show the typical osteolytic findings previously described in the literature. Due to the vascular nature of this tumor, radiation therapy and embolization have been described to control bleeding, and surgery has been described in at least one case to control severe hemorrhage.

CONCLUSION: Hepatocellular carcinoma metastasis to the mandible is a rare entity; however, this entity should be considered in a patient with known HCC and an oral mass. Although uncommon, the classic findings of bile formation on histopathology and a lytic lesion on imaging should make the diagnosis. Recommendations for treatment are based on the vascular nature of this tumor. The patient presented in this case report received the indicated palliative radiation therapy after the diagnosis was made.

Discussion:

On clinical presentation, HCC metastatic to the mandible often presents a mandibular mass accompanied by pain and trismus. The metastasis may present in the preauricular region and can be confused with a parotid neoplasm. Hypoesthesia the lisp and pathologic mandibular fractures are also presenting symptoms. Patients may also be anemic. Our case followed a typical presentation as our patient had progressive jaw pain and developed trismus. He also had a low hemocrit.

The present case was also typical in its radiographic presentation in that it showed a destructive, osteolytic mass on CT and panorex (see Fig 1). Other reports of HCC metastasis to the mandible show osteolytic lesions which lack sclerotic reaction. On panorex, the metastases appear as osteolytic lesions. Although not completed in our case, MRI of HCC metastatic to the mandible has been reported as a gadolinium enhancing lesion with high T1 and T2 signal.

In cases where metastatic HCC is suspected, FNA should be done instead of an open biopsy due to the hemorrhagic nature of the lesion. Although FNA is often diagnostic, few other reports have shown bile formation. At least one other report showed histology similar to ours on core biopsy, with cords and tubules of cells with multiple bile plugs. HepPar1 was positive in that biopsy and others. The FNA in the current case showed hypercellular smears with sheets of atypical cells in trabecular arrangements, and many of the cells contained yellow-green pigment, some of which was also found extracellularly (FIG 2A). Immunoperoxidase stain with HepPar1 confirmed a likely diagnosis of HCC based on bile formation in the H&E stains (FIG 2B).

Mandibular metastasis of HCC is an advanced presentation of the disease, and the majority of patients are dead within two years. In our present case, treatment was aborted two months after the mandibular metastasis was discovered due to progression of the primary tumors in the liver. Treatment modalities for the metastatic lesions are mostly palliative, including chemotherapy, radiation therapy, and embolization, which have been described to control hemorrhage. Surgery has been reserved for otherwise uncontrollable hemorrhage of the metastatic lesion, or in cases of solitary metastases to the mandible where the primary disease is well-controlled. Given this patient’s progressive disease burden and lack of hemorrhagic complications, surgical treatment was not necessary at this time. The patient is currently followed closely for any bleeding or worsening symptomatology.

Conclusion:

A metastatic process is well established in the differential diagnosis of mandibular tumors. However, HCC is rare and should be considered in patients with known HCC or in the work-up of an unknown primary. Along with a detailed history, physical exam, and imaging, definitive diagnosis can be achieved in the setting of a FNA showing bile formation as presented in this case. Further disease specific staining can confirm the diagnosis.

References:

8. Han L, Bhan R, Zak I, Husain M, Feng J, Vella S, Al-Abbadi MA. Metastatic hepatocellular carcinoma to the mandible: a case report of the mandibular metastasis appears as a lytic, destructive mass centered within the right mandibular ramus on CT with contrast. (Fig. 1).

Case Report:

A 55 year old man with cirrhosis, Hepatitis B and C, and multifocal hepatocellular carcinoma (HCC) presented with a three month history of an enlarging right mandibular mass. The patient had known metastases to the adrenal gland and was undergoing treatment with Sorafenib at the time of presentation. He also had a history of alcohol use and cirrhosis. He had had a ten pound weight loss in the preceding two months. The mass was painful, but the patient denied facial numbness. On physical exam, the patient had a tender, firm mass at the right angle of mandible which was three inches in diameter. The mass was not fluctuant or mobile. His oropharyngeal exam showed no other lesions, and his base of tongue and floor of mouth were soft. Flexible fiberoptic laryngoscopy revealed no abnormalities. His neck exam revealed no lymphadenopathy. He had no trismus at presentation, but development in the following weeks.

CT with contrast showed a lytic, destructive mass centered within the right mandibular ramus with erosion of the ramus. There was loss of the normal fat plane separating the lesion from the adjacent parotid glands and pterygoid muscle (Figs. 1).

The lesion was also demonstrated on panorex. FNA of the mandibular mass showed hypercellular smears with sheets of atypical cells in trabecular arrangements, surrounded by endothelial lined vessels. The cells were large with round nuclei, mild to moderate anisokurtosis, prominent nucleoli and amply granular cytoplasm. Many of the cells contained yellow-green pigment, some of which was also found extracellularly. This is consistent with metastatic HCC. Immunoperoxidase stain with HepPar1 was diffusely strongly positive, supporting this diagnosis (FIG. 2).

The patient was presented at our hospital multidisciplinary team conference. The recommendation was for palliative radiation therapy to control the patient’s symptoms, as he has known multi-organ metastatic disease. This patient received 7 days of palliative radiation therapy to the mandibular metastases for pain control for a total dose of 20 Gy. The endpoint was improvement on pain which was achieved subjectively for the patient.

Figure 1. HCC mandibular metastasis appears as a lytic, destructive mass centered within the right mandibular ramus on CT with contrast.

Figure 2A. FNA showing hypercellular smears with sheets of atypical cells, and many of the cells contain yellow-green pigment, some of which was also found extracellularly. (Fig. 2A).

Figure 2B. Immunoperoxidase stain with HepPar1 confirming diagnosis of HCC.