A case report: Brain metastasis of hepatocellular carcinoma

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Abstract

Introduction: Hepatocellular carcinoma (HCC) is the 5th most common malignancy in the world and 2nd most common cause of cancer related deaths. Though extra-hepatic metastases are seen in 64% of patients, metastasis in brain and skull is extremely rare.
Case description: A 53-year-old HBsAg-positive gentleman with known hepatocellular carcinoma receiving radiotherapy and chemotherapy presented with progressively enlarging swelling over the left side of the forehead. Imaging showed a left frontal extradural mass eroding the underlying skull and exerting a mass effect on the brain. As the primary HCC was controlled, differential diagnoses included eosinophilic granuloma, plasmacytoma, and intraosseous meningioma. The mass was excised, and histopathology revealed metastatic HCC. The postoperative period was uneventful, and radiotherapy to the scalp was added along with continuation of chemotherapy.
Conclusion: Skull and brain metastasis from primary HCC is rare. We report such a rare case with successful surgical management followed by adjuvant therapy.

Key words: Hepatocellular Carcinoma, scalp metastasis, radiotherapy and chemotherapy

Introduction

Hepatocellular carcinoma (HCC), a highly malignant neoplasms, is the 5th most common malignancy in the world and 2nd most common cause of cancer related deaths[1]. The disease is usually manifested in the 6th and 7th decades of life. The Extra-hepatic metastases are seen in 64% of the cases and rarely in cranial regions. The more common sites are lungs, regional lymph nodes, kidney, bone marrow and adrenal glands[2,3,4,5]. When a rapidly growing scalp swelling is encountered in a case of HCC, who is responding to chemotherapy, secondaries from HCC is not commonly thought of, but our case turn out to be a secondary from of HCC.

Case report

A 53-year-old gentleman presented to the Department of Neurosurgery with a progressively enlarging swelling over the left forehead. Initially pea-sized, the lesion increased to the size of a lemon over five weeks with progressively worsening pain. There was no history of discharge, redness, itching, nausea, vomiting, seizures, focal neurological deficit, or symptoms of raised intracranial pressure. No similar lesions were noted elsewhere in the body.

The patient was a known case of hepatocellular carcinoma diagnosed six months earlier. He was initially treated with Tablet Lenvatinib (4 mg), but due to inadequate tumor response and progression of disease, therapy was switched to oral Regorafenib, which achieved partial biochemical and radiological response. There was no relevant family history of similar illness.

On examination, the patient was alert, awake, and oriented. Karnofsky Performance Status was 80 and ECOG performance status was 1. He was icteric without palpable lymphadenopathy. Neurological examination was normal with no evidence of raised intracranial pressure.

Abdominal examination revealed mild right upper quadrant tenderness with negative Murphy's sign. Hepatosplenomegaly and palpable masses were absent in the abdomen. Neurological examination demonstrated intact higher mental functions, cranial nerves, and fundi. Motor and sensory examinations were normal. There were no signs of raised intracranial pressure. Rest of the systemic examination revealed no abnormality.

Local scalp examination revealed a solitary, non-tender, non-pulsatile hemispherical swelling measuring 5 cm in diameter over the left frontal region. The overlying skin was smooth without inflammatory changes but fixed to the mass and underlying structures.

Laboratory investigations revealed deranged coagulation profile, elevated ESR, elevated liver enzymes, hypoalbuminemia, hyperbilirubinemia, elevated serum alpha-

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fetoprotein, and positive HBsAg.

Abdominal ultrasonography and contrast-enhanced CT abdomen showed findings suggestive of HCC with multiple hepatic lesions.
(Figure 1)

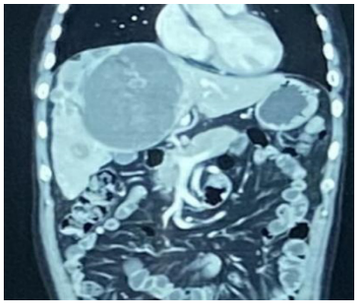

Figure 1: CECT of abdomen showing a large 13x12 cm contrast enhance mass with multiple other lesions probably secondaries in liver.

Non-contrast CT scan of head was done which showed a well-defined heterogeneously hyperdense lesion measuring 45x41x35 mm in left frontal region. Few areas of calcifications were noted within and along the periphery of the lesion. Few areas of hypodensities were noted within the lesion. The lesion was extending anteriorly for a length of 22.5 mm to involve scalp layer with a 31mm bony defect with irregular margin (Figure 2). The lesion extended intracranially for a length of 14.0 mm with the underlying dura intact. It was abutting and displacing the adjacent left frontal lobe of brain. However, there was no evidence of perilesional edema of underlying brain. The lesion was abutting superior sagittal sinus with loss of fat plane. There was no significant mass effect or midline shift or midbrain rotation. (Figure 3)

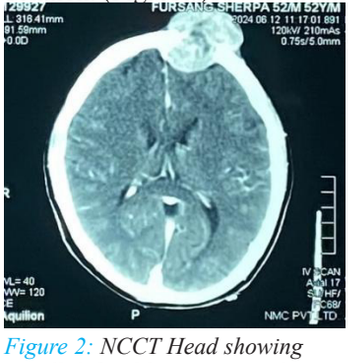

Figure 2: NCCT Head showing a well defined heterogenous lesion in frontall region with few area of hypodensities.

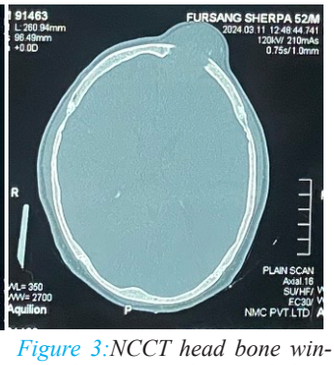

Figure 3:NCCT head bone window showing a defect in left frontal bone with irregular margin.

MRI brain further confirmed destruction of the frontal bone with extension into the scalp and cranial cavity.(Figure 4)

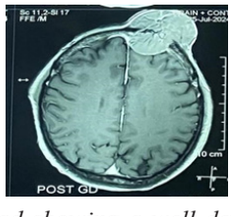

Figure 4: MRI Head showing a well defined lesion in the left frontal bone with destruction of bone and extension to cranial cavity with intact dura.

As the primary lesion appeared controlled, differential diagnoses included plasmacytoma and eosinophilic granuloma. Metastatic HCC was considered less likely. Systemic metastatic workup revealed no additional distant lesions, patient was planned for excision of the left frontal lesion.

The patient underwent surgical excision of the lesion through a bicoronal incision.. A solitary, firm, grayish blue subgaleal mass measuring 4 × 4 cm was identified, eroding a 5 × 5 cm portion of the frontal bone. The lesion extended into the extradural space but spared the dura (Figure 5). Wide excision of the mass, including overlying skin and involved bone, was performed. A plastic surgeon reconstructed the scalp defect using adjacent tissue flaps.

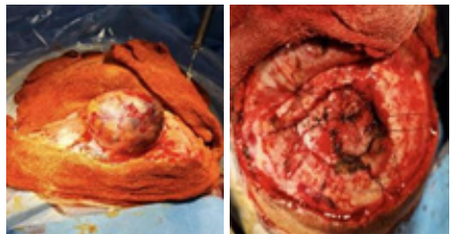

Figure 5: showing an intraoperative picture during excision showing a single subgaleal mass extending intracranially through bony defect with intact dura.

Postoperative period was uneventful. The histopathological report revealed it to be a metastatic lesion from the HCC. It showed encapsulated tissue comprising of tumor cells. These tumor cells were arranged in trabecular, pseudoacinar pattern, tubules and solid sheets. These tumor cells showed moderate to marked pleomorphism with increased nuclear-to-cytoplasmic ratios, round to oval nuclei, irregular nuclear membrane, vesicular to coarse chromatin, prominent nucleoli and moderate to abundant amount of eosinophilic granular cytoplasm. Some of the atypical cells showed clear granular cytoplasm. Few bizarre looking cells and few cells with intranuclear inclusions were also seen (Figure 6).

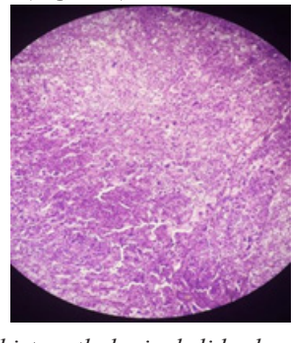

Figure 6: is histopathological slide showing the tumor cell with moderate to marked pleomorphism and increased N:C ratio, round to oval nuclei, irregular nuclear membrane, prominent nucleoli. Chemotherapy with oral regorafenib was resumed following complete wound healing, and adjuvant whole-brain radiotherapy (WBRT) was delivered to the scalp. The patient remains under regular oncological follow-up.

Discussion

Hepatocellular carcinoma (HCC) is the fifth most common

malignancies in the world and second most common cause of cancer related death globally. Its incidence is increasing worldwide because of the dissemination of hepatitis B and C virus infection. Patients with liver cirrhosis are at particularly high risk of developing HCC and should be monitored every six months to enable early detection when curative interventions such as hepatic resection, transplantation, or percutaneous therapies remain feasible[6].

HCC commonly metastasizes to the lungs, regional lymph nodes, peritoneum, and adrenal glands, but rarely to cranium. Shuangshoti et al[7]. The reported cranial metastases in only 1.3%–2.9% of cases. Historically, clinicians have paid limited attention to this phenomenon because cranial metastases are clinically uncommon, often mimic other skull lesions such as plasmacytoma or eosinophilic granuloma, and typically indicate advanced disease with poor prognosis[8].

The current literature includes a limited number of reported cases of cranial metastases from HCC (summarized in Table 1). Reported presentations range from asymptomatic skull lesions to acute neurological deterioration due to intracerebral hemorrhage. Table 1

Author	Distinctive presentation
Moriya et al 9	Brain metastasis seen in 1 year interval after hepatectomy for HCC.
Endo et al 10	Subgaleal and epidural metastasis presenting as epidural hemorrhage and died from hepatic failure
Peres et al 11	Cerebral metastasis presenting as initial finding of HCC
Tanabe et al12	Unusual presentation of brain metastasis from HCC- two case reports
Loo et al13	Two cases with cerebral metastasis presenting as initial findings of HCC
Salvati et al 14	Brain metastasis of HCC
Asahara et al15	Brain metastasis seen after hepatectomy for HCC in 5 cases
Kim et al16	Nervous system involvement by metastatic HCC
Yen et al17	Clinical and radiological pictures of HCC with intracranial metastasis
Shuangshoti et al7	Intracranial metastasis of hepatic carcinomas: a study of 9 cases within 28 years
Friedman et al18	A rare case with no identifiable risk factor for primary liver cancer
Bilge et al 1	HCC presenting with the initial manifestations of an intracranial mass lesion without any symptoms or signs suggestive of the primary hepatic site of the tumor

Yen et al17 reported that 90%15 of cases demonstrating hyperdense lesion on non-contrast computed tomography brain scan and 77% cases showed homogenous enhancement. In the non-skull involved group, 41% disclosed ring-shape enhancement and 87% had perifocal edema. 24% presented as intracerebral hemorrhage. Our patient had heterogeneously hyperdense lesion with few areas of hypodensities within the lesion however there were no evidence of perilesional oedema of underlying brain.

Most of HCC cases having lung metastasis, do not have cranial metastasis. In 66.7%, these cases have cranial metastasis with or without concurrent pulmonary metastasis[5,17]. However, no other simultaneous metastatic sites were found in our patient.

Cranial or intracranial metastases from HCC are generally symptomatic and can be life-threatening. Although technically feasible, surgical excision is reserved for accessible lesions not more than three, patients with reasonable hepatic function, primary malignancy well controlled and overall good prognosis[19]. Adjuvant radiotherapy, including whole-brain radiation therapy (WBRT) or stereotactic radiosurgery (SRS), can enhance local control and improve quality of life1.

With advancements in diagnostic imaging and systemic therapies, cranial metastases are being detected more frequently than before. However, prognosis remains poor, with overall survival measured in months even with multimodal therapy[20,21]. Early diagnosis is very important for improving the prognosis. Computed tomography (CT) and magnetic resonance imaging (MRI) are the two most commonly used imaging modalities for detecting brain lesions early[20,21].

Treatment requires an individualized consideration for each patient, depending on the clinical status (e.g., neurologic deficit, Child-Pugh class, life expectancy), disease burden (AFP level, extracranial disease control, especially the number of brain metastasis), and characteristics of the primary HCC (radiologic aspect, size, location)[22,23,24].

An integrative multidisciplinary approach for each case from diagnosis to treatment is always recommended24. Current options for cranial metastasis of HCC includes surgery, whole-brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), chemotherapy, targeted agents, immunotherapy, and supportive measures[24].

Even in patients with favorable prognostic factors who might benefit from an aggressive treatment, the goal of treatment is only to prolong survival and improve quality of life24. For those with short survival expectancy, stabilizing brain metastasis and palliative treatment is warranted24. Control of primary tumor (HCC), surgical excision of cranial mass followed by radiotherapy of cranium with appropriate chemotherapy has been found to improve overall survival as well as the quality of remaining life.

Conclusion

Brain and skull metastasis from hepatocellular carcinoma is rare but clinically significant. Early diagnosis and a multidisciplinary treatment strategy including surgery, radiotherapy, and systemic therapy can improve quality of life and survival outcomes in selected patients.

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