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CASE REPORT | PANCREAS

Incidental Diagnosis of MEN1 Syndrome in a Pediatric Patient Presenting With Obstructive Jaundice and Abdominal Pain

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Abstract

A 16-year-old adolescent boy presented with obstructive jaundice and was incidentally found to have a well-differentiated pancreatic endocrine neoplasm upon endoscopic ultrasound. The discovery of this tumor led to further investigation and the eventual diagnosis of MEN1 syndrome. The diagnosis of MEN1 can prove difficult, and lack of treatment has been shown to lead to early mortality. One must maintain clinical suspicion for this disease in the evaluation of patients presenting with suspicious lesions of unknown etiology, especially those involving the pancreas, anterior pituitary, and parathyroid glands.

Introduction

Pancreatic endocrine neoplasms are a rare malignancy that can be associated with multiple endocrine neoplasia type 1 (MEN1). Early diagnosis and intervention leads to decreased mortality. Therefore, one must maintain clinical suspicion of this syndrome in the analysis of patients who present with MEN1-associated tumors.

Case Report

A 16-year-old adolescent boy presented to an outside hospital with 1 week of jaundice, nausea, vomiting, and epigastric abdominal pain. Pertinent labs on presentation included AST 374 U/L, ALT 779 U/L, total bilirubin 3.27 mg/dL, and alkaline phosphatase 162 U/L. Historically, the patient had been referred to a pediatric endocrinologist for hypercalcemia and was found to have an elevated parathyroid hormone level with a low 25-hydroxyvitamin D level, prompting initiation of vitamin D supplementation, but was lost to follow-up. Abdominal ultrasound was performed and revealed cholelithiasis and a common bile duct (CBD) diameter of 6 mm. Abdominal/pelvic computed tomography (CT) revealed no abnormalities.

Due to high suspicion of a CBD stone, endoscopic ultrasound (EUS) found a maximal CBD diameter of 4.1 mm, with no evidence of biliary stone burden and several hypoechoic lesions in the uncinate, neck, body, and tail of the pancreas, the largest of which was a homogenous 10 x 12 mm lesion with well-defined borders (Figure 1). Fine-needle aspiration was performed on the largest lesion and revealed a well-differentiated pancreatic endocrine neoplasm (Figure 2). Esophagogastroduodenoscopy (EGD) revealed no evidence of gastric or duodenal carcinoids, and EUS did not discover any mediastinal lymphadenopathy or adrenal gland abnormalities. Pancreaticobiliary surgery recommended magnetic resonance imaging (MRI) using a pancreas protocol, which only revealed small foci of increased intensity, thought to represent lipomatosis. The patient's jaundice and gastrointestinal symptoms improved with time and were felt secondary to a biliary stone, which spontaneously passed; however, the incidental discovery of the pancreatic lesions of unknown etiology prompted further review of the patient's medical history with specific evaluation for MEN1 syndrome.

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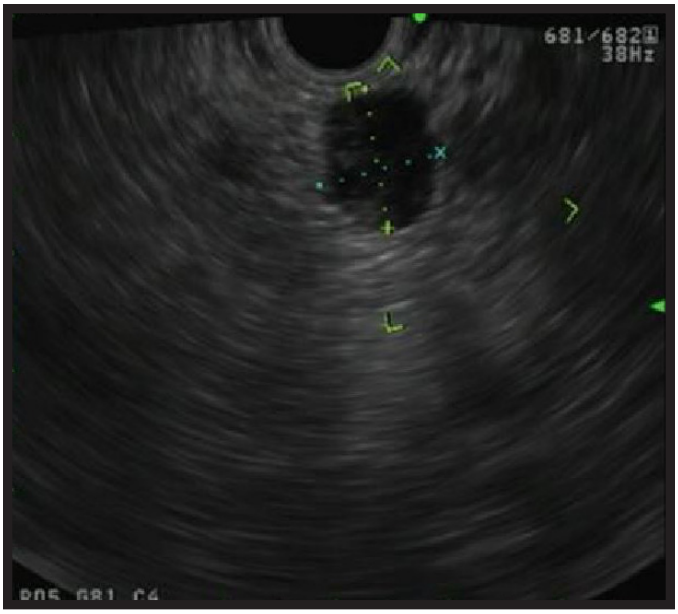

Figure 1. Endoscopic ultrasound revealing hypoechoic pancreatic lesion.

Ultrasound of the thyroid revealed nonspecific, 2–3-mm hypoechoic lesions, and brain MRI revealed a 9-mm hypoenhancing, sellar lesion (Figure 3). Chest CT revealed a nonspecific 2.0 x 3.9-cm anterior superior mediastinal lesion of intermediate attenuation, thought to represent residual thymic tissue. Laboratory analysis showed hemoglobin A1c 5.9%, prolactin 123 ng/mL, insulin-like growth factor-1 316 ng/mL, gastrin 25 pg/mL, chromogranin-A 6.0 ng/mL, vasoactive intestinal peptide 26 pg/mL, glucagon <134 pg/mL, and pancreatic polypeptide 722 pg/mL. Based on this constellation of a pituitary microprolactinoma, hyperparathyroidism, and a pancreatic neuroendocrine tumor, he was diagnosed with MEN1 syndrome. Cabergoline, a dopamine receptor agonist commonly used in prolactinomas for inhibition of prolactin secretion, was initiated. He subsequently underwent a pancreatic mass enucleation performed for tumor debulking, with a plan for surveillance of the remaining pancreatic lesions. Genetic testing revealed a gene mutation indicative of a diagnosis of MEN1 syndrome with autosomal dominant inheritance.

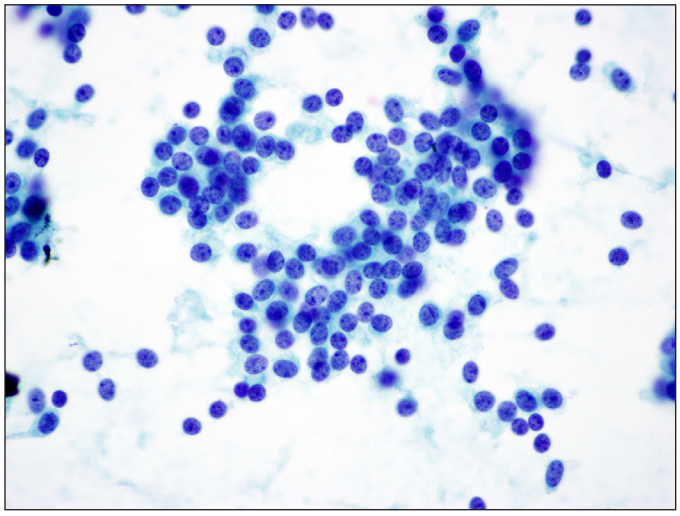

Figure 2. Papanicolaou stain demonstrating the characteristic findings of a pancreatic endocrine neoplasm, including cells with round uniform nuclei, inconspicuous nucleoli, and a coarsely stippled chromatin pattern (60x magnification).

Discussion

MEN1 is a genetic syndrome manifested most commonly as neoplasms of the anterior pituitary, parathyroid glands, and pancreas, but sometimes associated with lipomas, angiofibromas, carcinoid tumors, collagenomas, thyroid tumors, and adrenocortical tumors.[1,2] The associated genetic mutation either occurs sporadically or in an autosomal dominant fashion.[3] Diagnosis is made by the presence of either ≥2 associated tumors in an individual, ≥1 associated tumor in a first-degree relative of an afflicted individual, or indicative genetic analyses.[2] Thirty percent to 80% of patients with the MEN1 syndrome are found to have pancreatic islet cell tumors; however, pancreatic endocrine neoplasms have an annual incidence of less than 1 per 100,000 and are most frequently diagnosed in the sixth and seventh decades of life.[2,4]

Our case presents a unique clinical scenario for several reasons. The patient was young and his diagnosis via EUS was

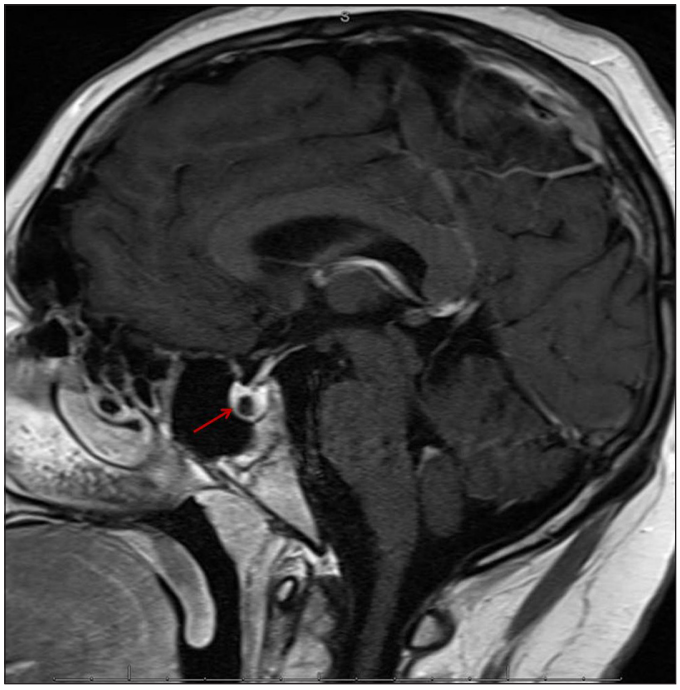

Figure 3. Brain MRI T1/FLAIR with contrast revealed a 5 x 9 x 6 mm hypoenhancing lesion (arrow) in the central aspect of the sella, likely representative of a microadenoma.

incidental, based on his presentation of obstructive jaundice. Our patient had also undergone CT and MRI of the pancreas, with the former revealing a normal study and the latter only indicative of pancreatic lipomatosis. Discovery of pancreatic lesions such as those seen in our patient can be difficult, and review of the literature supports EUS as one of the most sensitive means of detection.[3,5,6] EUS has demonstrated a sensitivity of 93% and a specificity of 95% in the diagnosis of all types of pancreatic neuroendocrine tumors, compared to a failure to localize rate of 40–60% in traditional imaging modalities.[7] We recommend the inclusion of EUS in the screening algorithm for pancreatic endocrine neoplasms if clinical suspicion for MEN1 syndrome remains high despite normal findings on more traditional imaging modalities such as MRI.

Treatment varies based on tumor location and generally involves medical therapy and/or surgical resection.[2] Guidelines currently recommend genetic testing for MEN1 syndrome confirmation in patients who meet the clinical criteria and in those with development of suspicious tumors.[3] Genetic screening also plays a large role in care once a diagnosis of MEN1 is made and focuses on analysis of chromosome 11q13, the location of the MEN1 gene.[2] Screening is typically performed in first-degree relatives of afflicted individuals, whether symptomatic or not, and is initially comprised of mutational analysis, with further biochemical and radiographic testing reserved for those identified as carriers of the MEN1 mutation.[3,8]

Disclosures

Author contributions: JD Jones wrote and edited the manuscript, and is the article guarantor. B. Cengia and J. Conway reviewed the manuscript. R. Pawa wrote, edited, and approved the manuscript.

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