

# Malignant Nonfunctioning Neuroendocrine Neoplasm of the Pancreas in a 10-Year-Old Child

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## Key Words

Pediatric pancreatic neoplasms · Neuroendocrine tumors · Whipple procedure

## Abstract

Malignant neoplasms of the pancreas are extremely rare in children and only represent a small percentage of pediatric cancer-related deaths. The paucity of cases reported in the literature, in addition to the lack of understanding of biologic behavior, has led to a lack of consensus concerning optimal management strategy. Presentation differs compared to adult counterparts and generally prognosis is improved even when lymph node metastases occur. Here we review the literature and report the case of a 10-year-old autistic female with a malignant nonfunctioning pancreatic endocrine neoplasm of the head of the pancreas successfully extirpated via pancreaticoduodenectomy.

## Case Report

A 10-year-old African American female presented to the pediatric gastroenterology clinic with nausea and a 25 pound weight loss. She had a history of significant speech delay which was concerning for autism. Video-EEG and chromosomal analysis were normal. Review of symptoms was negative for jaundice with no symptoms suggestive of reflux, ulcers, hypoglycemia, diarrhea or rashes. She was worked up for her symptomatology and was diagnosed with chronic pancreatitis. This child was initially treated symptomatically with prokinetic agents and anti-nausea medicine. However, during the work-up, she had persistent nausea and significant anorexia which led to an extensive work-up including routine laboratory, gastric emptying study, CT scanning, and EUS with biopsy. No preoperative hormonal studies were obtained. CT scan demonstrated a 2-cm well-circumscribed homogenous mass in the head of the pancreas with no apparent vessel invasion ([fig. 1](#)). This finding in addition to the weight loss was concerning for a malignant lesion leading to surgical consultation. Endoscopic ultrasound fine needle aspiration at that time demonstrated benign pancreatic aspirate with no evidence of malignancy. Pancreaticoduodenectomy was performed without complication and she was discharged home on postoperative day 7. Pathological examination diagnosed a 2-cm neuroendocrine tumor of the pancreas ([fig. 2](#)) with 4 of 26 lymph nodes positive for metastasis. At her

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3-week follow-up, she had recovered normal gastrointestinal function and was returning to school. Three-month follow-up at the gastroenterology clinic included repeat CT scans, CA 19-9 and CEA which were all normal. She is gaining weight and is free from recurrence.

## Discussion

Pancreatic neoplasms in children are rare and the natural history of most of these tumors is yet to be understood. It is estimated that they are responsible for only 0.2% of pediatric cancer-related deaths [1]. Our understanding of their behavior is limited and most reports are largely anecdotal. Pancreatic tumors are generally classified as epithelial or nonepithelial types. Epithelial tumors are further classified into exocrine and endocrine tumors. Exocrine tumors may be of acinar, ductal cell, or uncertain cell origin, and some tumors may arise from stem cells [2].

A variety of pancreatic tumors have been reported in children and/or adolescents: ductal adenocarcinoma, acinar cell carcinoma, pancreatoblastoma, solid pseudopapillary tumor, and pancreatic endocrine neoplasms (PENs). In addition, there are other tumors that either arise from nonpancreatic cells or secondarily involve the pancreas through direct extension [3, 4]. Cystic tumors include serous and mucinous cystadenomas and cyst adenocarcinomas, albeit there are no reports of childhood cystadenocarcinoma [5]. Warfel et al. suggested that these cystic lesions of the pancreas in children may represent congenital malformations similar to congenital cystic lesions of the lung as opposed to being actually neoplastic [6]. Pancreatic neoplasms in children tend to present late with abdominal pain, mass, or weight loss. Rarely do pediatric patients present with jaundice, mainly attributed to expansive growth rather than the infiltrative growth pattern seen in adults. Some tumors are large at presentation and may demonstrate areas of cystic degeneration or central hemorrhage.

One large review described a variety of malignant pediatric pancreatic tumors: solid pseudopapillary tumor (n = 7), pancreatoblastoma (n = 5), PEN (n = 2), peripheral neuroectodermal tumor (n = 2), and acinar cell carcinoma (n = 1). One PEN was a nonfunctioning tumor while the other was a malignant VIPoma [7]. Most cases previously reported in the literature as pancreatic ductal adenocarcinomas were probably misclassified.

Pancreatoblastoma is the most common pancreatic tumor of children. It was first described by Becker in 1957 as ‘infantile adenocarcinoma of the pancreas’ [8], and since, fewer than 75 cases have been reported [9]. Pancreatoblastoma occurs in the first decade of life, has a male predominance, and is associated with Beckwith-Wiedemann syndrome. These tumors are large, well-circumscribed solitary masses arising most commonly in the head of the pancreas, and like in other embryonal tumors, alpha-fetoprotein can be elevated [10]. Unfortunately, about one-third are metastatic at presentation, but in the absence of metastasis 5-year survival approaches 50%. Even after aggressive treatment, recurrence rates remain high and close observation is recommended. Numerous reports recently describe the response of pancreatoblastoma to chemo- or radiotherapy [11, 12]. Nevertheless, there are not enough data to support the widespread use of these modalities in an adjuvant or a neoadjuvant setting.

PENs arise from the cells within the islets of Langerhans. They are either sporadic or can occur in the setting of multiple endocrine neoplasia. In the setting of multiple endocrine neoplasia, PENs tend to occur at an earlier age compared to the sporadic form. Given their endocrine nature, these tumors may be either functioning or nonfunctioning

and may produce more than one hormonal peptide. Clinical syndromes when present are only related to the predominant hormone [10]. Of the PENs, only insulinomas, gastrinomas, and VIPomas have been reported in pediatric patients.

As in adults, insulinomas predominate and may present with Whipple's triad of fasting hypoglycemia, symptoms of hypoglycemia, and immediate resolution of symptoms with intravenous administration of glucose. While these tumors vary in size, they often occur in the body and tail of the pancreas. Insulinomas are usually less than 3 cm in size, present early with the clinical syndrome, and as in adults, are optimally treated with enucleation. Gastrinoma causes Zollinger-Ellison syndrome and patients may have multiple or recurrent peptic ulcers, classically in uncommon locations such as the postbulbar duodenum or proximal jejunum, that are refractory to medical management [13]. Gastrinoma and nonfunctioning PENs most commonly occur in or near the pancreatic head [10]. Very few glucagonomas are associated with a clinical syndrome and they tend to be much larger at presentation. Ideal treatment is complete resection or enucleation. When considering enucleation, intraoperative ultrasound is imperative since it demonstrates the relationship to the pancreatic duct. Patients with metastatic disease at presentation are often candidates for metastasectomy or debulking to decrease tumor burden. Most of these tumors are slow-growing and lengthy survival is often possible.

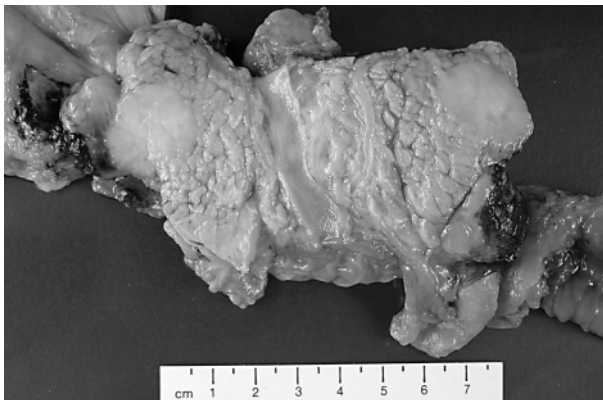
### Conclusion

Malignant neoplasms of the pancreas in children are uncommon. The number of cases reported in the literature is low and understanding of their biologic behavior and prognostic factors is limited. As in adults, investigation should include laboratory work as well as radiologic and endoscopic imaging. The use of preoperative baseline laboratory values may be helpful to monitor for recurrence. Resection is the only chance at cure and even confers a good prognosis in the presence of lymph node metastasis. Currently the use of chemotherapy or radiotherapy is anecdotal.

**Fig. 1.** Computed tomography of the abdomen demonstrating a hypodense mass in the head of the pancreas.



**Fig. 2.** Gross pathology demonstrating neuroendocrine tumor after pancreaticoduodenectomy.



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