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A Typical Neuropsychiatric Manifestation of Hepatocellular Carcinoma: A Case of Paraneoplastic Hypoglycemic Encephalopathy without Hepatic Failure or Brain Metastasis

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Key Learning Points

- HCC can cause hypoglycemia via IGF-II production even without liver failure.
- Neurological symptoms may mimic hepatic encephalopathy.
- Brain imaging and liver function tests help distinguish metabolic from structural or hepatic causes.
- Paraneoplastic syndromes should be part of the differential diagnosis in atypical HCC presentations.

1. Abstract

1.1. Background

Hepatocellular carcinoma (HCC) commonly presents with hepatic dysfunction, jaundice, or portal hypertension. Neurological manifestations usually occur secondary to hepatic encephalopathy or metastatic disease. However, paraneoplastic syndromes such as hypoglycemia-induced encephalopathy represent rare, yet important, atypical presentations.

1.2. Case Presentation

We report a 15-year-old girl with relapsed HCC who presented with acute neuropsychiatric symptoms including delirium, delusions, and hallucinations, in the absence of hepatic failure or cerebral metastasis. Laboratory investigations revealed normal liver synthetic function and ammonia levels only mildly elevated. Brain MRI showed no metastatic lesions. Her neurological symptoms were attributed to paraneoplastic hypoglycemia secondary to HCC.

1.3. Conclusion

This case highlights a rare paraneoplastic neurological presentation of HCC without hepatic failure, emphasizing the need for clinicians to consider metabolic and paraneoplastic etiologist when confronted with atypical neurological findings in liver cancer patients.

2. Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and a major cause of cancer- related mortality worldwide [1]. Neurological manifestations in HCC are typically due to hepatic encephalopathy or brain metastasis [2]. However, HCC can produce various paraneoplastic syndromes (PNS), such as erythrocytosis, hypercalcemia [3], porphyria cutanea trade, and rarely hypoglycaemia, resulting from ectopic secretion of insulin-like growth factors (IGF-II).

Paraneoplastic hypoglycaemia can present with diverse neurological symptoms ranging from confusion and delirium to seizures and coma. Recognition of this mechanism is crucial, as it may mimic hepatic encephalopathy but occurs in the absence of liver failure [4,5].

Table 1: Paraclinic tests.

parameter	result	Recent/comment
Total bilirubin	2 mg/dl	Slightly elevated
Albumin	4.2	Normal
PT	16	Mildly prolonged
PTT	32	Normal
Amonia	109	Mildly elevated
AST	45-68	Mildly elevated
ALT	61-84	Mildly elevated
Na	132	Mildly hyponatremic
BUN	12	Normal
Cr	0.8	Normal
HCO3	22.7	Normal
Ca	7.5	Mildly now

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3. Case Presentation

A 15-year-old girl with a known diagnosis of relapsed hepatocellular carcinoma was admitted due to new-onset altered mental status and neuropsychiatric symptoms. She exhibited delirium, delusions, and visual hallucinations, without focal neurological deficits or seizures. In physical examination the patient was afebrile and no jaundice and no signs of chronic liver failure (no ascites, spider nevi, or palmar erythema). Abdomen was non-tender, no shifting dullness. Neurological exam had no lateralizing signs.

Brain MRI: No evidence of metastatic lesions or structural abnormalities.

Abdominal CT: Tumoral involvement (peritoneal carcinomatosis) of the liver consistent with HCC recurrence; no portal vein thrombosis.

Given preserved hepatic function, absence of brain metastasis, and recurrent episodes of confusion temporally associated with low serum glucose, a paraneoplastic hypoglycemic encephalopathy was suspected. The hypoglycemia was attributed to excessive tumour secretion of incompletely processed big IGF-II, leading to increased glucose utilization and decreased gluconeogenesis.

4. Discussion

Neurological symptoms in HCC most often arise from two mechanisms:

1. Hepatic encephalopathy due to liver failure and hyperammonemia.

2. Brain metastasis leading to focal deficits or seizures [2].

However, in this case, neither mechanism was present. Instead, the patient's neuropsychiatric manifestations were secondary to paraneoplastic hypoglycemia, a rare but recognized metabolic complication of HCC [3,4].

Large or rapidly growing HCCs may produce an abnormal form of IGF-II, termed "big IGF-II," which mimics insulin by binding insulin receptors, thereby increasing glucose uptake by tissues and suppressing gluconeogenesis. The resultant hypoglycemia primarily affects the central nervous system, causing symptoms ranging from mild confusion to psychosis or coma [5].

Differential diagnosis of these situations include:

- Hepatic encephalopathy
- Metastatic brain lesions
- Sepsis or metabolic derangements
- Paraneoplastic syndromes

Paraneoplastic syndromes occur in 20–40% of HCC patients with these manifestations:

- Hypoglycemia due to IGF-II production
- Erythrocytosis due to erythropoietin secretion [4]
- Hypercalcemia due to PTH-related peptide
- Dermatologic or neurologic paraneoplastic effects (rare syndrome)

Recognition of paraneoplastic hypoglycemia in HCC is essential because neurological symptoms may be misattributed to hepatic encephalopathy, leading to inappropriate management. Early glucose correction and tumour control (via resection, embolization, or systemic therapy) are key to reversing symptoms [4,5].

5. Conclusion

This case illustrates an uncommon neurological presentation of hepatocellular carcinoma with paraneoplastic hypoglycemic encephalopathy in the absence of hepatic failure or cerebral metastasis. Clinicians should consider paraneoplastic causes in patients with HCC who develop neuropsychiatric manifestations despite preserved liver function, as timely recognition and metabolic correction can be life-saving.

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