An Adenoneuroendocrine Collision Tumor of the Pancreas: A Case Report

Disclosure: The authors did not report any financial relationships or conflicts of interest

Click for Supplemental Video

Presenting Author: Christine Chung, DO, General surgery resident PGY4, Department of General Surgery, HCA Swedish Medical Center, Englewood, CO, Englewood, CO


Introduction: A collision tumor is a neoplastic mass made up of two or more distinct cell populations that maintain distinct borders. Specifically, a mixed adenoneuroendocrine carcinoma (MANEC) is where a tumor has at least 30% adenocarcinoma component and at least 30% neuroendocrine carcinoma component.1

Pancreatic adenocarcinoma (PDAC) is rare but one of the most common malignant pancreatic tumors, whereas neuroendocrine pancreatic tumors are extremely rare at 1-2%.2 The incidence of the two as a combined neoplasm ranges only from 0.06-0.20%.2

Case presentation: We present a 57-year-old female with past medical history of lung cancer, COPD, and familial neurofibromatosis who presented with two months of nausea, vomiting, and epigastric abdominal pain. Imaging and endoscopic evaluation revealed extrinsic compression on the third portion of her duodenum. Fine needle aspiration (FNA) biopsies were obtained and were concerning for malignancy. On examination, her blood pressure was 179/84 mmHg, heart rate was 68 bpm, respiratory rate was 18, oxygen saturation was 100%, and temperature was 98.7°F. There were numerous neurofibromas noted mainly on the back and trunk and a few café au lait spots. The abdomen was soft but mildly tender to palpation. The rest of the examination was unremarkable. Initial labs revealed a CO2 of 36 mmol/L (range 22-31 mmol/L), an anion gap of 4 mEq/L (range 8-16 mEq/L), a BUN of 4 mg/dL (range 10-25 mg/dL), a creatinine of 0.60 mg/dL (0.70 – 1.40 mg/dL), a phosphorus level of 2.3 (range 2.6 – 4.9 mg/dL), and an ALT of 41 U/L (range <35 U/L). CA19-9 and CEA were both negative. All other lab values were within normal limits.

A CT chest abdomen & pelvis (CT CAP) was performed and showed a 4.2 x 2.8 cm focus of duodenal thickening and soft tissue prominence, concerning for duodenal neoplasm. The stomach appeared fluid-filled and dilated, suggesting a component of outlet obstruction. A 2.4 x 2.2 cm heterogeneously enhancing soft tissue nodule arising from the inferior aspect of the third portion of the duodenum was noted that may represent direct neoplastic extension versus an abnormal lymph node. Several enhancing nodular lesions involving the fourth portion of the duodenum and jejunum measuring up to 1.4 cm were also noted. A 3.7 x 2.8 cm right adrenal mass with pre-contrast attention of less than 10 was seen, consistent with an adrenal adenoma.

After ruling out a pheochromocytoma, the patient underwent an exploratory laparotomy, right adrenalectomy, pancreaticoduodenectomy, mesenteric nodal dissection, and portal nodal dissection. On final pathology, she was found to have a 4.7 cm pT3bN2M0R1 peri-ampullary combined poorly differentiated carcinoma and a well-differentiated grade 1 glandular neuroendocrine tumor (NET) with lymphovascular and perineural invasion. Three tumor deposits of poorly differentiated carcinoma involving the periduodenal/peripancreatic soft tissue were identified. The carcinoma and NET
components stained positive for chromogranin, CK7, and CDX2. Low-grade pancreatic intraepithelial neoplasia (PanIN-1) was also noted. One mesenteric lymph node was found to be involved by metastatic combined poorly differentiated carcinoma and well-differentiated grade 1 NET. In addition, 7 foci (<1.7 cm) of gastrointestinal stromal tumors (GISTs) were found in the duodenum with a final pathologic stage of mpT1N1M0R1 and a mitotic rate of <1 mitosis per 5 mm2. The GIST stained positive for KIT (CD117) and CD34.

She tolerated the procedure and did well in the immediate post-operative period, apart from a grade A pancreatic fistula. The patient was then seen by oncology and was started on Gemcitabine and Capecitabine. Unfortunately, she developed metastatic disease at 8 months post operatively and was placed on hospice.

Final/working diagnosis: We present a rare case of an adenoneuroendocrine pancreatic collision tumor with incidental GIST in a patient with NF-1. The exact pathologic mechanism of collision tumors is unknown, but there are four main theories in the literature. One is neoplastic heterogenicity, where two different neoplastic cells occur in the same area by chance. Second is cancerization theory, in which areas that have recurrent damage or high rate of turnover will have increased chance of developing separate neoplasms. Third is the interaction theory, which suggests that one neoplasm produces changes that induce an environment conducive to a second independent neoplasm. Fourth is that there is neoplastic heterogenicity during the formation of a neoplastic cell that results in dedifferentiation.

Imaging may reveal two separate components, heterogeneity, or abnormal accumulation in fluorodeoxyglucose-positron emission tomography (PET), but alone may not be sufficient to diagnose these tumors. Biopsies also cannot sample the entirety of the tumor. Thus, it is crucial to keep this differential in mind. Their presence significantly alters the biology of the tumor, and treatment is dependent on proper diagnosis. In the literature, collision tumors are most commonly found in the crania, lung, gastrosophageal junction, liver, rectum, bladder, and uterus, with the vast majority (96.2%) of tumors consisting of only two distinct components. MANECs are very rare, with only 0.23 cases per 1,000,000 individuals reported in 2000, and 1.16 cases per 1,000,000 individuals reported in 2016.

Furthermore, collision tumors are not easy to morphologically distinguish from composite tumors, in which two types of tumors are in close proximity with actual histologic merging of the different tumor cells. In more recent studies, immunohistochemistry has been a method utilized to help distinguish between the two tumors, but the diagnosis is usually not obtained until after surgical resection. Some studies recommend treating the more aggressive element, and thus the chemotherapeutic and radiation regimens are typically followed for PDAC in a collision tumor consisting of PDAC and a less aggressive tumor.

However, due to a small number of reported cases, clinical behavior or MANECs of the pancreas is still unclear and a standardized treatment protocol has not been established.

Management/Outcome/and or follow up: We report a rare case of a pancreatic collision tumor consisting of both pancreatic adenoneuroendocrine carcinoma and incidental GIST. Collision tumors and specifically MANECs of the pancreas are extremely rare and clinical behavior is unclear, and thus no standardized treatment exists. It is important to keep this differential in mind as preoperative diagnostics do not reliably identify these tumors, and treatment as well as prognosis may vary dependent on the tumor characteristics.
Learning Objectives:
- Differentiate between composite and collision tumors
- Discuss the four different theories for pathologic mechanism of collision tumors
- Diagnose, treat, and evaluate for collision tumors within their differential diagnoses