ACG CASE REPORTS JOURNAL

IMAGE | PANCREAS

Pancreatic Neuroendocrine Tumor-Induced Hyperammonemic Encephalopathy in the Absence of Hepatic Involvement

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CASE REPORT

A 47-year-old Hispanic man with a medical history of depression was sent from a psychiatric facility to the intensive care unit for decreased responsiveness. The family reported that the patient had become increasingly depressed with daily diarrhea and an unintentional 50-pound weight loss over the past 6 months. Alcohol level and drug screens were negative. Significant laboratory data revealed aspartate aminotransferase of 43 U/L, alanine aminotransferase of 126 U/L, prothrombin time of 16.1 s, and ammonia level of 163 μmol/L. Hepatitis panel, human immunodeficiency virus screen, autoimmune panel, and tumor markers (cancer antigen 19-9, alpha-fetoprotein) were unremarkable. Computed tomography (CT) and magnetic resonance imaging of the brain were negative. Abdominal CT revealed an intra-abdominal mass in the upper left quadrant, originating from the pancreas (Figure 1). CT-guided core needle biopsy with immunohistochemical staining positive for synaptophysin and chromogranin A, both under 400× magnification (Figure 2), supports the diagnosis of a well-differentiated, grade 1 of 3, pancreatic neuroendocrine tumor (PNET). Distal pancreatectomy with splenectomy followed, with negative pancreatic margins, and splenic and liver tissue negative for metastasis. The patient's confusion resolved.

PNETs are relatively rare, with a prevalence of approximately 1–4 per 100,000 population in the United States.[1] PNETs presenting with hyperammonemic encephalopathy (HE), as seen in our case, are uncommon. Many previously reported cases had liver metastases present.[2] In fact, 75%–80% of all PNETs have liver metastases at diagnosis,[2] making our case without the evidence of metastasis in the setting of severe hyperammonemic encephalopathy even more atypical. There are, however, previously documented cases in which metastatic PNETs presented with HE without evidence of liver failure or urea cycle dysfunction.[3] In a healthy liver, ammonia and its byproducts are typically cleared and prevented from entering the systemic circulation. In liver dysfunction or

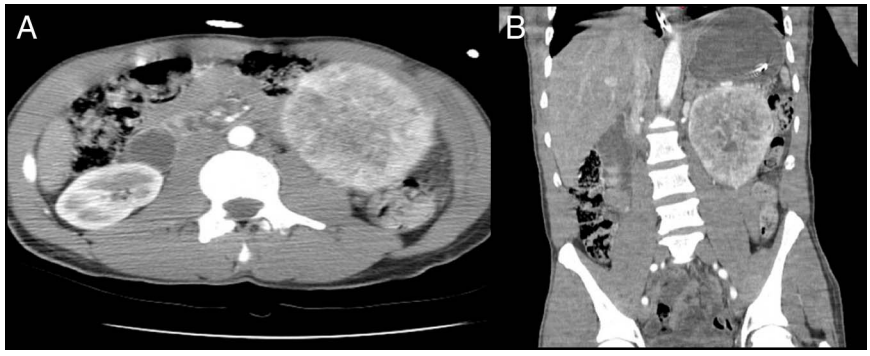

Figure 1. (A) Axial and (B) coronal view of abdominal computed tomography revealed an intra-abdominal mass in the upper left quadrant, originating from the pancreas.

ACG Case Rep J 2020;7:e00425. doi:10.14309/crj.0000000000000425. Published online: July 9, 2020

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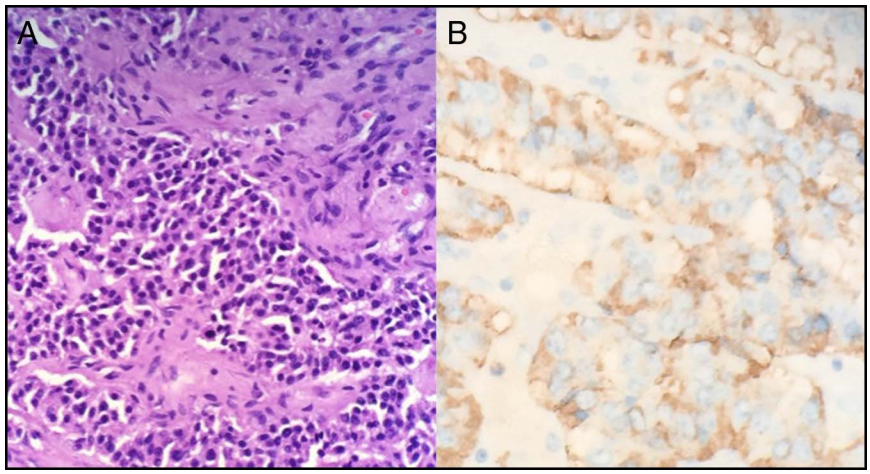

Figure 2. Pancreatic mass core biopsy immunohistochemical staining positive for (A) synaptophysin and (B) chromogranin A (400× magnification).

chronic liver disease, reduction in the metabolic capacity of the liver's urea cycle plus blood shunting adjacent to the hepatic sinusoids can lead to overaccumulation, neurocognitive changes, and cerebral edema—termed hepatic encephalopathy.

Alternative mechanisms for HE in the setting of PNETs have been proposed, many of which could suggest an etiology for the HE seen in our case involving no liver metastasis. First, unknown hormones or neurotransmitters produced by PNETs may predispose to the development of HE via a cascade of chemical signaling mechanisms.[4] In addition, amid an anatomically-intact liver, our patient's PNET may have facilitated a transtumoral or portosystemic shunt, further leading to the patient's symptom of HE.[5] In addition, PNETs often the cause severe diarrhea, leading to dehydration and intravascular volume depletion, which ultimately may enhance renal ammonia production and could contribute to our patient's HE. Our case highlights the importance of exploring extrahepatic etiologies in patients presenting with encephalopathy and elevated ammonia levels. In addition, the absence of liver metastasis in our case warrants further exploration into alternative mechanisms of HE that have previously been contemplated in cases of PNETs.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. AC Berry is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Previous presentation: This case was presented at the American College of Gastroenterology Annual Scientific Meeting, October 14-19, 2016; Las Vegas, Nevada.

Received January 23, 2020; Accepted May 8, 2020

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