

Orbital Metastasis as Initial Clinical Presentation in a Patient of Hepatocellular Carcinoma – A Rare Case with Review of Literature

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Abstract

Orbital metastasis, as the initial clinical presentation in hepatocellular carcinoma (HCC), is a rare manifestation. A 66-year-old male patient presented with a history of protrusion of the eyeballs, double vision, and swelling over the left side of the head for 8 months. Magnetic resonance imaging of the brain with orbit revealed a heterogeneous lesion in the left frontal lobe causing its destruction with intraorbital and intracranial extension. Triphasic contrast-enhanced computed tomography was suggestive of multiple hypodense areas in both lobes of the liver. Tissue diagnosis from the liver was suggestive of HCC. A diagnosis of multifocal HCC with orbital metastasis was made. The patient was treated with palliative radiotherapy and sorafenib. Orbital metastasis in HCC is rare. Prognosis is somber in such cases. The treatment should focus on providing palliation from symptoms.

Keywords

- hepatocellular carcinoma
- metastasis
- orbital
- palliation
- radiotherapy

Introduction

Orbital metastases are relatively uncommon accounting for 1 to 13% of all orbital tumors and occur in 2 to 5% of cancer patients.^{1–4} Hepatocellular carcinoma (HCC) is an aggressive malignancy, with 50 to 75% of patients developing metastases during the course of their disease.^{5,6} The most common sites of metastasis are the regional lymph nodes and lungs. The less common sites of distant metastases include bone, brain, adrenal glands, and skin.^{5,7,8}

The common malignancies metastasizing to the orbit are breast, lung, prostate, kidney, thyroid, and gastrointestinal.^{1,9–11} Orbital metastasis from HCC is a rare presentation with only a handful of cases reported in the literature. Herein, we report a rare case of orbital metastasis as the

initial clinical presentation in a patient with HCC with a brief review of the literature.

Case Report

A 66-year-old male patient presented with a history of protrusion of the eyeballs, double vision, and swelling over the left side of the head for 8 months. There was no history of jaundice, awareness of mass anywhere else in the body, loss of weight, and loss of appetite. On clinical examination, left eye proptosis with reduced visual acuity and conjunctival chemosis was present. A soft-tissue swelling measuring 4 cm × 4 cm was present in the left frontal region and orbit. Abdominal examination revealed hepatomegaly. The differential diagnosis at this stage included primary orbital

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neoplasm or metastatic tumor to the orbit. Baseline investigations including hemogram and kidney function tests were normal. Bilirubin was within normal limits, but liver enzymes were raised (aspartate transaminase: 87.3 U/L, alanine transaminase: 93.17 U/L, and alkaline phosphatase: 223 U/L). Serum α fetoprotein was found to be elevated (1000 ng/mL). Peripheral blood film examination did not show any abnormality. The patient tested positive for hepatitis C antibody. Magnetic resonance imaging (MRI) of the brain with orbit revealed a heterogeneous lesion in the left frontal lobe causing its destruction with intraorbital and intracranial extension (**Fig. 1**). Contrast-enhanced computed tomography of the chest was normal, and a triphasic scan of the abdomen showed multiple arterial hypervascular lesions in both lobes of the liver with washout in venous and delayed phases, suggestive of multifocal HCC. The largest lesion measured 2.5 cm \times 3.2 cm in the right lobe of the liver (**Fig. 2**). Multiple, small, similar arterial hypervascular lesions were seen in both lobes of the liver. Ultrasound-guided fine-needle aspiration cytology from the liver was suggestive of HCC (**Fig. 3**). The patient was treated with palliative radiotherapy of 30 Gy in 10 fractions to the left eye. The patient was subsequently started on sorafenib. MRI of the brain including the orbit was done after 3 months of radiotherapy, which revealed a significant reduction in the size of the lesion. Four months later, the patient developed lung metastasis and left iliac bone metastasis. He was given palliative radiotherapy of 20 Gy in five fractions to the left iliac bone, following which he had significant pain relief. The patient was given the option of second-line treatment with immune checkpoint inhibitors or second-line tyrosine kinase inhibitors, but he refused due to cost issues. The patient received intravenous zoledronic acid for 3 months. The patient is alive with progressive disease and is on palliative care.

Discussion

Metastasis to the orbit is a rare presentation in HCC. Breast constitutes the most common primary site, with 28 to 70% of orbital metastasis.¹¹ The common presenting symptoms of orbital metastases include diminished vision, pain, proptosis, double vision, awareness of mass, and limitation of extraocular movements. The differential diagnosis includes



Fig. 2 Contrast-enhanced computed tomography (CECT) showing a lesion in segment VI of the liver with small lesions in both lobes of the liver.

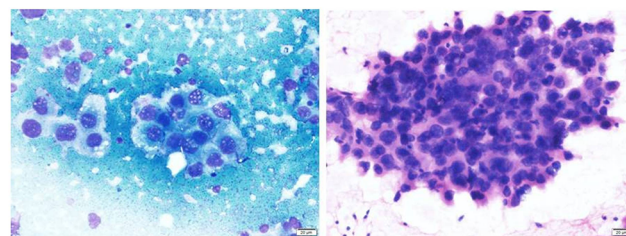


Fig. 3 The tumor cells were highly pleomorphic with coarse chromatin, prominent nucleoli, and moderate amount of cytoplasm. These tumor cells showed prominent cytoplasmic and nuclear vacuoles, and some of them showed intracytoplasmic bile pigment and intranuclear inclusions.

vascular lesions; lymphoproliferative lesions; tumors of the lacrimal gland and optic nerve; and metastatic tumors from the breast, lung, prostate, thyroid, and orbital chloroma in patients with acute myeloid leukemia or chronic myeloid leukemia.

The presence of orbital metastasis in HCC predicts a poor prognosis. In a series of 100 patients by Lubin et al,¹² the breast was the most common site in 53% of the patients, followed by the prostate in 12% and lungs in 8%. The most common clinical findings were limited to ocular motility (54%), proptosis (50%), and palpable mass (43%). The mean survival time after the orbital diagnosis was 20 months. Patients with metastatic carcinoid tumors had the longest mean survival (60 months) and patients with breast cancer had the

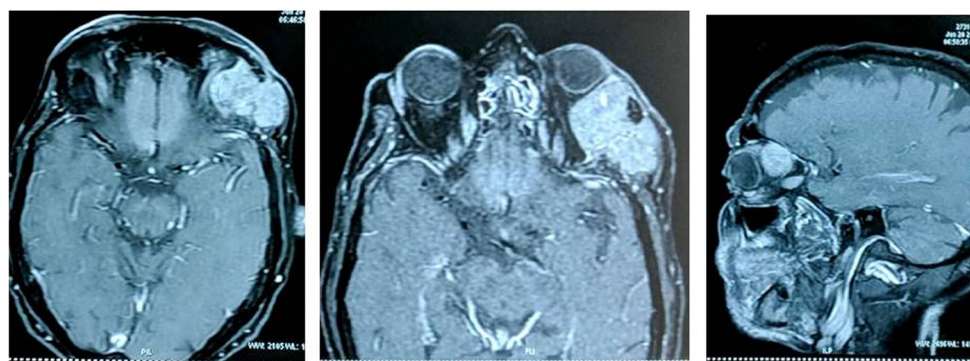


Fig. 1 Magnetic resonance imaging of the brain with orbit showing a heterogeneous lesion in the left frontal lobe causing its destruction with intraorbital and intracranial extensions.

second-longest mean survival (22 months) after diagnosis of orbital metastasis. In a series of 93 patients of orbital metastasis by Magliozzi et al,² HCC was the primary site in only one patient. Orbital metastases occur unilaterally in more than 90% of the patients.¹¹ To the best of our knowledge, 33 cases have been reported in the literature including case reports and series.^{2,5-8,13-34} Most of the patients were in the sixth and seventh decades of life.

Orbital metastasis, as the initial manifestation of disease, was present in 22 out of 33 patients (►Table 1). Our patient also presented with orbital metastasis as the initial presentation of the disease. A detailed history and thorough ophthalmic and general physical examination must be done in patients with orbital metastasis. Prompt referral to an oncologist is necessary for patients who present with orbital metastasis as the initial manifestation of the disease to rule

Table 1 Cases of orbital metastasis in hepatocellular carcinoma reported in the literature

Author	Year	Number of cases	Age	Gender	Orbital metastasis as the first manifestation of disease	Outcome
Lubin et al ¹²	1980	1	69	Male	Yes	Alive
Zubler et al ¹³	1981	1	64	Male	Yes	Died after 3 months
Wakisaka et al ¹⁴	1990	1	58	Male	Yes	Died after 11 months
Phanthumchinda and Hemachuda ¹⁵	1992	1	29	Female	Yes	Not mentioned
Kami et al ¹⁶	1994	1	60	Male	Yes	Died after 3 months
Tranfa et al ¹⁹	1994	1	85	Male	Yes	Not mentioned
Schwab et al ²⁰	1994	1	19	Male	Yes	Died 1 month
Hosokawa et al ²¹	1994	1	70	Male	No	Not mentioned
Loo et al ²²	1994	1	71	Female	Yes	Lost to follow-up after 3 months
Font et al ²³	1998	1	79	Female	Yes	Alive
Scolyer et al ²⁴	1999	1	78	Male	No	Not mentioned
Kim et al ⁷	2000	1	56	Female	Yes	Died after 2 months
Chen et al ²⁵	2003	1	69	Male	Yes	Orbital mass regressed
Oida et al ²⁶	2006	1	72	Male	No	Died after 4 months
Machado-Netto et al ¹⁷	2006	1	57	Male	Yes	Died after 15 months
Srinivasan and Krishnanand ⁵	2007	1	76	Female	Yes	Not mentioned
Hirunwiwatkul et al ⁸	2008	1	74	Female	Yes	Died after 2 months
Pitts et al ²⁷	2008	2	61 47	Female Male	Yes Yes	Both patients died with progressive disease
Fonseca Júnior et al ²⁸	2008	1	57	Male	Yes	Died after 15 months
Quick et al ⁶	2009	1	52	Male	No	Alive 20 months
Kolarević et al ²⁹	2011	1	70	Male	No	Died after 6 months
Mustapha and Madachi ³⁰	2011	1	25	Male	No	Not mentioned
Guerriero et al ³¹	2011	1	45	Male	No	Not mentioned
Eldesouky et al ¹⁸	2014	6	Range 47–70 Mean age 60.2 years	Male	3 cases	Survival of five cases ranged between 8 and 13 months with a mean of 10.2 (±2.3) months. One patient was receiving treatment (diagnosed for 6 months)
Téllez-Villajos et al ³²	2015	1	70	Female	No	Alive at 4 months
Madabhavi et al ³³	2020	1	72	Male	Yes	Alive at 7 months with stable disease
Protopapa et al ³⁴	2020	1	53	Male	Yes	Discharged after radiotherapy with little improvement

out primary at the earliest. Radiological investigations such as computed tomography and MRI are the principal means of evaluating orbital lesions. The potential risks of performing a biopsy of an orbital mass such as visual loss, bleeding, and diplopia, should always be weighed against the potential benefits, evaluating whether the management options are going to change as a result of the biopsy.

The intent of treatment in patients presenting with orbital metastasis is palliative as such metastasis suggests a haematogenous spread of disease. The aim of the treatment is to maximize the quality of life of such patients and to preserve visual function if possible. Radiotherapy is the mainstay of treatment in such patients as it will cause shrinkage of the lesion, control of symptoms, and visual preservation. Surgical resection is appropriate only in selected patients.

Orbital metastasis in HCC is rare. A high index of suspicion is required as proptosis and diplopia were the first manifestations of disease in the index case. Clinicians should be aware of such presentations. Prognosis in such patients remains dismal. The treatment should focus on providing relief from symptoms of the illness. Radiotherapy plays an important role in downsizing the lesion and symptom control.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms.

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Conflict of Interest

None declared.

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