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## Gastrointestinal

# Pancreatocolonic fistulization secondary to pancreatic adenocarcinoma presenting as unexplained halitosis

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## ABSTRACT

Pancreatic cancer is often detected in late stages, which contributes to its grim prognosis. Although the manifestations of pancreatic cancer most often include nonspecific gastrointestinal complaints, we report a case with the sole initial complaint of halitosis and subsequent diagnostic workup demonstrating a pancreatic mass with secondary pancreatocolonic fistulization. The etiologies of and the radiological findings pertaining to halitosis, the presenting symptoms and imaging studies relevant to the diagnosis of pancreatic cancer, and the imaging and clinical findings of pancreatic fistulization are discussed.

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## Case report

A 77-year-old man with a medical history of long-standing insulin-dependent diabetes mellitus presented to a gastroenterology clinic at the urging of his wife because of her perception that the patient had developed severe, feculent halitosis. This odor had not improved with oral hygiene and dental consultation had not been helpful. The patient noted slight unintentional weight loss over the past 3 months but was otherwise asymptomatic. The patient had a prior episode of reportedly idiopathic acute pancreatitis 7 years previously.

Laboratory testing demonstrated normal liver function test results. Amylase and lipase levels were both within normal limits. Fluoroscopic barium esophagography to investigate the possibility of a Zenker diverticulum demonstrated no luminal irregularities or dysmotility. Because of this history of unexplained pancreatitis and weight loss, computed axial tomography of the chest, abdomen, and pelvis was obtained, revealing an irregular, up to 8-cm pancreatic tail mass abutting the stomach and the transverse colon (Fig. 1).

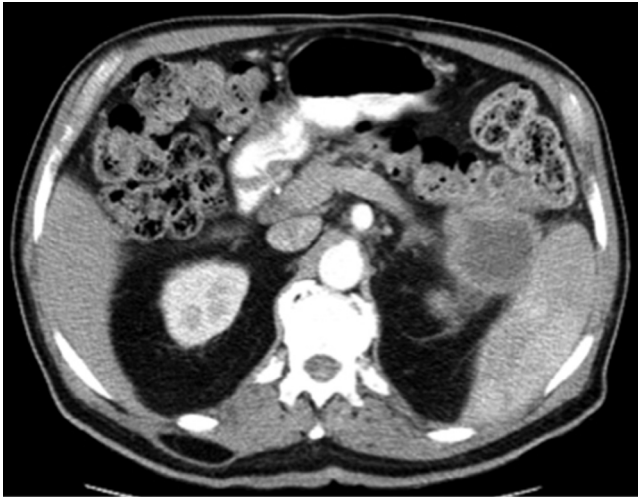
Endoscopic ultrasonography (EUS) revealed an irregular, hypochoic mass with poorly defined borders and evidence of invasion into the small bowel, and fine needle aspiration of the

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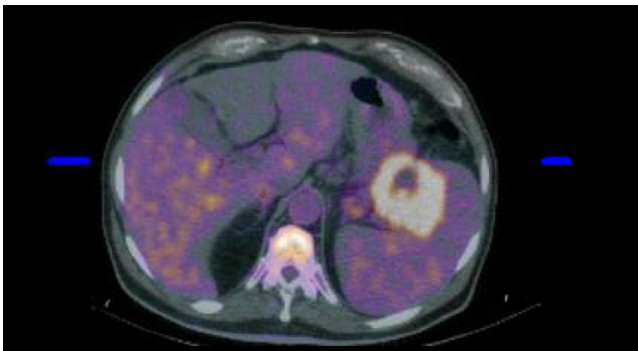
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**Fig. 1 – Axial and sagittal projections of the patient’s contrast-enhanced computed tomography of the abdomen demonstrate an approximately 7 × 8 × 7 cm mass with central hypodensity arising from the tail of the pancreas. Fat planes between the mass and the stomach, the transverse colon, the spleen, and the left kidney are completely effaced. There is thickening of the walls of the stomach and the transverse colon immediately adjacent to the pancreatic mass.**

pancreatic mass demonstrated adenocarcinoma. Fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT) was ordered for further characterization of the mass, initial staging, and to serve as a baseline to assess for response to treatment. 18F-FDG PET/CT demonstrated a large, peripherally hypermetabolic and centrally necrotic heterogeneous mass in the left upper abdominal quadrant centered in the tail of the pancreas and inseparable from multiple surrounding structures (Fig. 2). PET/CT did not demonstrate evidence of distant metastatic disease or occult lesions in the



**Fig. 2 – Axial fused Fluorine-18 fluorodeoxyglucose positron emission tomography computed tomography of the abdomen show intense peripheral hypermetabolic activity associated with the pancreatic mass, which is inseparable from the spleen and the proximal greater curvature of the stomach. The mass demonstrates central photopenia likely consistent with tumor necrosis.**



**Fig. 3 – Coronal computed tomography of the abdomen demonstrates a large, ill-defined hypodense mass centered in the region of the pancreatic tail with invasion into the wall of the greater curvature of the stomach, the spleen, and the left kidney. The boxed “A” indicates that this is anterior view from a multiplanar reformat.**

liver or distant sites. The lack of distant metastases was one of the justifications for taking the patient to surgery.

After evaluation by medical and surgical oncology, the patient began chemotherapy with gemcitabine and abraxane, with subsequent tumor progression. The chemotherapy regimen was switched to a combination therapy utilizing fluorouracil, irinotecan, oxaliplatin, and folinic acid. After 6 cycles of FOLFIRINOX, CT demonstrated a decrease in size of the primary tumor and no new areas of disease.

Preoperative imaging after 6 months of neoadjuvant chemotherapy demonstrated an increase in the size of the mass with invasion of the posterior wall of the stomach, the colonic splenic flexure, the anterior aspect of the spleen, and the superior pole of the left kidney (Fig. 3). Additionally, there was a suggestion of fistulization with the transverse colon as evidenced by air within the mass (Fig. 4). The patient underwent exploratory laparotomy, partial gastrectomy, partial colectomy, partial omentectomy, distal pancreatectomy, splenectomy, left nephrectomy, and duodenal resection, with T3N1 disease staging. The presence of a pancreaticocolonic fistula was confirmed during surgery. Two months postoperatively, the patient remains with good performance status. Halitosis resolved in the immediate postoperative period without recurrence.

## Discussion

Pancreatic cancer is a diagnosis with grim 1 and 5-year survival rates [1]. It is generally believed that the poor prognosis



**Fig. 4 – CT of the abdomen performed 6 months after the initial scan demonstrates significant interval growth of the patient’s centrally necrotic pancreatic tail mass to approximately 8 × 10 × 8 cm. There is fistulization with the transverse colon as evidenced by air within the mass; additionally, there is worsened invasion of the spleen and left kidney.**

in most cases of pancreatic cancer is attributable, in part, to the advanced stage at which most such tumors are detected. The retroperitoneal location of the pancreas allows many pancreatic cancers, especially those outside the head of the pancreas, opportunity for extensive growth and spread before symptoms develop. These symptoms, when present, are often nonspecific gastrointestinal complaints that patients and clinicians can easily ascribe to more common, benign etiologies. In this case, intractable halitosis was the sole complaint motivating this patient to seek care.

There is controversy as to whether disease of the gastrointestinal tract can contribute to halitosis, as the gastroesophageal junction is usually closed [2]. Zenker diverticulum, a well known but rare cause of halitosis (due to bacterial digestion of retained food) is usually diagnosed by barium swallow or videofluoroscopy [3]. Achalasia and hiatal hernias can also contribute to halitosis, similarly caused by food retention, and can be diagnosed by barium swallow or other modalities [4]. Maldigestion and fermentation from small intestinal bacterial overgrowth or from exocrine pancreatic insufficiency may additionally contribute to halitosis [5]. In this patient, results of the evaluation for all of these causes of extraoral halitosis were negative.

Pancreatic cancer is the fourth leading cause of malignancy-related death, among men and women, in the United States. As 85% of these cancers are of exocrine cellular origin, we will restrict our discussion to these cases. The vast majority of patients diagnosed with pancreatic cancer will die from this disease [1]. The only curative modality for pancreatic cancer is surgery, but only 15%-20% of patients are candidates for

resection at the time of diagnosis. Even after optimal resection, the 5-year survival rate is only 30% for patients with negative nodes [6].

Although the classical presentation of pancreatic head cancer with obstructive jaundice is well known, the symptoms of pancreatic cancer are often vague and subtle. These include pain, typically of a gnawing quality that is felt in the back, anorexia, early satiety, and weight loss. Up to a quarter of patients with pancreatic cancer have no pain at diagnosis, and the presence of pain is associated with disease that is already unresectable. The onset of diabetes mellitus at an advanced age is a distinct sign of possible pancreatic malignancy that is often overlooked [7].

Multiple imaging modalities are useful in the diagnosis of pancreatic adenocarcinoma (PDAC). A recent meta-analysis found that differences in sensitivity, specificity, and diagnostic accuracy between magnetic resonance imaging (MRI), CT, transabdominal ultrasound, and EUS failed to reach statistical significance [8]. Although the sensitivity of transabdominal ultrasound varies throughout the literature, it is still often used as an initial test because of its wide availability and relatively low cost; this is balanced by limitations caused by the technical demands and operator variability inherent to the procedure [8-11]. CT is the most commonly utilized modality for the evaluation of PDAC; its sensitivity ranges from 89% to 97% for tumors larger than 1.5 cm [12]. Studies have failed to demonstrate differences in the effectiveness of MRI vs CT in the detection of PDAC, although MRI has been suggested to be more useful in small tumors [11]. EUS has been found to have an excellent sensitivity for pancreatic cancer, with a negative predictive value approaching 100%. The use of EUS has a key role in cases in which there is strong clinical suspicion, but other modalities have failed to show a lesion [11].

Gastrointestinal fistulization is a known complication of acute pancreatitis, which has been reported to occur in up to 5.7% of patients. Kochhar et al. cited the colon and duodenum as the most common locations for fistulization, together accounting for 80% of cases of pancreatic fistulization. Of those with fistulization, only 45% had a history of surgical or percutaneous interventions; thus, 55% were considered spontaneous [13]. In contrast, fistulization resulting from pancreatic masses is rare with only 1 report, in a case of intraductal papillary mucinous neoplasm, encountered on extensive review of the literature [14]. Colonic wall thickening is the hallmark of colonic involvement in acute pancreatitis and may radiographically predict a worse prognosis. Rectally administered, water-soluble contrast enemas may be useful in diagnosing pancreatocolonic fistulae [15].

Halitosis as the sole presenting sign of pancreatic cancer, as in our patient, appears to be quite rare, with only 1 other report found in the literature [16]. Although a meta-analysis by Silva et al. revealed the prevalence of halitosis to be perhaps as high as 31.8% [17], the vast majority (80%-90%) of cases are caused by oral factors confined to the tongue, teeth, and gums [18]. Extraoral causes of halitosis are rare, although the odor may be similar to oral halitosis because of common volatile sulfur compounds produced by certain bacteria [19]. There are many extraoral causes of halitosis; including multiple respiratory and pharyngeal abnormalities, for which imaging studies including CT and chest x-ray may be helpful in the



diagnosis, including chronic sinusitis and nasal obstruction [20], pneumonia or pulmonary abscess, bronchiectasis, or tonsilloliths [21].

For our patient, development of halitosis preceded direct radiological evidence of a fistula, that is, air within the pancreatic mass or identification of a fistula tract. However, there were secondary signs of fistulization with stomach and colonic wall thickening on the patient's initial imaging studies. Pathophysiologically, we propose that microscopic evidence of fistulization or bacterial translocation through a permeable, likely necrotic bowel wall may explain the clinical evidence of halitosis while preceding overt evidence of fistula formation radiographically. It is notable that the patient's halitosis resolved in the immediate postoperative period with obliteration of the fistulous connection between the upper gastrointestinal tract and the large bowel.

In conclusion, we present a rare case of pancreatic cancer with an initial presentation of severe feculent halitosis. This striking juxtaposition of the common and almost always benign complaint of halitosis with the dire diagnosis of pancreatic malignancy has been reported only once before [16]. Although quite uncommon, in combination with other warning signs such as unintentional weight loss and a history of unexplained pancreatitis, the presence of pancreatointestinal fistulization caused by malignancy should be added to the differential diagnosis. Increased awareness of this uncommon presentation may occasionally result in early detection and improved outcomes for some cases of PDAC.

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