Introduction

Cancers are the main cause of mortality and health problem worldwide, and Hepatocellular carcinoma (HCC) is recognized as one of the most frequent malignancies in the world (1,2). It is considered as the fifth most common cancer and the second leading cause of cancer deaths around the world. Hepatitis B infection is the greatest risk factor for HCC in most geographic areas, with the highest rates in China, Taiwan, and Korea (3,4). Extrahepatic metastasis is also common, and the most frequently affected sites are the lungs, regional lymph nodes, kidney, bone marrow, and adrenals (5,6).

Brain metastasis from hepatocellular carcinoma (BMHCC) is relatively rare, with an approximate rate of 1-6% (7,8). Although the interval between diagnosis of primary cancer and detection of brain metastasis ranged from 2 to 54 months (1,9), the prognosis of these patients is poor with a survival period of a few weeks with low quality of life. However, no standard therapeutic strategy has been reported to date to increase survival in patients with unresectable tumors; early diagnosis could improve the chance of curative surgical resection (8).

The present study describes a rare case of HCC presenting with the initial manifestations of an intracranial mass lesion. The diagnosis could not be made until she was admitted to the hospital with a loss of consciences and hypertension (3,10). Eventually, the lesion was diagnosed as a brain metastasis of hepatocellular carcinoma from pathological results (11).

Case Report

A 74-year-old female was admitted to our hospital due to abdominal pain on his right side as a chief complaint. The patient’s medical history was negative for chronic HBV-related hepatitis. The patient was oriented and did not have pathologic reflexes. His initial laboratory examination revealed blood cell counts and blood glucose were within normal limits, Coagulation factors were also within normal limits, and his coagulability was as follows: prothrombin time (PT): 11.5 seconds, international normalized ratio (INR): 1.42, activated partial thromboplastin time (PTT): 28 seconds, Hepatic-related factors were as follows: glutamic oxaloacetic transaminase (AST): 28 IU/L, glutamic pyruvic transaminase (ALT): 45 IU/L, alkaline phosphatase (ALP): 290 U/L, alpha-fetoprotein: 352 ng/mL. Bilirubin, Serum electrolyte levels (Mg, Na, and Phosphorous), urinalysis was within the normal range as
Brain metastases of hepatocellular carcinoma

well.

Thorax-abdomen-pelvic CT revealed a hyperdense mass lesion with irregular margins and 42×47×8 mm in size in the right lobe of the liver (7th & 8th segments) with extension near the radial margin, moderate portal inflammation and mild to moderate steatosis and no evidence of cirrhosis, but no other organs were involved, and there was no symptom of metastasis (Figure 1).

![Figure 1. CT image of the lesion in the liver](image1)

A core needle biopsy was also done, and finally, hepatocellular carcinoma had been diagnosed based on computed tomography (CT images), high AFP level (alpha-fetoprotein), and biopsy.

The patient underwent sorafenib for treatment, and she had experienced a stable condition. 3 years after that, the patient was admitted to the emergency department due to hypertension and loss of consciences (GCS<5). However, she had been well previously, and no history of head trauma, the patient was hospitalized due to loss of consciences.

Computed tomography (CT) and MRI of the patient’s head revealed multiple intracranial masses and homogenous enhancement by post-contrast CT that confirmed brain metastasis of hepatocellular carcinoma (Figure 2). The interval between diagnosis of primary cancer and detection of brain metastasis was 36 months. The mean survival period was only 3mo after diagnosis of brain metastasis. The patients with HCC metastasized to brain died of neurologic causes rather than hepatic failure. The present study revealed a 74-year-old female had hyperdense mass lesion 42×47×8 mm in size by contrast and non-contrast computed tomography scan. His bilirubin and liver enzymes level was normal. She had neither ascites nor a history of hepatic encephalopathy. She had no symptoms of fatty liver, and eventually, she was died because of intracranial hemorrhage (2,17).

In conclusion, the rarity of this type of case gives the clinician the suspicion of such associations when confronted with a patient with liver dysfunction, and neurologic findings, and further studies are needed to elucidate the impact of the presence of extrahepatic metastases on survival in patients with brain metastasis from HCC.

![Figure 2. CT image of the metastatic lesions in the brain.](image2)

Discussion

Hepatocellular carcinoma (HCC) is possibly curable if discovered in its initial stages. HCC is one of the most frequently occurring malignancies in Asia (12). The number of new HCC patients is approximately 500,000 to 1 million per year and is increasing (2). HCC shows both intrahepatic and extrahepatic metastasis. The most common extrahepatic metastases are the lung, regional lymph nodes, peritoneum, and adrenal glands, but rarely to brain with an approximate rate of 1-6% that is associated with an extremely poor prognosis (13,14).

Although the brain is not the most common site for metastatic disease for HCC, some investigators have predicted that the incidence of brain metastases will increase in the future as more patients survive longer (15,16).

The interval between diagnosis of primary cancer and detection of brain metastasis ranged from 2 to 54 months. The mean survival period was only 3mo after diagnosis of brain metastasis. The patients with HCC metastasized to brain died of neurologic causes rather than hepatic failure. The present study revealed a 74-year-old female had hyperdense mass lesion 42×47×8 mm in size by contrast and non-contrast computed tomography scan. His bilirubin and liver enzymes level was normal. She had neither ascites nor a history of hepatic encephalopathy. She had no symptoms of fatty liver, and eventually, she was died because of intracranial hemorrhage (2,17).

In conclusion, the rarity of this type of case gives the clinician the suspicion of such associations when confronted with a patient with liver dysfunction, and neurologic findings, and further studies are needed to elucidate the impact of the presence of extrahepatic metastases on survival in patients with brain metastasis from HCC.

References

1. Tune B, Filik L, Tezer-Filik I, Sahin B. Brain metastasis of hepatocellular carcinoma: a case report and review of the literature. World J Gastroenterol 2004;10:1688-9.
2. Fujihara H, Chikazu D, Saijo H, Suenaga H, Mori Y, Iino M, et al. Metastasis of hepatocellular carcinoma into the mandible with radiographic findings mimicking a radicular cyst: a case report. J Endod 2010;36:1593-6.
3. Jiang X-B, Ke C, Zhang G-H, Zhang X-H, Sai K, Chen Z-P, et al. Brain metastases from hepatocellular carcinoma: clinical features and prognostic factors. BMC cancer 2012;12:49.
4. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:69-90.
5. Chedid MF, Krue CR, Pinto MA, Grezzana-Filho TJ, Leipnitz I, Krue LD, et al. Hepatocellular carcinoma: diagnosis and operative management. Arq Bras Cir Dig 2017;30:272-8.
6. Kanda M, Tateishi R, Yoshida H, Sato T, Masuzaki R, Okin T, et al. Extrahepatic metastasis of hepatocellular carcinoma: incidence and risk factors. Liver Int 2008;28:1256-63.
7. Seinfeld J, Wagner AS, Kleinschmidt-DeMasters B. Brain metastases from hepatocellular carcinoma in US patients. Journal of neuro-oncology 2006;76:93-8.
8. Wang S, Wang A, Lin J, Xie Y, Wu L, Huang H, et al. Brain metastases from hepatocellular carcinoma: recent advances and future avenues. Oncotarget 2017;8:25814.
9. Chang L, Chen Y-L, Kao M-C. Intracranial metastasis of hepatocellular carcinoma: review of 45 cases. Surg Neurol 2004;62:172-7.
10. Schiff ER. Case Study in the Management of Patients with Hepatocellular Carcinoma. Management of Patients with Viral Hepatitis 2004;183-8.
11. Uka K, Aikata H, Takaki S, Shirakawa H, Jeong SC, Yamashina K, et al. Clinical features and prognosis of patients with extrahepatic metastases from hepatocellular carcinoma. World J Gastroenterol 2007;13:414-20.
12. Kulkarni RS, Anand AS, Patel AA, Shah SA. Hepatocellular carcinoma presenting as rapidly growing sternal mass: an unusual presentation. J Cancer Metastasis Treat 2016;2:41-3.
13. Hiraoka A, Horiike N, Koizumi Y, Tazuya N, Ichiryu M, Nakahara H, et al. Brain metastasis from hepatocellular carcinoma treated with a cyber-knife. Intern Med 2008;47:1993-6.
14. Jung H-K, Lee D-S, Yoon S-S, Kim H-J. Systemic metastasis of hepatocellular carcinoma responsive to multidisciplinary treatment including debulking surgery. Ann Surg Treat Res 2014;86:100-4.
15. DEMİR M, DUMAN TT, ÜYETÜRK Ü, DÜZCÜ SE, BAŞAR BB. An incidentally Diagnosed Hepatocellular Carcinoma That Exhibited Unusual Metastasis. Turkish J Oncol 2019;34.
16. Jang SY, Kim CH, Cheong JH, Kim JM. Concomitant subdural hemorrhage and intracerebral hemorrhage due to brain metastasis of the hepatocellular carcinoma. Brain Tumor Res Treat 2015;3:48-51.
17. Han JH, Kim DG, Park JC, Chung H-T, Paek SH, Chung YS. Little response of cerebral metastasis from hepatocellular carcinoma to any treatments. J Korean Neurosurg Soc 2010;47:325-331.