

# Isolated Progressive Enlargement of Head Mass as the First Symptom: A Rare Case Report of Cranial Metastasis of Hepatocellular Carcinoma and Literature Review

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## Case report

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# Abstract

**Background:** This article presents a rare case of skull metastasis of primary hepatocellular carcinoma that manifests the isolated progressive enlargement of the head mass as the first symptom.

**Case presentation:** A 65-year-old female patient presented an isolated painless mass in the head, which grew rapidly over the last month. Head CT revealed a 6.4 cm×5.6cm osteolytic destruction in the right parietal bone. MRI further revealed that the occupation was significantly enhanced in the T1 reinforced phase. The patient underwent total surgical resection. Postoperative pathology confirmed that the head mass was the skull metastasis from hepatocellular carcinoma (HCC).

**Conclusion:** The case of skull metastasis from primary hepatocellular carcinoma is rare, and HCC patient with intracranial metastasis tends to have a rather poor prognosis. Surgical excision of the metastatic mass and radiotherapy can improve the life quality and prolong the survival time of the patient.

## Background

Hepatocellular carcinoma rarely metastasizes to the bone system, as the reported incidence of skull metastases is as low as about 0.5 to 1.6 percent<sup>1,2</sup>. Consistently, the case of progressive enlargement of isolated head mass as the first symptom for HCC is extremely rare<sup>3,4</sup>. Here, we report a case of skull metastasis of hepatocellular carcinoma, and conduct the literature review.

## Case Description

A 65-year-old female patient admitted to the neurosurgery department of our hospital was diagnosed with an isolated progressive enlargement head mass. Over the past six months before admission, she occasionally felt dizzy. Three months before admission, the patient accidentally found a mass in the right parietal bone during the haircut. One month before admission, the patient felt that the mass had been enlarged significantly. About one week before admission, the mass was several times larger than the size of 3 months ago. The patient reported a history of hypertension for 15 years, an event of acute appendicitis 30 years ago and received appendectomy. She also underwent surgery of Lumbar disc herniation 23 years ago.

## After Admission:

### Physical examination

A solitary painless head mass (about 6.4 cm×5.6cm in diameter) was observed in her right parietal region. The other physical examination did not confirm hepatic disease-related signs, such as liver palm, spider nevus and so on. After Cerebral infarction, her left limb muscle strength was down to grade Ⅱ, while the other limbs remained normal.

### Laboratory examination

Alanine aminotransferase (ALT) was 83 U/L (normal value 0–50 U/L). In addition, other laboratory indicators, including liver function, coagulation function and so on, were normal.

## Image examination

B ultrasound test found that the subcutaneous soft tissue in the range of about 67×25mm was hypoechoic, the boundary was unclear, the local skull bone cortex continuity was interrupted. Moreover, the internal signal showed a 53×26mm hypoechoic zone, along with the external hypoechoic rim. The findings indicated that the head subcutaneous soft tissue is hypoechoic, and the possibility of hematoma should be considered.

Abdominal B ultrasound revealed fatty liver, and no space-occupying lesions could be determined in gallbladder, pancreas, and spleen. Skull CT examination showed that the right parietal bone was destroyed and a soft tissue mass sized about 6.4× 5.6cm was (Fig. 1). MRI examination showed that the right parietal bone destruction and surrounding soft tissue mass (about 6.4×5.6 cm in size) with uneven enhancement. (Fig. 2).

**Treatment:** The patient accepted the resection of the space-occupying lesion in the right hemisphere. Sarcomatous tumor located outside the epidural was determined by intraoperative pathological analysis. The tumor had invaded the surface of the superior sagittal sinus. Then we resected the tumor completely, and found that the tumor capsule was intact, and that the cut surface was like beige fish. Postoperative immunohistochemistry suggested: GFAP (-). SYN (-). AE1/AE3(+). SOX10(-). CGA (-). VIM (-). CD99(-). TFE3(-). Ki-67(30%+). CK18(+). CK19(-). P63(-). TTF1(-). CD56(-). CEA (-). SMA (-). PAX8(-). GATA3(-). TG (-). HMB45(-). CK7(-). CK20(-). HePpar-1(+). GPC-3(+). CD34(-). ERG (-). SALL4(-). SYN (-). S100(-). The results of Immune markers were in agreement with the diagnosis of metastatic hepatocellular carcinoma, and the proliferation of cancer cells was medium (Fig. 3).

Postoperative pathology showed a convex oblate mass sized of 6.7×6.7×2cm, whose section was gray yellow and solid. Apparently, the mass seemed to have a capsule. Microscopic analysis showed that the tumor tissue has a dense arrangement, and forms the solid cancer nest and adenoid structure. A large number of blood sinuses could be seen in the stroma, which was indicative of hepatocellular metastatic carcinoma. All the tumor cells were consistently round in shape (Fig. 4).

The abdominal CT plain scan and enhancement examination found primary liver occupation (Fig. 5);

Postoperative laboratory examination indicated that the expression of liver tumor markers, including carbohydrate antigen 125,199, carcinoembryonic antigen, alpha fetoprotein, was still within the normal range.

## Discussion And Conclusions

The patients with hepatocellular carcinoma usually had a dismal prognosis<sup>5</sup>. The short therapeutic time window for extrahepatic metastases is usually in the late stages<sup>6</sup>. The common sites of extrahepatic metastasis of hepatocellular carcinoma include regional lymph nodes, lungs, bones and so on<sup>7</sup>. Among them, hepatocellular carcinoma bone metastasis often occurs in vertebrae, pelvis, ribs, skull and so on<sup>5</sup>. Previous literatures reported that the incidence of skull metastasis in hepatocellular carcinoma was roughly

0.5%-1.6%<sup>8,9</sup>. The prognosis of patients with skull metastasis of hepatocellular carcinoma was poor and the overall survival time was notoriously short in an average of 8 to 9 months<sup>10</sup>. In this case, the surgical indication was clear due to severe destruction of skull bone and infiltration of the sagittal sinus induced by the tumor<sup>11</sup>. Of note, the patient only manifested isolated and progressive enlargement head mass as the first symptom, and there was no obvious abnormality in the expression of the liver and tumor markers. After the surgical operation, only abdominal enhancement CT suggested that the left lobe of the liver is occupied.

A thorough searching of the literature in a vast variety of languages was performed to find all the available articles that describe skull metastasis from hepatocellular carcinoma, since January 1957<sup>12-62</sup>, one hundred and seven articles with the keywords of "skull metastasis AND hepatocellular carcinoma", 35 articles with "((skull metastasis [All Fields])) AND (hepatocellular carcinoma)" were found. These studies formed the basis of this review (Table 1). We found that the cases of cranium metastases from hepatocellular carcinoma were much prevalent than that of skull base metastasis, and such disparity could be attributable to the difficulty to find or to diagnose the skull base metastasis. More cases have been reported in recent years, partly due to the prolonged life expectancy of the population and the development of diagnosis technology<sup>63</sup>.

In light of the diagnosis and treatment of the patients with skull metastasis from hepatocellular carcinoma in this case, the author puts forward the following suggestions. Firstly, in terms of the diagnosis of progressive enlargement of scalp mass, if CT examination suggests osteolytic destruction of the skull, MRI examination further revealed that the occupation was significantly enhanced in T1 reinforced phase, with equal or low signal in T1 and T2 image, then the possibility of malignant tumor skull metastasis should be considered<sup>64</sup>. Secondly, in terms of clinical intervention, given the poor prognosis of patients with skull metastasis of hepatocellular carcinoma is poor<sup>4</sup>, the treatment regimens should be individualized by the combined therapy of surgical removal, radiotherapy, palliative treatment and so on<sup>1</sup>. Thirdly, in terms of operation, since the tumor tissue has an abundant blood supply<sup>65</sup>, blood (including blood products associated with coagulation) should be prepared before surgery to prevent significant intraoperative bleeding. In this case<sup>63</sup>, a large amount of bleeding began after scalp incision.

Based on the review of these cases, we find that skull metastasis from hepatocellular carcinoma a rare case<sup>63</sup>, and that the symptom of cranial metastasis of primary hepatocellular carcinoma is no specific. The liver function may not be compromised significantly, and the patient has no specific signs. When dealing with cases of a head mass that rapidly increases within the short term and shows osteolytic bone destruction by CT examination, we should consider skull metastasis as the potential diagnosis<sup>65</sup>. An early and active intervention can improve the life quality and prolong the overall survival time of the patient<sup>66</sup>.

## Declarations

### Ethics approval and consent to participate

We confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

Written informed consent has been obtained from the patient to have case details and any accompanying images published.

### **Consent for publication**

Written informed consent for publication was obtained from all participants.

### **Availability of data and materials**

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors report no conflicts of interest in this work.

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### **Author contributions**

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Written consent was obtained from the patient for publication of this case report.

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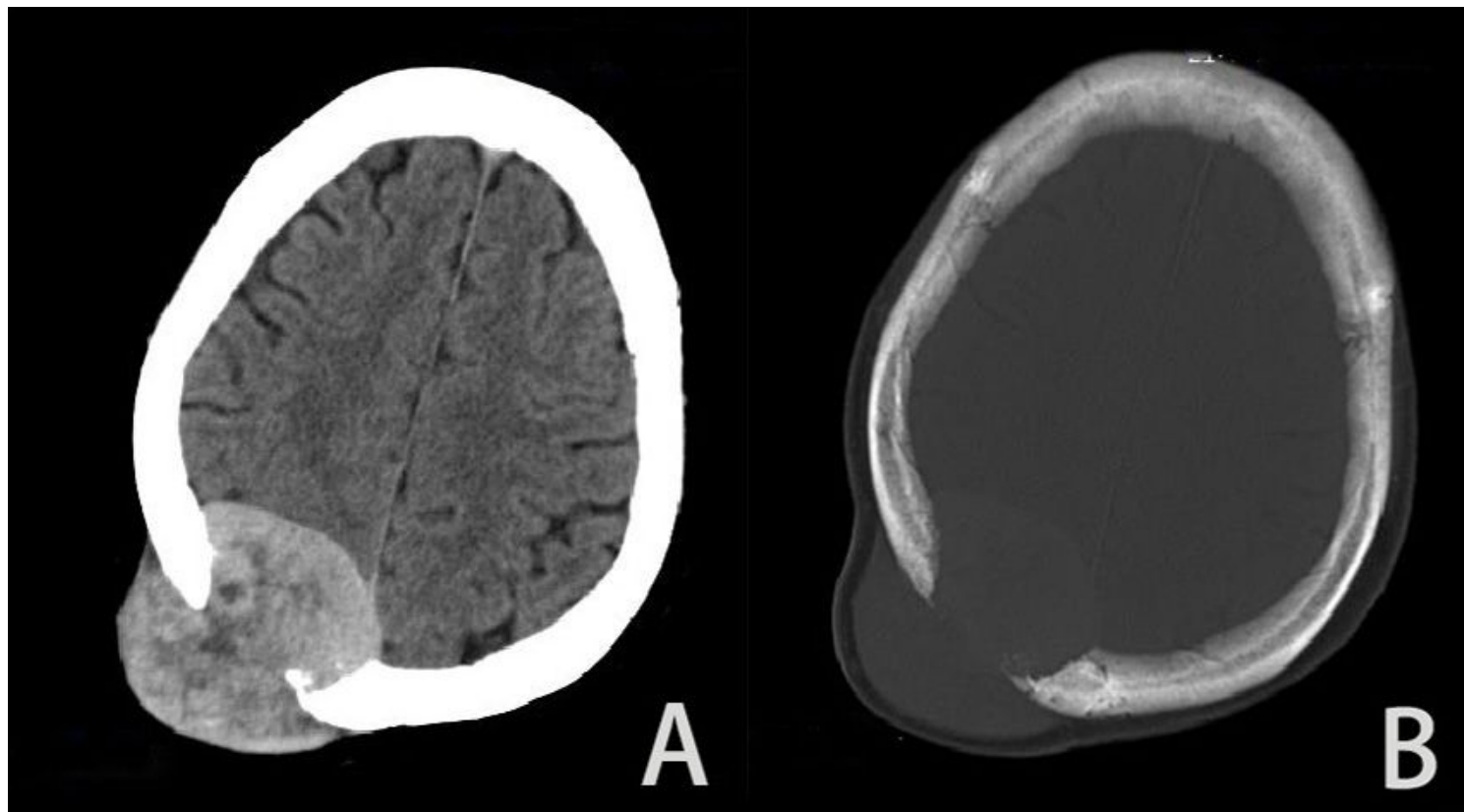
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## Tables

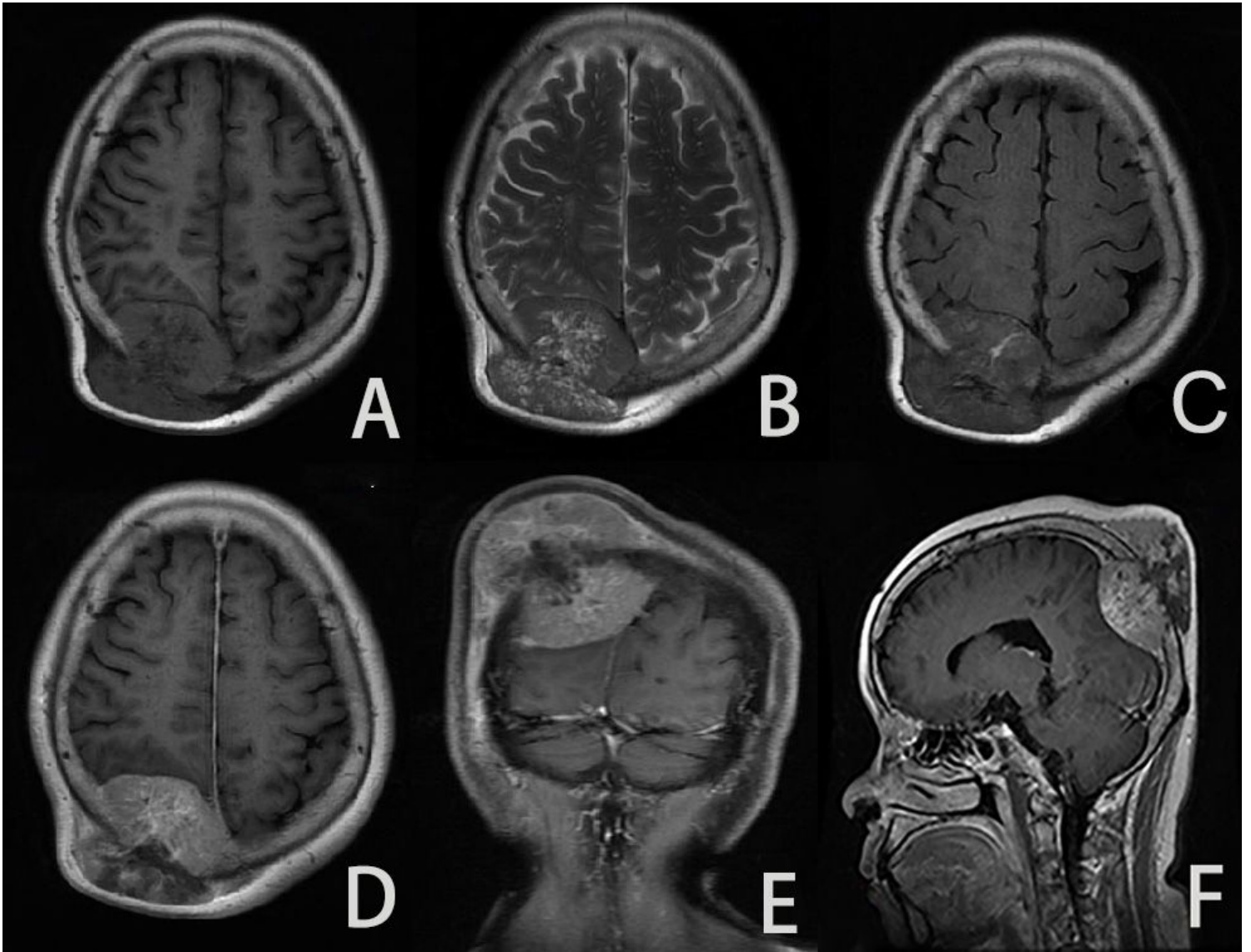
Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

## Figures



**Figure 1**

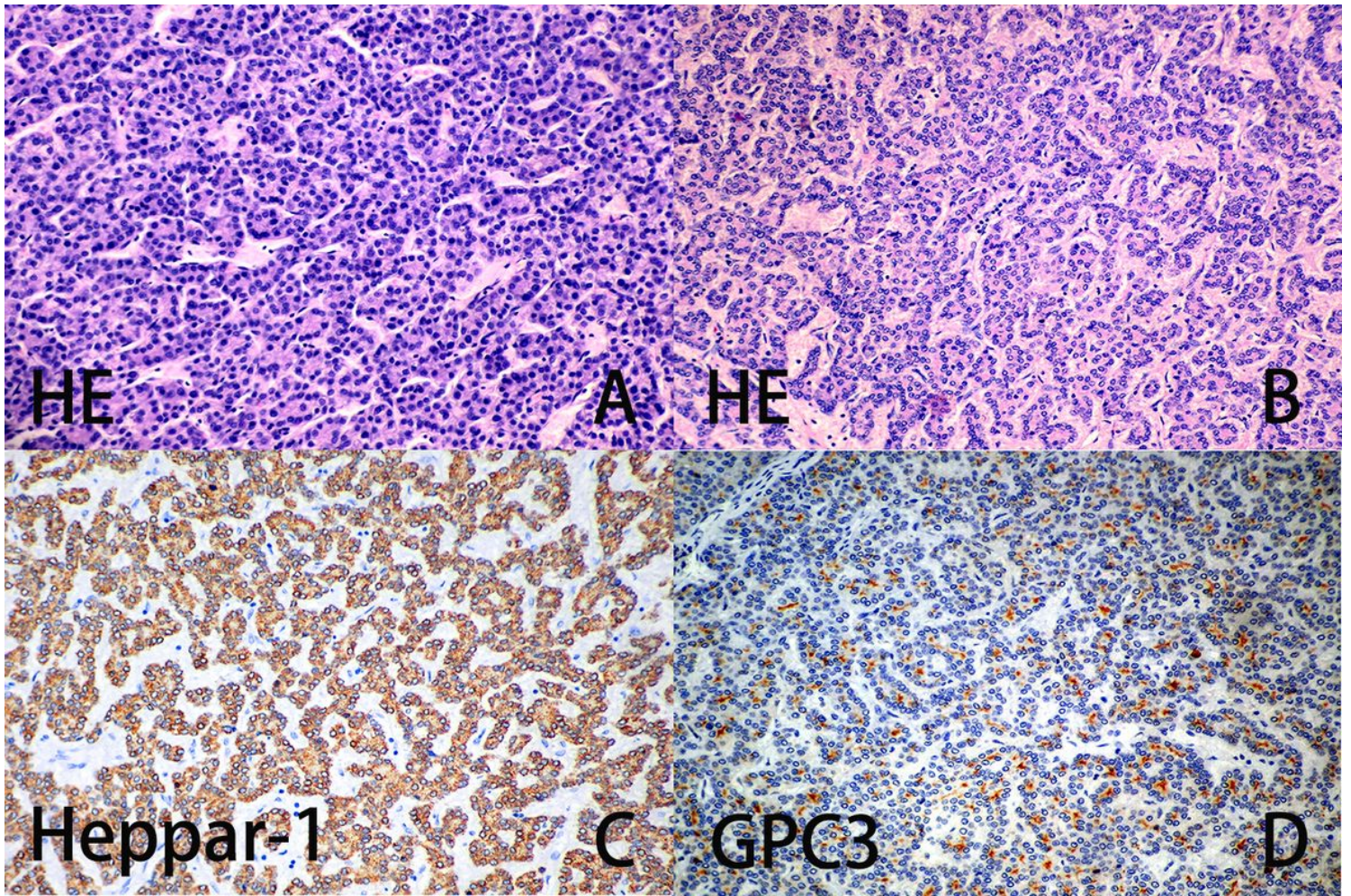
CT plain scan of the skull showed a mass of occipital mass with a slightly higher density (Fig. A), 6.4×5.6cm in diameter, exhibiting a clear boundary of the mass, uneven internal density, growth across the skull and displacement near the brain parenchyma. Bone window (Fig. B) indicated local bone destruction of the right parietal bone.



**Figure 2**

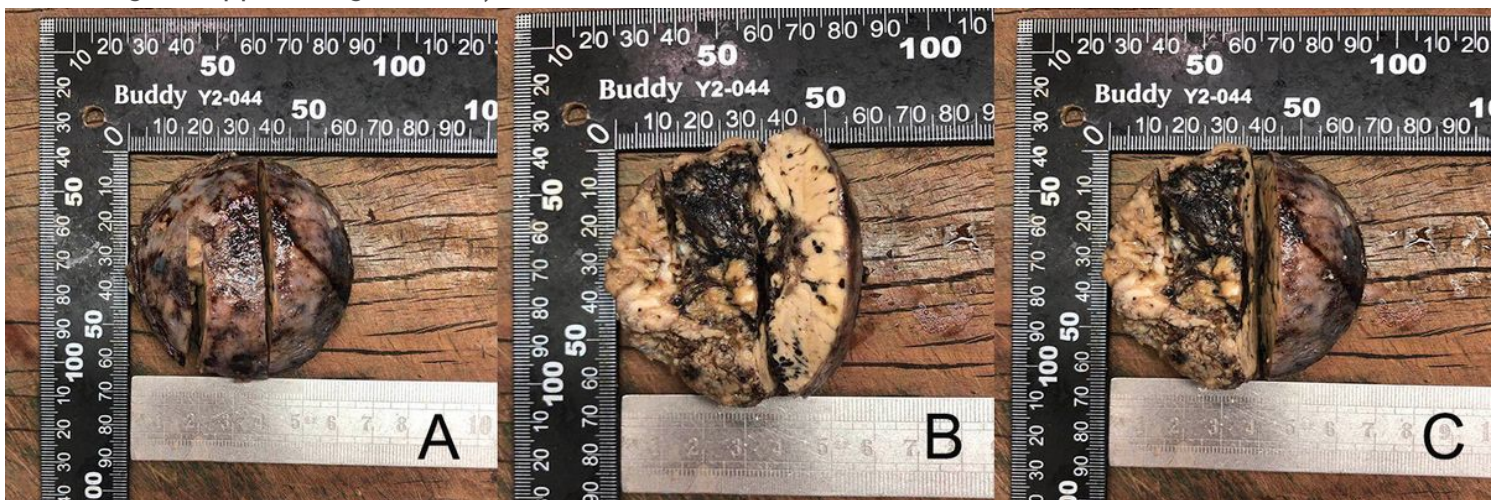
Magnetic resonance imaging of the brain showed an occipital mass. T1WI (Fig. A) ; T2WI (Fig. B,) ; FLAIR (Fig. C.). An internal slice of long T2 signal found clear transcranial growth, no brain edema, and destruction of the local skull. After the contrast, (Figure D-F,) significant uneven enhancement of mass Axial, coronal, sagittal T1 enhanced. The adjacent meninges were enhanced.





**Figure 3**

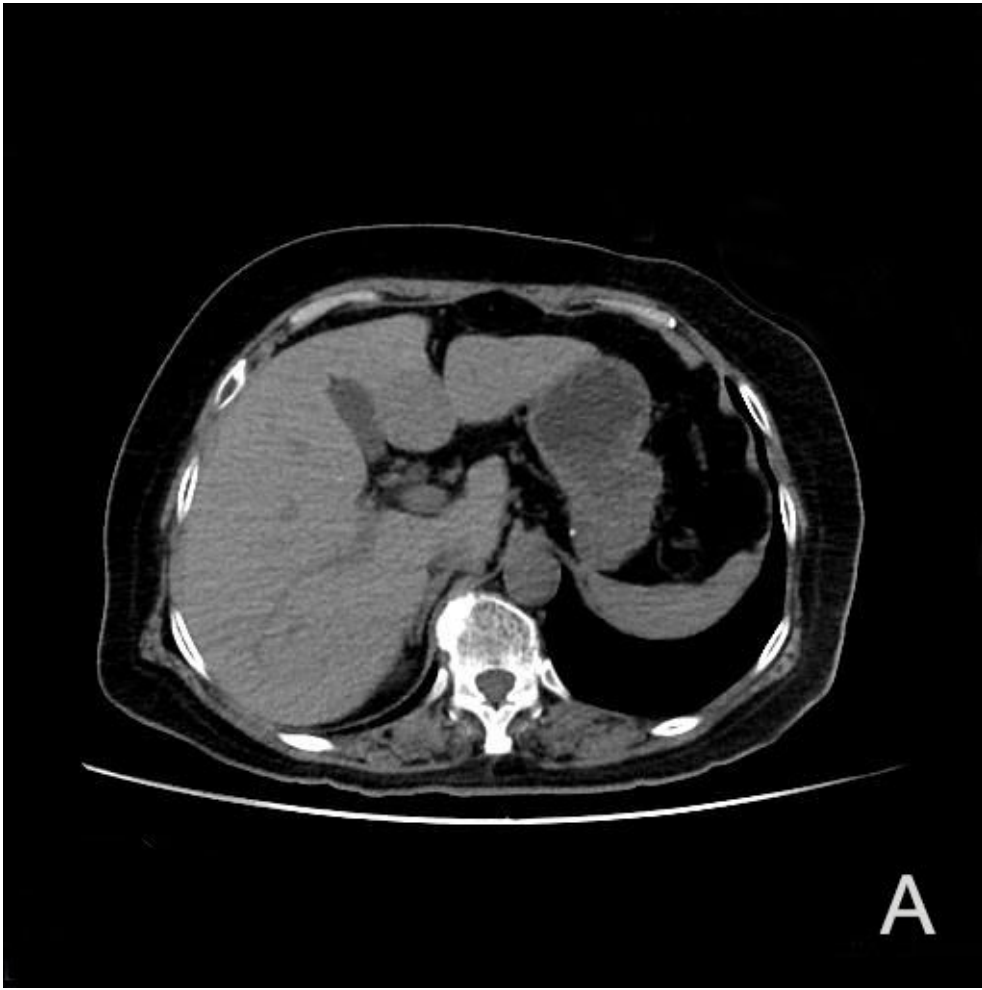
Postoperative immunohistochemistry analysis suggested metastatic hepatocellular carcinoma. (Fig. A. B. HE stains; Fig. C Heppar-1; Fig. D. GPC3)



**Figure 4**

An oblate mass sized of 6.7×6.7×2cm is visible to the naked eye. The cut surface seemed grayish yellow and dark red, and the capsule was intact. (Figure A, B, C).





**Figure 5**

CT image observed a nodule sized of 3.8cm in diameter in the left lobe of the liver. Enhanced scanning found that the arterial phase was enhanced, and that the portal and venous phases showed relatively low density. These finds were indicative of liver cancer.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [table.xlsx](#)