Pancreatic Carcinoid Tumor in a Pediatric Patient

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Patient: Female, 9-year-old
Final Diagnosis: Carcinoid tumor
Symptoms: Easy fatigability • weakness • back pain • easy bruising
Clinical Procedure: Distal pancreatectomy and splenectomy
Specialty: Endocrinology and Metabolic • Surgery

Objective: Unknown etiology
Background: Carcinoid tumors are well-differentiated tumors that develop from neuroendocrine cells. They are rare tumors and occur most commonly in the gastrointestinal tract, followed by the pulmonary system. They usually present with abdominal pain or cough or persistent pneumonia. They are usually diagnosed with computed tomography (CT) or magnetic resonance imaging (MRI) of the chest or abdomen. The cornerstone of treatment is surgical resection. There are rare reported cases of carcinoid tumor presenting in the pancreas as gastrinoma or insulinoma and are associated with multiple endocrine neoplasia type 1 (MEN1).

Case Report: We report a case of an otherwise healthy 9-year-old girl who presented with manifestations of Cushing syndrome (easy fatigability, weakness, back pain, easy bruising, hirsutism, acne, skin discoloration [pigmentation], and blurred vision). She was diagnosed with incidental carcinoid tumor in the pancreas based on hypertension and typical stigmata. She underwent distal pancreatectomy and splenectomy. The histopathology showed a well-differentiated neuroendocrine tumor with G2. The diagnosis of concurrent Cushing syndrome and carcinoid syndrome can be challenging, as it is rare. It is important to screen for MEN syndrome when Cushing syndrome occurs in a child, as there is a high rate of transition to malignancy. They are usually diagnosed with ACTH, cortisol, and imaging.

Conclusions: Incidental hypertension in children is not common and mandates further investigation and clinical work-up to look for endocrinopathies such as Cushing syndrome and carcinoid syndrome. As the literature on such cases is scant, further reporting of cases is needed.

Keywords: Case Reports • Cushing Syndrome • Neuroendocrine Tumors

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Background

Carcinoid tumors are well-differentiated tumors that develop from neuroendocrine cells [1]. The phrase “carcinoid tumor” was first described in 1907, when it was called karzinoide (“carcinoma-like”) for its rapid growth [2]. These tumors contain many neurosecretory granules that secrete serotonin, histamine, dopamine, and prostaglandins [1]. They are rare, with 4-8 cases per 100 000 in clinical and pathological settings [3,4] and there are few cases published in the literature. The most common site of carcinoid tumors is in the gastrointestinal tract, followed by the pulmonary system [5]. Among those, almost 13% of cases had distant metastases at time of presentation [5]. They usually present with abdominal symptoms (eg, pain) or respiratory symptoms (eg, cough and persistent pneumonia). They are usually diagnosed with computed tomography (CT) or magnetic resonance imaging (MRI) of the chest or abdomen [1]. The cornerstone of treatment is surgical resection. There are rare reported cases of carcinoid tumor presenting in the pancreas as gastrinoma or insulinoma and associated with multiple endocrine neoplasia type 1 (MEN1) [2]. We report a case of a girl with Cushing syndrome who was incidentally diagnosed with carcinoid syndrome.

Case Report

A 9-year old girl, who was healthy until 2 months before the first hospital admission, was presented when she developed face puffiness (moon face) and increase in weight. Accompanying symptoms included easy fatigability, weakness, back pain preventing her from walking unsupported, easy bruising, hirsutism, acne, skin discoloration (pigmentation), and blurred vision. There was no history of previous trauma. There was no history of fever, loss of appetite, vomiting, change of bowel habits, cough, or preceding illnesses. She was born full-term, had a complete immunization history, and uneventful perinatal history. There was no family history of chronic or heritable diseases. Clinical examination showed high blood pressure 140/80 mmHg, and stigmata of Cushing syndrome.

The patient was diagnosed with Cushing syndrome in a government hospital with clinical suspicion based on hypertension and typical stigmata. Extremely high plasma cortisol was detected by an overnight dexamethasone test. ACTH and severe hypokalemia indicated ectopic Cushing syndrome. CT abdomen showed a retroperitoneal mass inseparable from the pancreatic body/tail. She was then transferred to a tertiary hospital for surgical management. She was admitted to the pediatric intensive care unit (PICU) because she was hypertensive. Her laboratory test results were: dexamethasone suppression test was 167 mcg/dl (normal level 0-2 mcg/dl), and also found to have severe hypokalemia 1.9 mmol/L (normal value 3-5 mmol/L). Complete blood count (CBC) showed no leukocytosis, low platelets 60×10^9/mcl (normal value 150-400×10^9/mcl). She had high levels of ACTH 1424 pg/mL (normal value 11-82 pg/mL), DHEA >27 000 mcg/dl (normal value 29-412 mcg/dl), testosterone 18.3 ng/dl (normal value 15-70 ng/dl), serum cortisol level 4239 mg/m^2/day (normal value 6-8 mg/m^2/day). Her liver profile was normal. An urgent MRI brain was done and showed no intracranial masses, with an unremarkable pituitary gland. CT neck, chest, abdomen, and pelvic (CAP) showed a retroperitoneal mass inseparable from the pancreatic body/tail, bilateral adrenal hyperplasia, and small bilateral lung bases atelectasis with suggestion of minimal bilateral pleural effusion. She was managed conservatively. She was started on antihypertensive and diuretic medications (amlodipine, enalapril, atenolol, furosemide, and spironolactone) along with potassium correction and gastric protection. Upon starting the medications, her blood pressure and electrolytes normalized. She further underwent an MRI abdomen to confirm the diagnosis, which showed a pancreatic mass, most likely a neuroendocrine tumor, with adrenal hyperplasia (Figures 1-3). She was prepared for pancreatocexomy, and she received 1 unit of platelets preoperatively.

She underwent distal pancreatectomy and splenectomy. The initial approach was laparoscopic; however, minimally invasive surgery was converted to laparotomy because there was significant bleeding from the pancreatic body, so dissection of the distal pancreas was done to control the bleeding. The mass was found to be located at the body and tail of the pancreas. Splenectomy was performed as it was adhesive to the tumor and there was significant bleeding. A drain in the left side was inserted. The estimated blood loss was 1000 ml. The patient received 2 units of platelets intraoperatively. The patient was intubated and transferred to the Pediatric Intensive Care Unit (PICU).

The patient was extubated on postoperative day 1. Her high blood pressure was controlled with 2 antihypertensive medications. Her pleural effusion was managed medically with 2 diuretics. Her echocardiogram (ECHO) showed good left ventricular function, with ejection fraction of 55%. Her carcinoid syndrome was managed with octreotide. She received pain medications (morphine and paracetamol) and antibiotics (ceftriaxone and metronidazole) for surgical prophylaxis, but this was continued for 20 days as the patient was febrile with positive cultures. She was hypokalemic, received potassium chloride replacement, and was started on hydrocortisone according to Endocrinology recommendations. Her lab test results showed creatinine 29 µmol/L (normal value 53-97.2 µmol/L), normalization of potassium and sodium (3.6 mmol/L and 140 mmol/L respectively), serum calcium level 2.06 mmol/L (normal level 2.2-2.7 mmol/L), and serum magnesium level 0.54 mmol/L (normal level 0.85-1.10 mmol/L). She underwent replacement of calcium and magnesium. CBC showed no leukocytosis, hemoglobin 83 g/L (normal value 121-151 g/L), and...
platelets $80 \times 10^9$ (normal value $150-400 \times 10^9$/mcL). An ultrasound (US) of the abdomen showed no pleural effusion and no intraabdominal collection. The drain amylase and lipase were normal. The abdomen was soft and lax. The wound was dry and clean. Ceftriaxone was stopped because she developed penicillin allergy. Hydrocortisone was tapered by Endocrinology to 10 mg q8h. She was clinically and vitally stable. She was prepared for discharge.

She stayed 4 days in the PICU and then was transferred to the pediatric ward. She was followed by the Pediatric Endocrinology team. She received hydrocortisone 25 mg q8h and insulin to control her hyperglycemic episodes.

Using the TNM staging system $T3N0M0$, histopathology showed a well-differentiated neuroendocrine tumor with $G2$ (pending the Ki67 result) and a $pT3$ tumor limited to greater than 4 cm. There were no lymph nodes. The pancreas was positive for malignancy and the spleen was negative. The tumor cells were positive for CD56, NSE, synaptophysin, chromogranin, E-cadherin, and EMA. B-catenin showed membranous/cytoplasmic staining. Panekeratin was negative.

She was discharged on day 25 from admission with an abdominal drain. We plan to perform a DOTA scan to rule out metastatic disease or residual disease to assess for the need to receive chemotherapy. Also, a baseline of 24-h urinary 5-hydroxyindoleacetic acid (5-HIAA) and serum chromogranin A was recommended.

**Discussion**

We describe a pediatric patient who was diagnosed with Cushing syndrome and carcinoid syndrome in the pancreas, which is extremely rare and important to diagnose due to the high risk of malignancy [6].

A systemic review reported that 15% of cases of Cushing syndrome are caused by ectopic adrenocorticotropic secretions leading to metastasis [7]. Also, a large 15-year retrospective study in Mexico showed only 16 patients had neuroendocrine tumors, of which the mean age was 36 years, nearly 3/4 of the cases were in the bronchus, 2 were in the thymus, and 1 consisted of a corticomedullary tumor [8]. Clinical presentation is often hard to assess because symptoms can be misleading. For instance, patients can present with infections or Cushing syndrome in 70% of the cases with suspicion of lung cancer or pituitary origin; therefore, diagnosis is usually made.
late in ectopic cases [7]. They are usually diagnosed with high ACTH nonresponsive, cortisol, with further hormonal level that can indicate an ectopic site of origin. For instance, 5-HIAA and calcitonin are suggestive of lung and thymus origin, whereas gastrin, glucagon, calcitonin, insulin, and VIP are suggestive of pancreatic origin [6]. In addition to laboratory diagnosis, imaging is often utilized. A computed tomography (CT) chest, abdomen, and pelvis with contrast is often ordered to delineate the site of the ectopic lesion [9], and if it is not found, a nucleotide scan is often the next step [10]. Surgical management is usually the first modality for treatment. If treatment was refractory to surgery, second-line treatment includes medications and radiotherapy. Medications include pituitary targeted therapy (somatostatin analog and dopamine agonists), new therapy (retinoid acid, heat shock protein 90 inhibition, epidermal growth factor inhibition, and cyclin kinase), and even steroids [11]. There is only 1 reported case of concurrent Cushing syndrome and bronchial carcinoid syndrome, in 12-year-old child, which was diagnosed with laboratory tests, CT chest, and CT-guided biopsy [12]. The follow-up and prognosis of such ectopic tumors are not studied broadly. However, a 10-year follow-up study by Scott et al found that nearly 70% had no recurrence and had complete reversal of Cushing syndrome, 30% died with no causes related to the tumor, and 7% had recurrence of the tumor [13].

Conclusions

Incidental hypertension in children is not common and mandates further clinical and investigative work-up to look for endocrinopathies such as Cushing syndrome and carcinoid syndrome. As the literature is scant on such cases, further reporting of cases is needed on this topic.

Declaration of Figures’ Authenticity

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