Journal of Neurosurgery and Clinical Neurology

Case Report

Volume 4 Issue 01

Craniocerebral Metastases of Hepatocellular Carcinoma

El Hadji Cheikh Ndiaye SY*, Hugues Ghislain Atakla, Daouda Wague, Mbaye Thioub, Maguette Mbaye, Alioune Badara Thiam, Momar Codé BA

Neurosurgery Department, Fann's national teaching hospital, Dakar, Senegal

***Corresponding Author:** El hadji Cheikh Ndiaye SY, Neurosurgery Department, Fann's national teaching hospital, Dakar, Senegal.

Received date: 10 July 2023; **Accepted date:** 03 August 2023; **Published date:** 09 August 2023

Citation: SY E-H C N, Atakla HG, Wague D, Thioub M, Mbaye M, et al. (2023) Craniocerebral Metastases of Hepatocellular Carcinoma. Journal of Neurosurgery and Clinical Neurology 4(01): https://doi.org/10.38207/JNCN/2023/AUG040103

Abstract

Brain metastases are the natural outcome of any cancerous process. However, the susceptibility of cancers to be the cause of brain metastases varies according to the primary site and the histological nature of the tumor. They are currently considered the most common malignant brain tumors seen in adults and therefore deserve particular attention. As the primary cancer is still far from known, CBM poses a twofold problem: confirming the secondary nature of the neoformation and guiding the search for the primary site, bearing in mind that in 15 to 20 % of cases, the primary tumor remains unknown. Although extrahepatic metastases from hepatocellular carcinoma are not uncommon, intracranial metastases are relatively rare and have an inferior prognosis. Diagnosis is straightforward, based firstly on diagnosing the primary lesion (hepatocellular carcinoma) and then correlating it with the histopathology of the brain metastasis. In the Neurosurgery Department of the Fann University Hospital, we conducted a retrospective descriptive study of three cases of craniocerebral metastases of hepatocellular carcinoma over 2 years from January 2019 to December 2022. This study aimed to investigate the epidemiological, clinical, paraclinical, therapeutic, and evolutionary aspects.

Keywords: brain metastases, hepatocellular carcinoma, bone lysis

Introduction

Hepatocellular carcinoma (HCC) is one of the world's most common cancers. Its incidence is increasing and is closely associated with advanced liver disease **[1]**. In 2008, hepatocellular carcinoma was the 5th and 7th most common cancer in adult men and women, respectively. It is the 2nd and 6th most common cause of cancer death in men and women worldwide **[2]**. Cirrhosis, whatever its origin, increases the risk of HCC, especially if it is due to hepatitis C (HCV), hepatitis B (HBV), or hereditary hemochromatosis (HH) **[3,4]**.

HCC can be diagnosed with certainty based on radiological criteria, with or without biological data (alpha-feto-protein assay), without histology, which is only carried out when these methods are inconclusive **[5]**. Craniobrain metastases (CBM) of HCC are very rare. Even in endemic regions, brain metastases from HCC are so rare that their incidence is only around 0.2 % **[6]**. The diagnosis of CBM is suspected based on clinical and paraclinical data with brain imaging, particularly magnetic resonance imaging. The diagnosis is confirmed by histology. Once the diagnosis of brain metastases has been established, the choice of treatment takes into account several parameters, the most important of which are the patient's general condition, the single or multiple appearance of the brain lesion, its topography, histology, the existence of other extra-cerebral metastatic locations and the treatment of the primary cancer. The treatment options are surgery, conventional radiotherapy, radiosurgery, chemotherapy, and recently trans-arterial chemo-embolization (TACE) **[6,7]**. The prognosis in cases of CBM is still not fully understood. Only a few exclusive studies have reported that the forecast is so unfavorable when HCC spreads to intracranial structures, including the skull and brain, that the median survival time was only 1 to 2 months **[7,8]**. We report the case of 3 patients followed in our department for cranioencephalic metastases whose etiological investigation revealed an HCC carcinoma.

Observations

Case N° 1

The patient was 30 years old and was admitted to the hospital for management of confusion with intracranial hypertension that had been evolving for 1 month in the presence of a left frontoparietal swelling for which no further medical consultation had been carried out. An investigation carried out with the parents revealed generalized tonic-clonic convulsive seizures. The patient was known to be a chronic carrier of HBsAg. The clinical examination revealed a relatively good general condition with a Karnofski index of 70 %. The conjunctiva and mucous membranes were normal-colored and not icteric. The abdominal investigation revealed a slight tenderness in the right hypochondrium with no palpable mass or ascites. On

palpation, there was also a soft left frontoparietal swelling of firm consistency with healthy, painless skin. The neurological examination concluded that there was an intracranial hypertension syndrome, a cortical irritation syndrome with persistent disturbance of consciousness in the late post-critical phase. Cerebral CT scan **(Figure 1)**.

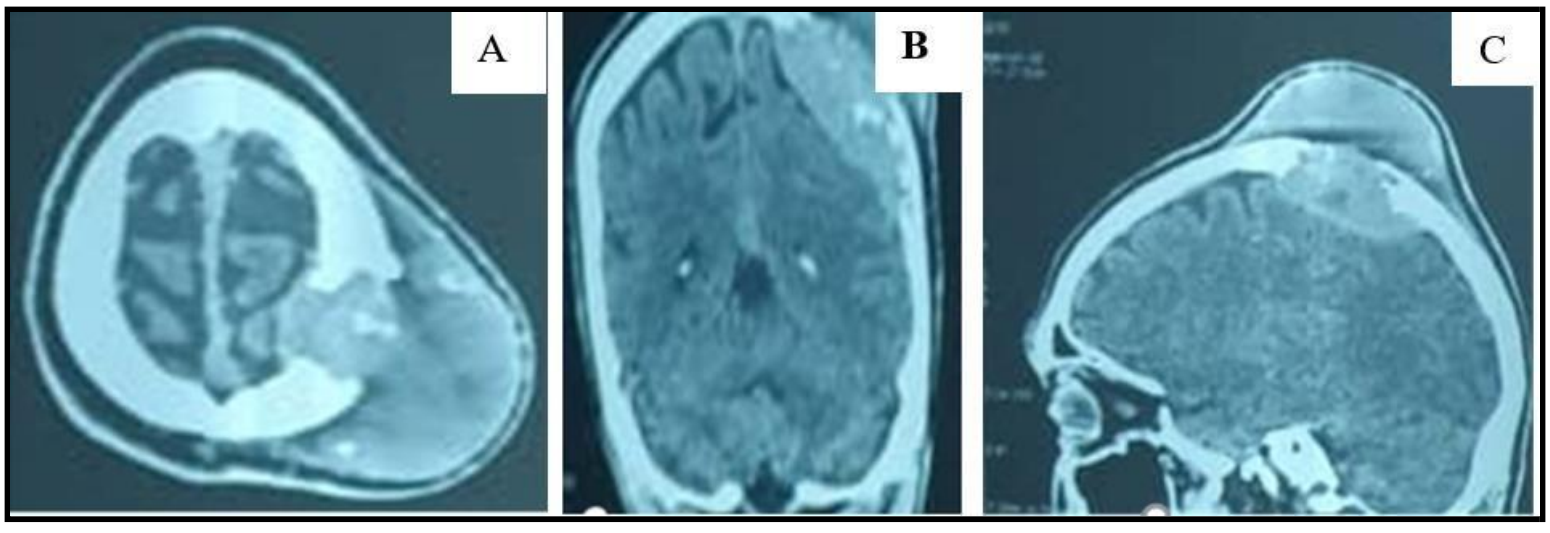

Figure 1: Cerebral CT scan injected in the parenchymal window and axial section (A), sagittal (B) and coronal (C) reconstruction, showing a contrasting endo and exocranial tissue process with localised bone lysis in the left parietal region.

Abdominal ultrasound revealed a liver of normal size with regular contours, heterogeneous in relation to the presence of hyperechoic nodules. The chest X-ray was without particularity. The liver function tests revealed hepatocellular failure syndrome (disturbance of liver function with elevated ASAT/ALAT greater than 3 times normal, low prothrombin rate (PT) and hyperbilirubinaemia). An alpha-feto protein level was requested but not performed. He underwent surgical excision and biopsy of the mass **(Figure 2)**.

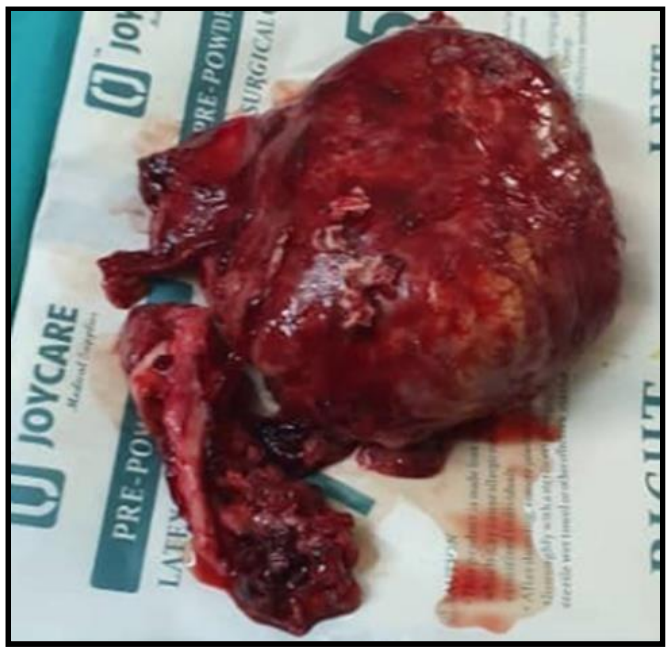

Figure 2: Operating specimen

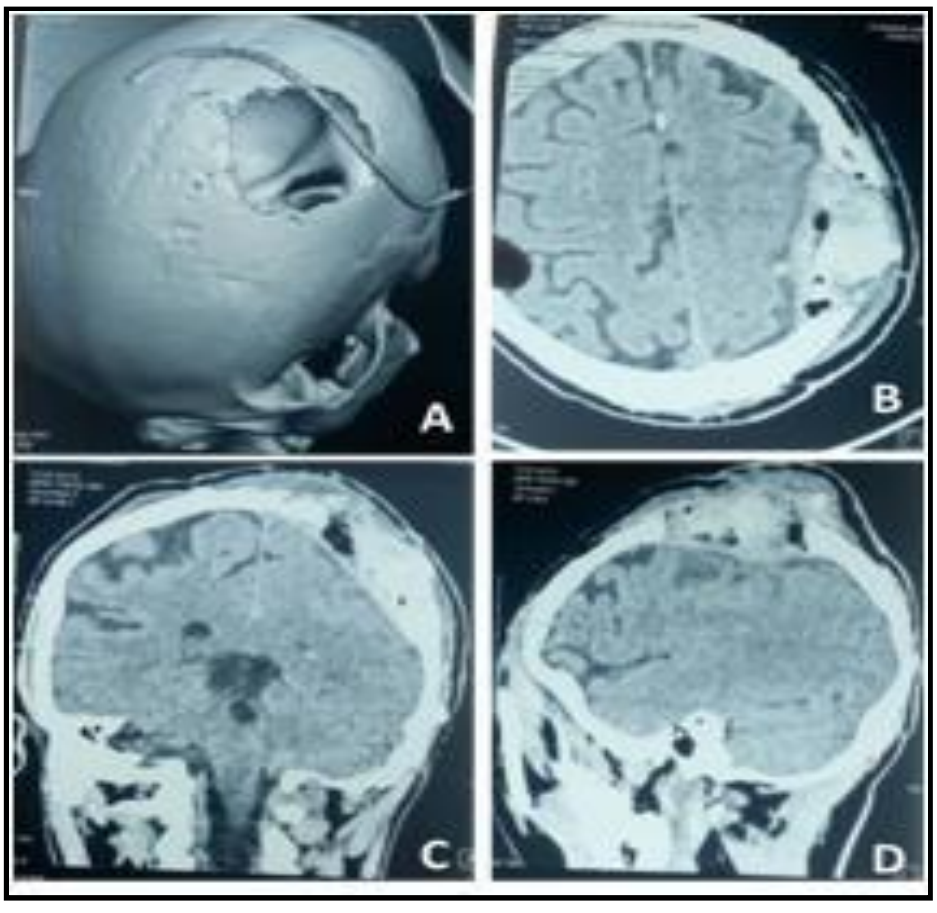

Figure 3: Postoperative cerebral CT scan

Case N° 2

This was a young man, aged 35, whom we followed up on for a painless, non-inflammatory right parietal swelling associated with headaches and no vomiting. The history-taking revealed no specific pathological history. His general condition was poor, with a Karnofski index (KI) of 60 %, but he was hemodynamically stable. He had a distended abdomen with a nonpalpable liver, abdominal curvature, and collateral venous circulation. There was also a firm right parietal swelling with little pain on palpation and healthy skin. The neurological examination was in favor of intracranial hypertension syndrome. Analysis of the other systems was unremarkable, apart from the conjunctivae and mucous membranes, which were icteric **(Figures A, B, C)**. The stools were discolored, and the urine was dark.

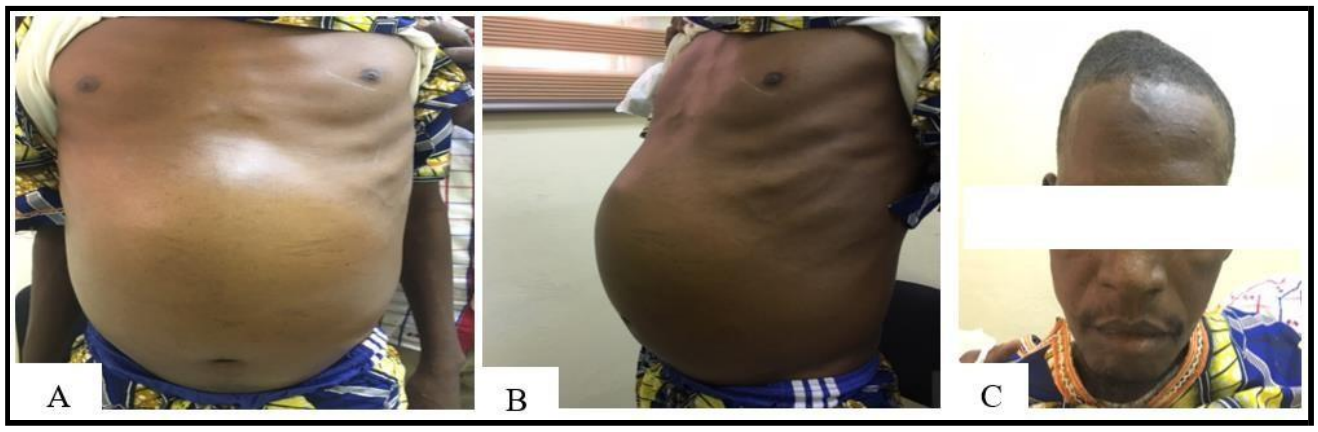

Figure 4: Profuse ascites (A: front view, B: lateral view, C: right parietal swelling).

Abdominal ultrasound revealed a large, dysmorphic, heterogeneous liver with hyperechoic nodules and copious ascites. The chest X-ray was normal. Cerebral computed tomography (CT) was consistent with a neoplastic process **(figure 5)**.

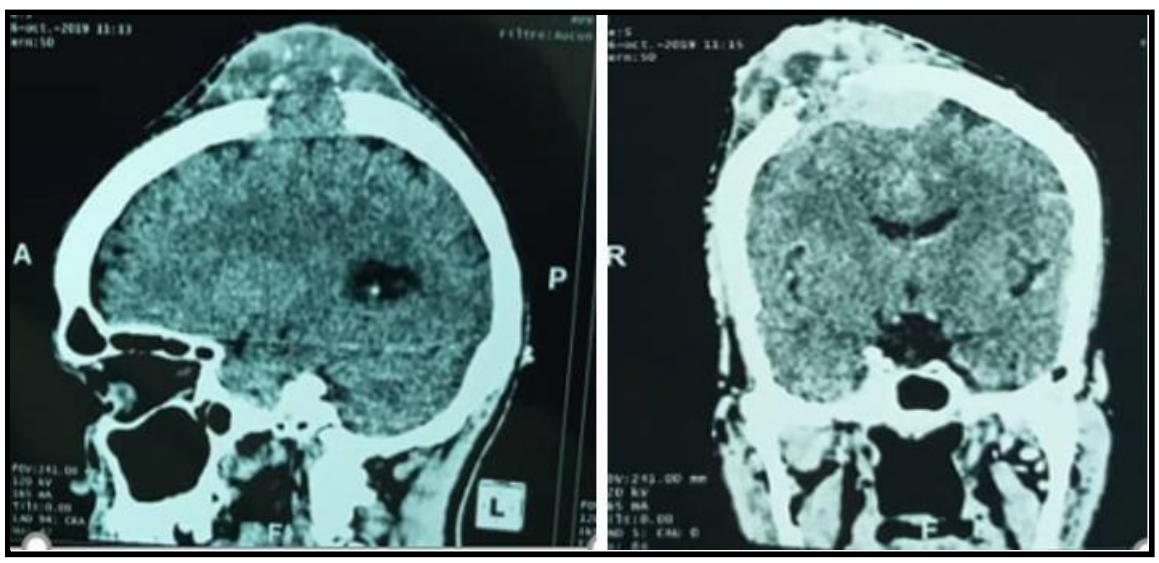

Figure 5: Cerebral CT scan in a parachymal window, sagittal (A) and coronal (B) reconstruction: right fronto-parietal craniocerebral tumour mass taking up the PDC with exocranial extension and bone lysis.

Given the craniocerebral lesion and liver lesions, the diagnosis of CM on probable HCC was retained, and he underwent total removal of the tissue portion of the tumor and a biopsy of the tumor mass. The patient also underwent conservative treatment due to his poor general condition. He was transferred to digestive surgery to manage ascites and hepatomegaly, where he died 15 days later.

Case N° 3

The patient was a 66-year-old woman with altered consciousness associated with a language disorder of the aphasic type and weakness of the right hemisphere, with no evidence of vomiting or convulsive seizures. Questioning revealed no particular pathological history. She was in good general condition with 90 % KI and hemodynamically stable. The neurological examination revealed a disorder of consciousness with a GCS of 7/15 (E2V1M4) subject to aphasia, anisocoria with tight right miosis that was not very reactive, and a right pyramidal syndrome with a craniofacial predominance (MS 0/5, MI 03/5). Abdominal examination revealed slight pain on palpation in the right hypochondrium.

A biological assessment revealed a disturbance in liver function with ASAT/ALAT greater than 2 times average. The alpha-fetoprotein level was not measured. She underwent a CT biopsy of the hepatic lesion, which revealed a 45x42x46 mm heterogeneous segment 6 hepatic tissue mass spontaneously hypodense and enhanced by arterial and portal contrast. A cerebral CT scan **(Figure 6)** showed a spontaneously iso-dense heterogeneous extra-axial expansive process of the left parietal wall, strongly enhanced by contrast agent, with bone lysis, soft tissue infiltration, and sub factorial involvement.

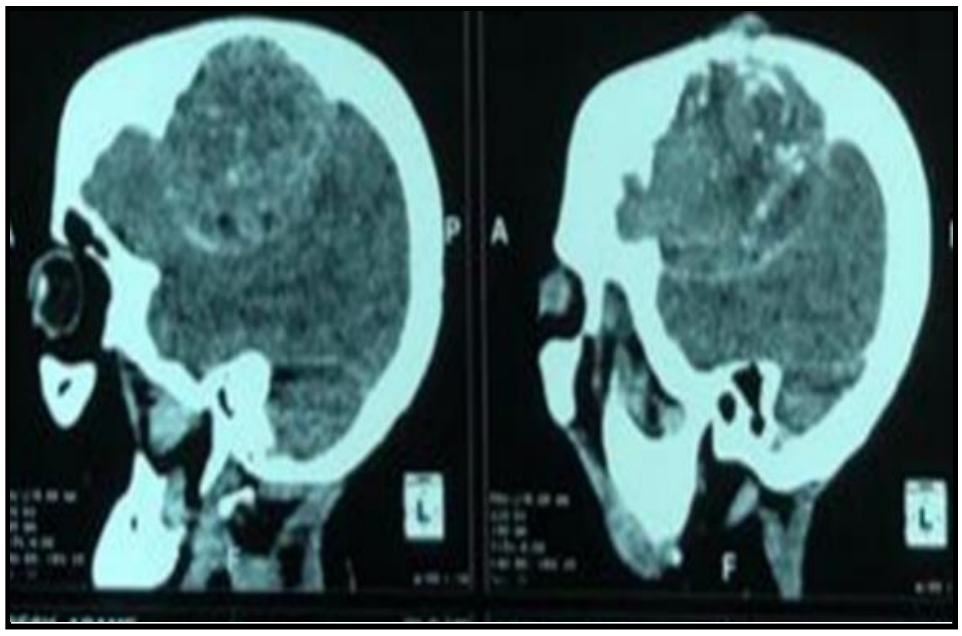

Figure 6: Cerebral CT scan with PDC injection, parenchymal windows, sagittal reconstructions.

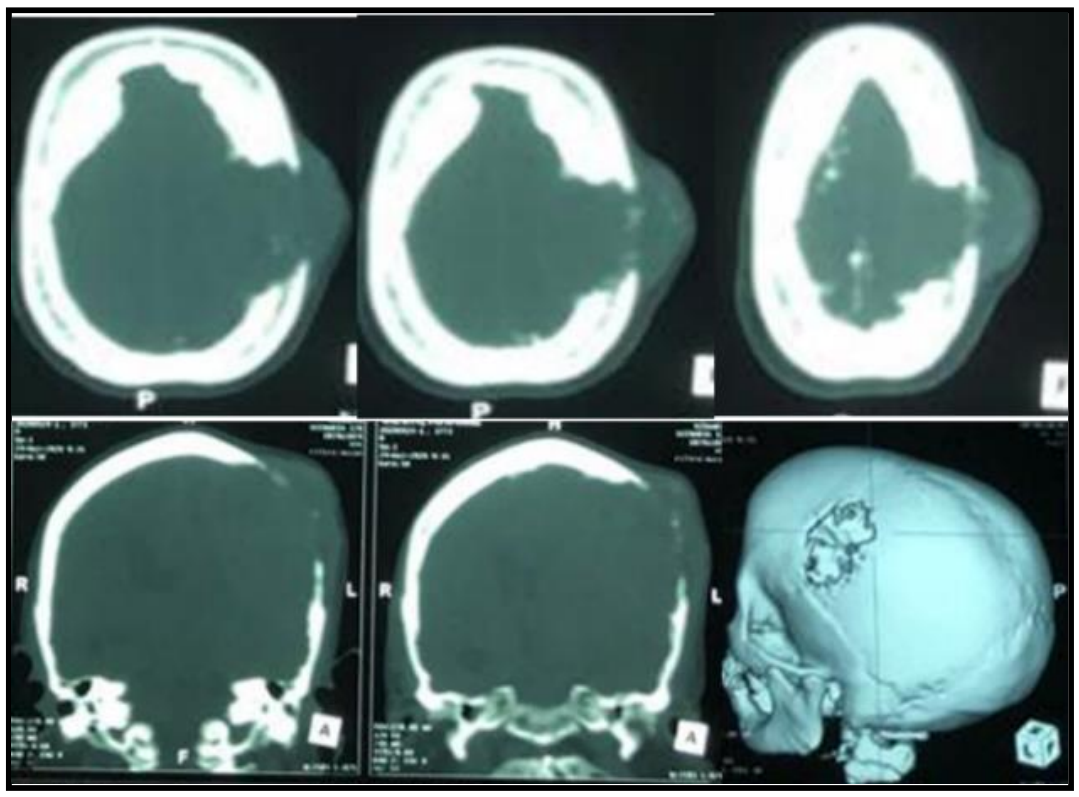

Figure 7: Cerebral CT scan with bone window, axial sections with coronal (A), sagittal and 3D (B) reconstructions.

She was treated with corticosteroids (Solumedrol 240mg/day). The diagnosis of a secondary cranioencephalic lesion was retained. A tumour resection with biopsy was indicated, but the patient died before undergoing surgery. The patient died 10 days after her consultation and the anatomopathology examination of the liver biopsy came back in favor of HCC after her death.

Discussion

Epidemiological aspect

In this work, we report the case of 3 patients diagnosed in our department with metastatic HCC. Of these, 2 were male, with a sex ratio of 2. Although the size of our sample was small to allow comparison, some data in the literature show that the predominance is often male **(Table I)**.

Table I: Male (M)/female (F) sex ratio: comparison between different studies **[8-10].**

Author	year	Sex-ratio
Ling Chang MD et al	2004	8
Choi Hye Jin et al	2009	3,13
Jung Ho Han et al	2010	5,66
Notre étude	2023	2

The mean age of the three patients was 43.67 years, with extremes of 30 and 66 years. By comparing this result with those observed in several studies **(Table II)**, we note that the mean age of appearance of intracranial metastases was relatively earlier in our study. However, it should be emphasised that the small size of our sample does not allow us to draw any conclusions from this observation.

Table II: Comparison of the mean age of onset of HCC with other studies **[11-13].**

Author	year	Sex-ratio
Yu-Yun Shao et all [11]	2011	54
Xiao-Bing Jiang et all [12]	2012	48,5
Moon-Soo Han et all [13]	2013	62
Notre étude	2023	43,67

The patients in this study were not being followed for any known cancer. Symptoms related to the craniocerebral lesion were the revealing signs of primary cancer. In other words, all three of our patients had metastatic disease. Doualeh Ali **[14]** reports that 80% of his patients presented with revelatory brain metastases, which means that in these patients, the primary cancer was unknown on admission. This is in contrast to Moon-Soo Han et al. **[11]**, whose primary was known to be CHC and was followed up in their hospital. Out of 5015 patients with HCC diagnosed and treated between 2001 and 2012, 33 were retrospectively confirmed to have brain metastases from HCC. In another series, Choi Hye Jin et al. **[8]** reported that between 1995 and 2006, 6919 patients with hepatocellular carcinoma were treated at the Yonsei University Health System. Of these, 62 (0.9 %) had a diagnosis of brain metastasis. The primary site was also known in other studies, such as that of Yu-Yun Shao et al. **[11]** and Xiao-Bing Jiang et al. **[12]**.

The Karnofsky index (KI) is a significant factor in local treatment decisions. Our patients had a 60 %, 70 %, and 90 % KI in our work. In the Senegalese series by Mane **[15]**, 58 % of his patients had a KI greater than or equal to 70, 42 % had a KI of 60, and none had a KI of 20 or 10.

Doualeh Ali **[14]** found an IK greater than or equal to 70 in approximately 90 % of his patients.

The neurological signs found in our work were pyramidal syndrome in one of our patients, cortical irritation syndrome in one of our patients, and consciousness disorders in one of our patients, with a Glasgow Score of 9/15. Doualeh Ali **[14]** found intracranial hypertension syndrome in the first place, affecting 90 % of patients; secondly, pyramidal syndrome with 70 %, and thirdly cortical irritation syndrome with 50 %. The cerebellar syndrome is found in only 20 % of our patients. Consciousness disorders are not so rare, occurring in 35 % of cases. In the Moroccan series by Pratic **[16]**, an HTIC syndrome was found in 83.3% of cases, dominated by headaches, motor deficits in 53.3 %, and epileptic seizures in 10% of cases.

Extra-neurological signs pointing to primary cancer were found in two patients with digestive symptoms (cholestasis syndrome, portal hypertension syndrome, hepatomegaly, and tenderness in the right hypochondrium).

In the Senegalese series by Doualeh Ali **[14]**, extra-neurological symptoms pointing to a primary were found in 30 % of his patients.

Etiological investigation

An etiological investigation in search of digestive cancer in general and hepatic cancer, in particular, responsible for the CM studied, was carried out with a thoracic-abdominal-pelvic CT scan in one of our patients, an abdominal ultrasound in two of our patients, a chest X-ray in two of our patients and, biologically, hepatocellular insufficiency was found in two of our patients, and the alpha-fetoprotein level was requested but not done in all of our patients. This test revealed a primary lesion such as HCC in all our patients. Contrary to other studies, such as that by Doualeh Ali **[14]**, which looked for primary cancer using TAP scans in 85 % of cases, chest X-rays in only 10 % of patients, and tumor marker assays in only one patient with a single PSA. The latter was able to locate primary cancer in 65 % of cases, a result attributable to the sensitivity of the thoracic-abdominal-pelvic scanner. In decreasing order of frequency, the primary tumors found were bronchopulmonary cancer in 35 % of our series, breast cancer in 25 %, and colon cancer in 5 %, while no primary liver tumor was found.

The etiological investigation in the Moroccan series by Pratic **[16]** found the primary in only 20 % of cases and, in decreasing order of frequency, reported bronchopulmonary cancers in 60 % of patients and colon cancers in 20 % of cases.

Therapeutic aspect

Our three patients with cerebral metastases had been treated symptomatically with stage II analgesics, anti-oedematous agents, and anticonvulsants. Surgical excision has several advantages: in addition to enabling histological diagnosis, it has an immediate decompressive effect by reducing the tumor mass and associated cerebral edema, thus facilitating the action of radiotherapy and inducing prolonged remissions or even cures. In principle, the indication for surgical treatment of MC should be discussed within a multidisciplinary team. The essential criteria for discussion are the brain lesion's number and topography, primary cancer's histology, the patient's age and functional status (Karnofsky score), systemic dissemination of cancer, and therapeutic control of the primary cancer. All our patients underwent curative surgery with surgical removal of the mass. Unlike the series by Doualeh **[14]**, which was a surgical series, all the patients in the study had undergone surgery, with 75% having had curative surgery with partial or total removal and the remaining 25 % having had palliative surgery.

Radiotherapy can be used to treat both single and multiple metastases. It may be curative to treat an existing metastasis, prophylactic to

prevent its occurrence, or, more commonly, palliative to relieve the symptoms of incurable brain metastases. Conventional external radiotherapy remains the treatment of choice for CM. It is often the only therapeutic option in the presence of multiple CMs or the case of a single CM when the systemic extension of cancer or the location of the lesion contraindicates surgery. Like Mane and collaborators **[15]**, 84 % of those patients underwent radiotherapy, and 2 of our three underwent radiotherapy. This was done with a Cobalt, the only radiotherapy treatment device available in Senegal. As in the Pratic series **[16]**, 16.7 % of patients underwent conventional encephalic radiotherapy with a 30 Grays regimen in 10 sessions.

Anatomopathology

Pathological examination of the surgical **specimen** confirmed the diagnosis of craniocerebral metastasis of HCC. A scan biopsy of the liver lesion confirmed the nature of the primary lesion (hepatocellular carcinoma) in all 3 patients.

Evolutionary aspects

The short-term evolution of all our patients was unfavorable, with a 100% death rate. Contrary to Jung Ho Han et al. **[17]** In a study conducted in 2010 in Korea, we reported a median survival time of only 8 weeks and an actuarial survival rate of approximately 8% at one year; we found a median survival of 18 days, with extremes ranging from 10 days to 1 Month. The small sample size in our study does not allow conclusive results to be obtained. However, we believe this high percentage of deaths is linked to late consultation, delayed diagnosis of the primary site, late cerebral manifestations, and the absence or delay of adequate adjuvant treatment (chemotherapy and radiotherapy).

Conclusion

Despite the malignancy and high frequency of hepatocellular carcinoma, craniobrain metastases are rare, with a high mortality rate. The prognosis is poor, with death in this case. The forecast is poor, with a death rate of 100 % in this observation, for a median survival of 18 days, with extremes ranging from 10 days to 31 days. Delayed diagnosis and limited therapeutic resources reinforce this poor outcome. The development of radio-embolization and chemoembolization could delay the onset of fatal complications of the disease.

Abbreviations:

HCC: Hepatocellular Carcinoma

HH: Hemochromatosis

TACE: Transarterial Chemo Embolisation

KI: Karnofsky Index

CM: Contrast Medium

TAP: Thoraco-Abdominal-Pelvic

References

1. Hartke J, Johnson M, Ghabril M (2017) The diagnosis and treatment of hepatocellular carcinoma. Semin Diagn Pathol. 34(2): 153-159.
2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, et al. (2011) Global cancer statistics. CA: a cancer, journal for clinicians. 61(2): 69-90.
3. Lok AS, Seeff LB, Morgan TR, di Bisceglie AM, Sterling RK, et al. (2009) Incidence of hepatocellular carcinoma and associated risk factors in hepatitis C-related advanced liver disease. Gastroenterology. 136(1): 138-48.
4. Niederau C, Lange S, Heintges T, Erhardt A, Buschkamp M, et al. (1998) Prognosis of chronic hepatitis C: results of a large, prospective cohort study. Hepatology (Baltimore, Md). 28(6): 1687- 95.
5. Llovet JM, Bruix J (2003) Systematic review of randomized trials for unresectable hepatocellular carcinoma: chemoembolization improves survival. Hepatology. 37(2): 429-42.
6. Kim M, Na DL, Park SH, Jeon BS, Roh JK (1998) Nervous system involvement by metastatic hepatocellular carcinoma. J Neurooncol. 36(1): 85-90.
7. Chang L, Chen YL, Kao MC (2004) Intracranial metastasis of hepatocellular carcinoma : review of 45 cases. Surg Neurol. 62(2): 172-177.
8. Choi HJ, Cho BC, Sohn JH, Shin SJ, Kim SH, et al. (2009) Brain metastases from hepatocellular carcinoma : prognostic factors and outcome : brain metastasis from HCC. J Neurooncol. 91(3): 307-313.
9. Chang L, Chen YL, Kao MC (2004) Intracranial Metastasis of Hepatocellular Carcinoma: Review of 45 Cases.» Department of Neurosurgery, National Taiwan University Hospital, Taipei, Taiwan. 62(2): 172–177.
10. Han JH, Kim DG, Park JC, Chung HT, Paek SH, et al. (2010) Little Response of Cerebral Metastasis from Hepatocellular Carcinoma to Any Treatments.» J Korean Neurosurg Soc. 47(5): 325–331.
11. Han MS, Moon KS, Lee KH, Cho SB, Lim SH, et al. (2013) Brain metastasis from hepatocellular carcinoma: the role of surgery as a prognostic factor. BMC Cancer. 13: 567.
12. Yu-Yun Shao, Li-Chun Lu et al. Incidence croissante des métastases cérébrales chez les patients.» Oncologue, 2011: 82–86.

13. Bing, et Chao Ke et al. (2012) Métastases cérébrales du carcinomehépatocellulaire: caractéristiques cliniques et facteurs pronostiques. Cancer BMC, n° 49(2012): 12.
14. Doualeh Ali K (2018) Métastases cérébrales : Aspects épidémiologiques, diagnostiques, thérapeutiques et évolutifs. À propos de 20 cas. These Med. 211.UCAD.
15. Mane M (2012) La prise en charge des métastases cérébrales des cancers solides a l'Institut Joliot-Curie de Dakar: à propos de 50 cas. Thèse Med.2012.121. UCAD.
16. Pratic F, Lmejjati M, Ait Ben Ali A (2012) Profil épidémiologique des métastases cérébrales: expérience du service de neurochirurgie du CHU de Mohamed VI Marrakech. These Med. Université Cadiayyad.
17. Han JH, Kim DG, Park JC, Chung HT, Paek SH, et al. (2010) Little Response of Cerebral Metastasis from Hepatocellular Carcinoma to Any Treatments, J Korean Neurosurg Soc. 47(5): 325-331.