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Case report

Primary hepatoid adenocarcinoma of the orbit



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ABSTRACT

Purpose: To report a case of primary hepatoid adenocarcinoma of the orbit.

Observations: An adult patient was referred for evaluation of an orbital mass. Histopathology of the orbital biopsy indicated a carcinoma with hepatoid features. Laboratory studies revealed normal liver function tests, elevated serum alpha-fetoprotein, and whole-body positron emission tomography/computed tomography scan showed no evidence of liver involvement or an alternative primary origin. **Conclusions and importance:** To the authors' knowledge, this is the first reported case of primary hepatoid adenocarcinoma of the orbit.

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1. Introduction

Hepatoid adenocarcinoma (HAC) is a rare extrahepatic malignant tumor that is characterized by a histologic resemblance to hepatocellular carcinoma (HCC). HAC is most commonly reported in the stomach, and has been identified in multiple abdominal-pelvic organs, the lungs, and other sites.^{1–8} Typically, patients with HAC present with elevated serum alpha-fetoprotein (AFP), and with tumor immunohistochemistry positivity for AFP, however both of these features are variable in reports.¹ Although HAC of the skull base has recently been reported, to our knowledge, it has not yet been reported as a primary tumor of the orbit.⁸

2. Case report

A 63-year-old female was referred for evaluation of an orbital mass. The patient noted several weeks of left sided eyelid swelling, and vertical diplopia. Past medical history included diabetes mellitus, hypertension, asthma, and arthritis. The patient had no history of alcohol abuse, cancer, hepatitis B or C, cirrhosis, or immune compromise.

On examination, the patient's visual acuity was 20/40 OD and 20/60 OS. On confrontational testing, there was a superior visual

field cut in the left eye. There was an afferent pupillary defect on the left. Extraocular movements were limited in supraduction and abduction on the left side. Hertel measurements were 13/14 mm (OD/OS), and the left globe was inferiorly displaced. Marginal reflex distance-1 measurements were 3/1 mm (OD/OS). The anterior segment exam was unremarkable.

CT scan of the orbits demonstrated an extraconal, ovoid, enhancing solid mass in the superior left orbit measuring 23 × 21 × 21 mm, destroying the roof of the left orbit with extension into the left anterior cranial fossa and left frontal sinus (Fig. 1).

Orbitotomy with biopsy and de-bulking of the mass was performed through an upper eyelid crease approach. Upon biopsy brisk hemorrhage was encountered and required hemostatic matrix (FloSeal, Baxter Healthcare Corporation, Hayward, CA) to control bleeding. Histopathology of the mass revealed large, round epithelioid cells with abundant eosinophilic cytoplasm and a very high mitotic rate. Immunohistochemistry revealed diffuse weak cytoplasmic staining for keratin (AE1/3 & CAM5.2), diffuse cytoplasmic staining for arginase-1, extensive cytoplasmic staining to HepPar-1, focal weak cytoplasmic staining to glypican-3, and extensive weak canalicular pattern staining to polyclonal CEA (Fig. 2). The tumor demonstrated negative staining for AFP, chromogranin A, synaptophysin, CD56, and S-100 protein. These features indicated a carcinoma with hepatocarcinoma features.

Laboratory studies revealed normal liver AST, ALT, and total bilirubin levels. Serum alpha-fetoprotein (AFP) was mildly elevated at 8.5 ng/ml (reference range < 6.1 ng/ml). A whole body combined

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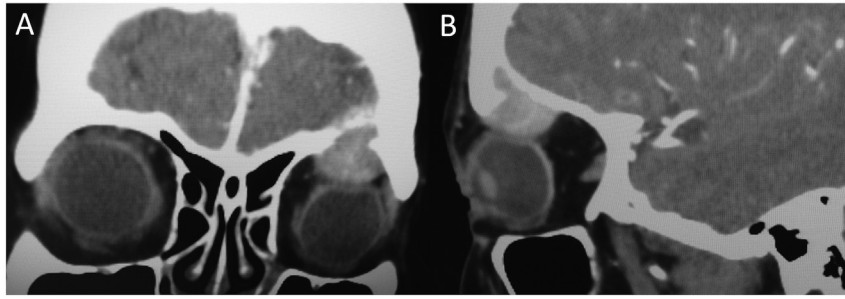


Fig. 1. Computed tomography scan of the orbits demonstrating an extraconal, left orbital mass destroying the roof with extension into the anterior cranial fossa and frontal sinus as seen on coronal (A) and sagittal (B) views.

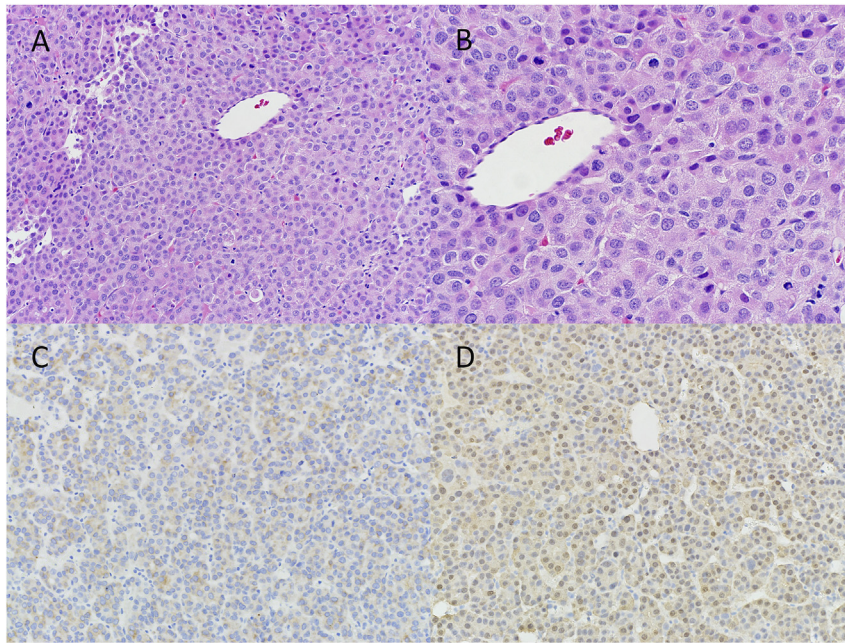


Fig. 2. The mass was composed of large round epithelioid cells with abundant eosinophilic cytoplasm and a high mitotic rate (A: hematoxylin and eosin stain, 10x; and B: hematoxylin and eosin stain, 20x). Positive immunohistochemical stains included keratin proteins (AE1/3 & CAM5.2 antibody cocktail) (C: 20x) and arginase-1 (D: 20x).

PET/CT scan revealed a hypermetabolic solid left orbital mass and lytic lesions within the sternum, right posterior seventh rib, and T9 vertebral body felt to represent metastatic disease. There was no evidence of liver involvement. Given these findings, the patient was given a diagnosis of primary hepatoid adenocarcinoma of the orbit with metastatic spread. Repeat imaging with MRI of the brain and

orbits two months after the initial CT scan revealed significant interval progression (Fig. 3).

The patient received 40 Gy of external beam radiation to the orbit. Despite radiation, the tumor continued to progress rapidly with worsening intracranial extension. Given the patient's rapid clinical deterioration, chemotherapy was deferred. The patient

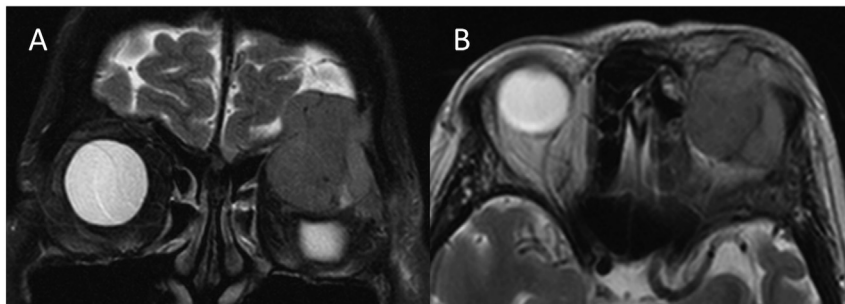


Fig. 3. Magnetic resonance imaging of the brain and orbits demonstrating enlargement and worsening intracranial extension of the left orbital mass as seen on coronal (A) and axial (B) views.

elected to be placed on hospice care and unfortunately died shortly thereafter, approximately 4 months after the initial diagnosis.

3. Discussion

Hepatoid adenocarcinoma (HAC) is a rare and typically aggressive extrahepatic tumor which resembles hepatocellular carcinoma (HCC) and is most commonly reported in abdominal–pelvic organs and the lungs.^{1–7} It has also been recently reported in the anterior skull base.⁸ To our knowledge, this is the first case of primary HAC of the orbit, although it must be acknowledged that the tumor may have originated in the frontal sinus or frontal bone.

Patients with HAC commonly present with an elevated serum AFP.¹ The tumor resembles HCC in both morphology and immunophenotype. Histologically, HAC appears as large polygonal cells with abundant eosinophilic cytoplasm proliferating in a trabecular or sheet-like fashion.⁸ Immunohistochemistry profile is consistent with hepatoid differentiation, with up to 91.6% of cases staining positively for alpha-fetoprotein (AFP).¹ Although our patient's serum AFP was elevated, the tumor was negative for AFP staining. There is no specific immunohistochemical stain that can differentiate HAC from HCC.¹

Diagnosis of HAC relies on confirmation of an extrahepatic tumor with a histopathologic profile mimicking HCC in the absence of primary HCC on systemic work-up. The main consideration for an orbital tumor with hepatoid features and elevated serum AFP is metastatic HCC to the orbit, which is a well-documented entity.⁹ Primary HCC should be ruled out with imaging. In this case, a combined whole body PET/CT scan was performed, which showed no evidence of liver lesions or an alternative primary origin. PET alone, which uses a glucose analog tagged with a positron-emitting isotope of fluorine (FDG), is not sufficiently sensitive for detecting primary HCC, because not all HCCs are FDG avid.¹⁰ A disproportionate number of metastatic HCCs, however, are FDG avid and would be detected by PET.¹⁰ The addition of CT images to PET, as was done in this case, significantly increases the yield when the lesion is not FDG avid, since 90% of HCC are visible on unenhanced CT.¹¹ Also of note, primary HCCs with extrahepatic metastatic spread tend to be large (>5 cm),¹² and large primary HCCs are more readily detectable on both PET and CT scans.^{10,13} Therefore, the authors believe that the PET/CT performed in this case was sufficient to rule out primary HCC.

This and previous reports indicate HAC to be an aggressive tumor with poor prognosis.^{1–8} Treatment is not well defined but previous strategies have included surgical excision or de-bulking, chemotherapy, and radiation.^{2–8} Unfortunately, our patient's tumor was highly aggressive and continued to rapidly progress despite surgical de-bulking and radiotherapy. The optimal treatment for HAC remains unknown.

Patient consent

The patient was deceased at the time of preparation of this report, however written consent was obtained from the patient's next-of-kin for publication of personal information.

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Conflict of interest

The following authors have no financial disclosures: JBA, FLG, MMB, MRV, RCK.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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