Case Report

Unusual Presentation of Aggressive Neuroendocrine Tumor

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Abstract

Neuroendocrine tumors (NETs) are rare neoplasms that occur in 1 out of 100,000 people in the United States and can occur in any body tissue, although most commonly located in the lung and small intestine. They arise from various neuroendocrine cells and, while many are benign, malignant cases are reported. While NETs are known to excessively produce hormones, 50% of NETs are non-functional in nature and clinically silent.[1,2] This feature can allow the tumor to grow to massive sizes or metastasize to other organs, making early recognition and treatment difficult and dramatically changing prognosis. It is reported that 40-93% of gastrointestinal NETs metastasize to the liver.[1]

The following report is a rare case of a massive metastatic liver neuroendocrine tumor found incidentally in a 47-year-old gentleman who presented to the emergency department complaining of seizures. The pathophysiology, etiology, and treatment options for metastatic liver tumor from NETs will be discussed.

Introduction

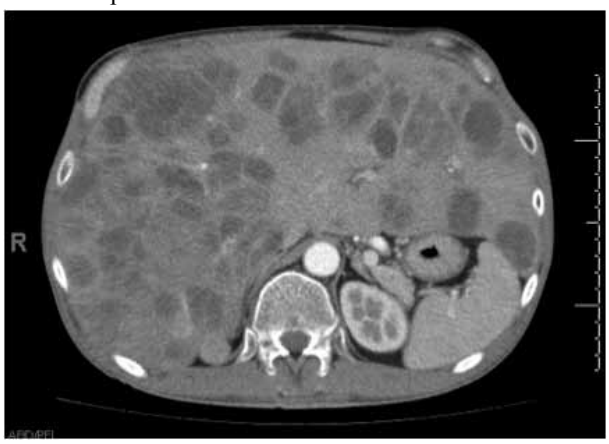
Neuroendocrine tumors (NETs) are uncommon groups of heterogeneous neoplasms that occur in roughly around 1 out of 100,000 people in the United States.[1,2] While NETs are uncommon in our population, metastatic disease to the liver is very common, ranging from 40-93% of the gastrointestinal NETs and is a major cause of morbidity related to these neoplasms. While NETs can occur in a wide variety of organ systems, they most commonly occur in the bronchopulmonary and gastrointestinal tract.[1,5]

Case Report

A 47-year-old Caucasian gentleman, with a past medical history significant for seizure disorder, presented to the emergency department with intractable seizures. He described getting a strange feeling in his head prior to the seizures. The patient was unable to recall what happened after the episode. He denied any epigastric discomfort, weight loss, dysphasia, nausea, emesis, constipation, or diarrhea.

On physical examination, the patient's vital signs were stable. Neurological examination was benign. All other systems were within normal limits except for his abdominal examination. His abdomen was firm and distended. Organomegaly was appreciated with the liver edge to be estimated 8-10 cm below the costal margin. At that time, ultrasound of the abdomen was obtained, which revealed hepatomegaly with diffusely inhomogeneous echotexture and splenomegaly.

Figure 1: Axial view demonstrating hepatomegaly with multiple lesions.



Subsequently, CT scan of the abdomen and pelvis with oral and intravenous contrast was obtained for further evaluation. The CT scan demonstrated massive hepatomegaly spanning the abdomen from the left flank wall to the right flank wall over a distance of 27 cm (Figure 1). The liver also extended from the dome of the diaphragm into the right hemipelvis measuring 36 cm in length (Figure 2). The appearance of the liver was suggestive of extensive metastatic disease. There was also a large mass extending towards the tail of the pancreas (Figure 3).

Figure 2: Coronal reformatted image demonstrating the liver occupying majority of the abdominal space.

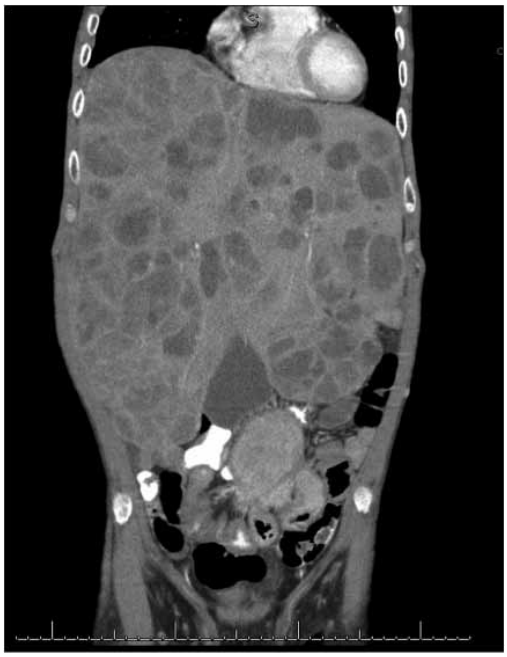
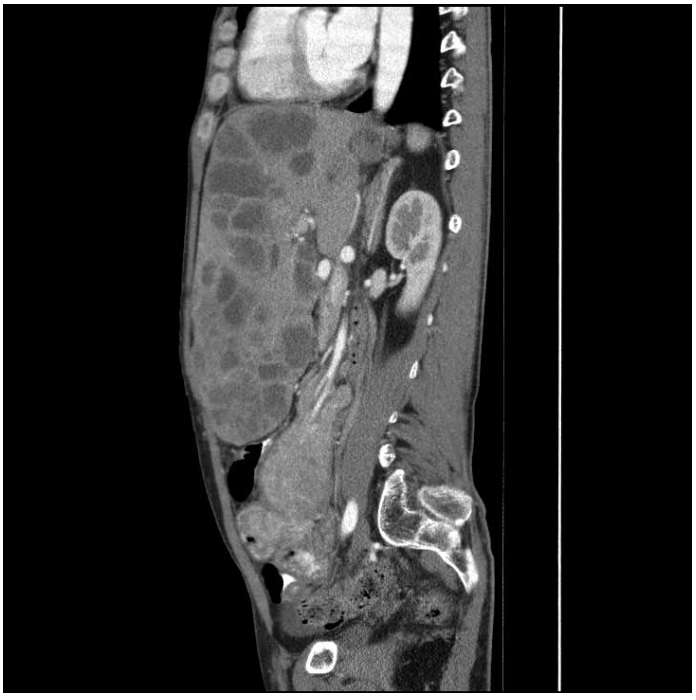


Figure 3: This parasagittal view suggests site of origin to be pancreatic with caudal displacement secondary to massive hepatic enlargement.



Subsequently, a core needle biopsy of the liver was obtained, which demonstrated a nested and organoid growth pattern comprised of relatively uniform tumor cells. Mild nuclear pleomorphism was present. No mitoses were identified. No necrosis was noted. Furthermore, immunohistochemical stains were performed to characterize the tumor cells. The results showed positivity for chromogranin, synaptophysin, and Neuron-specific enolase (NSE) of the tumor cells. The thyroid transcription factor 1 (TTF-1) stain was negative. A diagnosis of neuroendocrine carcinoma grade I was made at this time.

Discussion

Neuroendocrine tumors (NETs) are rare groups of neoplasms that can commonly metastasize to the liver.[1,2,4] While NETs have the ability to secrete polypeptides with hormonal activity (functional), roughly around 50% of NETs can be categorized as non-functional in nature.[1] Examples of functional NETs are Carcinoid, VIPoma, Insulinoma, Prolactinoma, Pheochromocytoma, and Gastrinoma. These NETs usually present clinically based on which hormone they secrete excessively. The concern with non-functional NETs is that they can be clinically silent until they reach a large size.[1] It is estimated that the median survival duration for NETs that metastasize to the liver is 72 months.[5] While treatment for NETs is specific for their location, systemic symptoms, and type, the following will explain the treatment options for NETs that metastasize to the liver.

Currently, the gold standard for treatment for liver metastases from NETs is resection. Surgical resection achieves a survival rate of 60-80% at five years out with a mortality of 0-5%.[1,2] While resection is the gold standard, there are other modalities that are used for palliative treatment. Radiofrequency ablation (RFA) is a modality for a certain select group of patients. RFA can be considered for the following conditions: lesions less than 3 cm, palliation of carcinoid symptoms, patients medically unsuitable for surgical resection, and/or management for recurrent lesions after primary resection.[2]

Another modality for palliative treatment for unresectable metastatic liver lesions is embolization. This technique acts by targeting the tumor's blood supply. While the majority of blood supply to the liver is made up by the portal vein, NET's primary blood supply is via the hepatic artery. This modality shows a 50-96% response rate in reduction in size of lesions.[2] This technique can also be used to subselectively direct medication towards the lesion. There are recent studies showing the use of miriplatin-lipiodol emulsion for chemoembolization. The results showed a significant reduction in size of the liver lesions.[3] Another case from 2004 showed a considerable reduction in size of liver lesions from a patient receiving chemoembolization with four cycles of peptide radioreceptor therapy with 111Lu-otcreotate. This case also demonstrated a significant reduction of Chromogranin A serum markers.[1] Most recently, a study was performed using doxorubicin-impregnated drug-eluting bead as chemoembolization. This study, which was performed on 18 patients, showed similar reduction in progression of disease as comparable to previous chemoembolization studies.[5]

Liver transplantation is another form of treatment that is only considered in a select few. Patients considered for transplant should have no extrahepatic disease with controlled primary tumor and meet the Milan criteria. Transplantation shows a 47-96% five-year survival rate. Five-year recurrence rate was also found to be 24-80%.[1,2]

In conclusion, treatment options for NETs with hepatic metastases have increased in recent years. While liver resection is currently the gold standard of treatment, other modalities are currently available for palliative treatment. In the case of this patient, during his further evaluation by oncology his disease progressed rapidly, and he succumbed prior to initiation of appropriate therapy. Brian Harris, PhD, MD, FAAR, is Diagnostic Radiologist at Quantum Imaging and Therapeutic Associates, Inc., in Harrisburg, PA.

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Potential Financial Conflicts of Interest: By AJCM® policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article that might create any potential conflict of interest. The author has stated that no such relationships exist.

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