Case Report

Clivus metastasis of hepatocellular carcinoma causing hypopituitarism

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Abstract

Hepatocellular carcinoma usually metastasizes within the liver. Extrahepatic sites are less common but most frequently involve regional lymph nodes, lungs, adrenals and bones. Metastatic hepatocellular carcinoma to the skull is an uncommon occurrence with only a few case reports documented in the literature. We report a case of metastatic hepatocellular carcinoma to the clivus in a 67-year-old male who presented with headache, vertical diplopia, left ptosis and hypopituitarism.

Keywords: bone, hepatocellular carcinoma, hypopituitarism, metastasis, skull

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy [1-4]. It is associated with chronic viral hepatitis B and C as well as cirrhosis [2,3]. Intrahepatic metastases are relatively common, extrahepatic metastases are unusual with lung, adrenal, bone and regional lymph nodes being the most common sites [1-4]. Herein, we report a case of a 69-year-old male who developed metastatic hepatocellular carcinoma to the clivus with associated hypopituitarism. This report will briefly review the literature on hepatocellular carcinoma metastases to the skull.

Case

A 67-year-old man with a history of hypertension, hyperlipidemia, chronic obstructive pulmonary disease, coronary heart disease, chronic hepatitis C and polysubstance abuse (alcohol, tobacco and heroin) presented initially with headache, vertical diplopia and left ptosis. The physical examination was significant for left oculomotor nerve palsy. Magnetic resonance imaging (MRI) of the brain showed a 2.4x2.4x1.5 cm mass arising from the superior aspect of the clivus with extension into the sella and left cavernous sinus and displacement of the pituitary gland to the right and the infundibulum anteriorly. The mass was seen to abut the dorsal margin of the cavernous segment of the left internal carotid artery without vessel narrowing. Computed tomography (CT) scans of the chest, abdomen and pelvis showed a cirrhotic

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liver with a 6.8 cm mass in hepatic segments VI and VII. MRI of the liver showed a 6.8 cm hepatocellular carcinoma in hepatic segments VI/VII and a 1.1 cm lesion in hepatic segment VIII.

Laboratory testing showed elevated alpha fetoprotein (AFP) 12.5 ng/mL (reference range <11.0 ng/mL), mild hyperprolactinemia 24.9 ng/mL (reference range 4.0-15.2 ng/mL) and hypopituitarism. Hormone levels were: follicular stimulating hormone (FSH) 0.2 mU/mL (reference range 1.5-12.4 mU/mL), luteinizing hormone (LH) <0.1 mU/mL (reference range 1.8-10.8 mU/mL), testosterone 76 ng/dL (reference range 193-824 ng/dL), insulin-like growth factor 1 (IGF-1) 33 ng/mL (reference range 34-240 ng/mL), thyroid stimulating hormone (TSH) 0.543 uU/mL (reference range 0.4-5.5 uU/mL), free T4 0.6 ng/dL (reference range 0.9-1.7 ng/dL), T3 90 ng/dL (reference range 79-165 ng/dL), growth hormone (GH) 1.46 ng/mL (reference <1.00 ng/mL), adrenocorticotropic hormone (ACTH) 25 pg/mL (reference <<47 pg/mL) and morning cortisol 4.3 ug/dL (reference range 5.3-22.5 ug/dL).

The patient underwent an endoscopic, endonasal trans-clival approach for partial resection of the skull base mass. Intraoperative frozen section consultation of the biopsied clival mass revealed metastatic hepatocellular carcinoma. Histopathological examination of the paraffin-embedded specimen revealed bile producing, pleomorphic cells with variable amounts of eosinophilic cytoplasm arranged in a trabecular and to a lesser extent in an acinar pattern [Figure 1]. The nuclei showed varying degrees of atypia with prominent nucleoli and occasional intranuclear vacuoles. The bone invasion was identified [Figure 2]. This pattern was consistent with metastatic hepatocellular carcinoma. Immunohistochemical stain for arginase-1 (prediluted; Ventana Medical Systems, Tucson, Arizona, USA) showed diffuse positive staining, supporting the diagnosis.

Figure 1. Metastatic hepatocellular carcinoma with small foci of brown staining bile material (hematoxylin and eosin, original magnification 200X).

Figure 2. Epithelioid cells of metastatic hepatocellular carcinoma adjacent to bone and bone marrow elements in the clivus (hematoxylin and eosin, original magnification 200X).
Discussion

Hepatocellular carcinoma is one of the most common malignancies worldwide [1-4]. Metastasis tends to occur in later stages of the disease with the liver being the most common site [3,4]. The most common extrahepatic sites are lung and abdominal lymph nodes, with bone involvement being rare [1-6]. When HCC metastasizes to the bone, it usually does so to the vertebrae, pelvis and ribs [1,2,4,7]. Skull metastases are uncommon and occur in only about 0.4-1.6% of patients with HCC [1,4,7]. These patients typically present with pain associated with the mass and cranial nerve deficits [8,9]. Intracranial bleeding such as epidural [6] and subdural [7] hematomas have also been reported but was not seen in the current case.

Metastases specifically to the clivus are even rarer. In a series of 47 patients with clival metastases, DeConde et al identified five cases of HCC, though only three patients had HCC confirmed histologically. The other two patients were presumptively diagnosed based on imaging and clinical history [10]. Four patients were male. Three patients had hepatitis C and two had hepatitis B. Four presented with abducens nerve palsy and one with a headache. One patient had ptosis and two patients had multiple cranial nerve palsies on presentation.

Our patient not only presented with a rare anatomical location for HCC metastasis confirmed histologically but also presented with hypopituitarism, likely related to mass effect on the pituitary, given the extension of the tumor into the sella. The pituitary gland was seen to be flattened into the right aspect of the sella on MRI. A similar case of clival and pituitary HCC metastasis presenting with panhypopituitarism had a slightly different hormone profile [11]. In addition to low FSH, LH, free T4 and cortisol levels, our patient also had decreased IGF-1 and testosterone. Compared to the normal prolactin and GH levels in the previously reported patient, our patient’s prolactin and GH were both elevated.

Differential diagnoses of clival masses based on imaging are chordoma (40% of all cases), chondrosarcoma, metastases from other primaries [8] and meningioma. Histologically, chordoma, chondrosarcoma and meningioma can usually be ruled out. The classic picture of chordoma is that of cords and nests of physaliphorous cells embedded in a myxoid stroma. In chondrosarcoma, tumor cells produce a cartilaginous matrix. There are many histologic variants of meningiomas, most of which are low-grade tumors. The most common type consists of eosinophilic syncytial cells arranged in a whorled pattern. Histologically, the most challenging differential is metastases from other primaries. Especially poorly differentiated HCC without bile production and hepatocellular morphology can look similar to other poorly differentiated metastases and might not be distinguishable without immunohistochemical stains such as arginase, which is a good marker of HCC.

Conflict of interest

All authors declare that they have no conflict of interest.

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References