

## CASE REPORT

# Metastatic Signet-Ring Cell Carcinoma Presenting as Acute Pancreatitis

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### ABSTRACT

**Introduction** Signet-ring cell carcinoma can arise from virtually all organs. Most signet-ring cell carcinoma arise from stomach (90%), while occurrence elsewhere within the gastrointestinal accounts for less than 1% of gastrointestinal malignancies. Signet-ring cell carcinoma may present with significant phenotypic variability, including cutaneous metastases<sup>7</sup>, though primary symptoms involving the pancreas are rare. **Case report** A Forty-eight-year-old male with no past medical history presented to the emergency department with abdominal pain, nausea, and vomiting. Laboratory data revealed normal electrolytes and liver function tests but a lipase of 525 units/liter. Computed tomography scan demonstrated soft-tissue stranding surrounding the pancreas with extensive mesenteric lymphadenopathy. He denied alcohol intake and additional data, including, IgG4, triglycerides and abdominal ultrasound were unrevealing. He was treated for acute pancreatitis. Following discharge he re-presented to the emergency department one week later with abdominal pain and jaundice. His liver function test were concerning for an obstructive process with alkaline phosphatase of 300IU/L, total bilirubin of 11.7 mg/dL, direct bilirubin of 7.5 mg/dL without transaminitis. Endoscopic retrograde cholangio pancreatography and endoscopic ultrasound demonstrated a heterogeneous mass at the pancreatic head. Fine needle aspiration of the mass and nodes revealed pathology consistent with signet-ring cell carcinoma with BRAF, KRAS, and TP53 mutations. Immunophenotype staining was pankeratin, keratin20, and CDX2 positive and cytokeratin7 negative, most consistent with a lower gastrointestinal primary. An esophagogastroduodenoscopy with random gastric biopsies was negative. **Discussion** We present a rare case of signet-ring cell carcinoma presenting as acute pancreatitis. Our case had an esophagogastroduodenoscopy with negative biopsies along with imaging that was unremarkable for any gastric primary. While there are few case reports that have had pancreatitis associated with signet-ring cell carcinoma, nearly all reported cases were from Ampulla of Vater metastasis which was not observed in our case. In conclusion we hope that by presenting our case we can broaden our knowledge of clinical scenarios of signet-ring cell carcinoma to hasten diagnosis and, subsequently, treatment.

### INTRODUCTION

Signet-ring cell carcinoma (SRCC), an uncommon subtype of adenocarcinoma, can arise from virtually all organs. The classical signet ring appearance is related to the production of sufficient intracytoplasmic mucin to compress the nucleus against the periphery of the cell wall [1]. Most SRCC arise from stomach (90% of all signet ring carcinoma) and accounts for approximately 25% of all gastric cancer. Occurrence elsewhere within the gastrointestinal tract is far less common, and accounts for less than 1% of all other gastrointestinal malignancies [2]. While the majority of SRCC are gastric in origin, usually signs of metastasis are evident at the time of presentation. Intra-abdominal metastases tend to

involve the serosal surface, retroperitoneum, gastric mucosa, and ovaries [3, 4]. Gastric SRCC preferentially involves lymph nodes and peritoneal surfaces [5]. Colonic SRCC is typified by diffuse intramural infiltration, with lymph node involvement and peritoneal surface metastasis. While it is usually possible to determine the primary origin, extensive examination fails to demonstrate the primary site in approximately 3-5% of oncology cases [6]. Because identification of the primary site of cancer usually dictates the treatment and expected prognosis, the inability to identify a primary site of cancer poses many challenges. Immunohistochemical studies can be useful in suggesting an origin and therefore may guide investigations and management options. We present the case of a previously healthy 48-year old male presenting with acute pancreatitis from metastatic SRCC to the head of the pancreas from unconfirmed primary origin.

### CASE REPORT

A Forty-eight-year old male with no significant past medical history presented to the Emergency Department (ED) with three days of post-prandial abdominal pain, nausea and vomiting. Laboratory data obtained in the ED revealed normal electrolytes and liver function tests. He was however noted to have a lipase of 525 units/liter. A CT scan of the abdomen and pelvis demonstrated diffuse soft tissue stranding surrounding the pancreas

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**Keywords** Carcinoma; Signet Ring Cell; Pancreatitis

**Abbreviations** CT computed tomography; ED emergency department; EGD esophagogastroduodenoscopy; ERCP endoscopic retrograde cholangio pancreatography; EUS endoscopic ultrasound; SRCC signet-ring cell carcinoma

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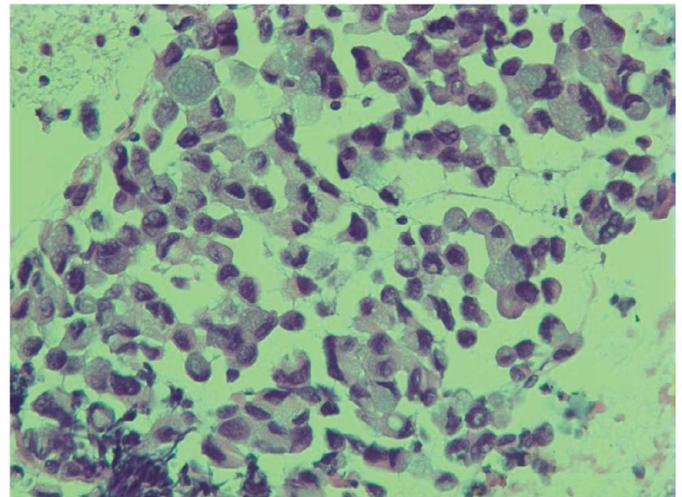
without evidence of gallstones and extensive mesenteric and retroperitoneal lymphadenopathy. He was treated conservatively for pancreatitis and evaluation for potential etiologies was undertaken. He denied any recent or excessive alcohol intake and additional data, including IgG4, triglycerides and an abdominal ultrasound were unrevealing. He responded appropriately to conservative management and was discharged with scheduled follow up in the gastroenterology clinic. He re-presented to the ED one week later with recurrent, post-prandial abdominal pain and jaundice. He was found to have liver function tests concerning for an obstructive process with alkaline phosphatase of 300 IU/L, total bilirubin of 11.7 mg/dL, direct bilirubin of 7.5 mg/dL without transaminitis. The patient subsequently underwent ERCP and EUS, which demonstrated a round, heterogeneous mass at the pancreatic head as well as a congested and edematous major papilla that appeared fibrosed. Fine needle aspiration of the pancreatic mass and lymph nodes revealed pathology consistent with signet-ring cell adenocarcinoma (**Figure 1**) with BRAF, KRAS, and TP53 genetic mutations. Immunophenotype staining was positive for pankeratin, keratin 20 (**Figure 2**), and CDX2 (**Figure 3**), and was negative for cytokeratin 7 (**Figure 4**) most consistent with a lower gastrointestinal primary. Furthermore, tumor markers, including CA-19-9 and CEA were sent and noted to be elevated. He underwent percutaneous transhepatic cholangiography with biliary drainage to facilitate biliary decompression. An EGD with random gastric biopsies was negative, as was a colonoscopy. Following discharge he was transferred to the Oncology service where he completed 6 sessions of FOLFOX treatment for Stage IV signet-ring cell adenocarcinoma over the next 6 weeks. Unfortunately, repeat imaging at that time demonstrated further metastasis to the lungs bilaterally and L2-L4 vertebral bodies.

## DISCUSSION

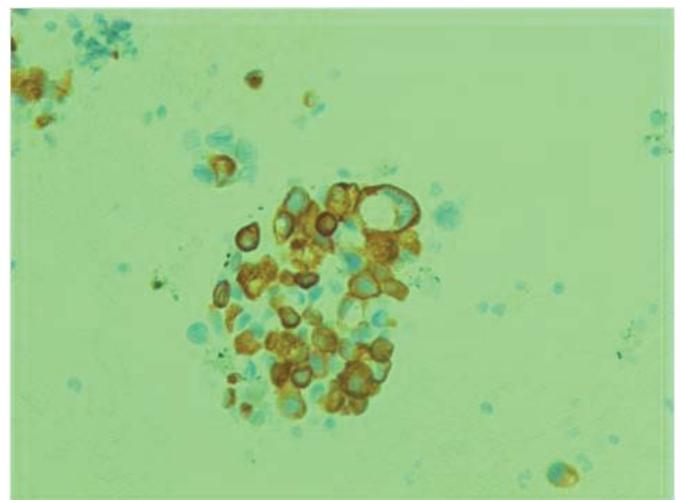
Signet-ring cell carcinoma (SRCC) is an uncommon variant of adenocarcinoma, in which intracytoplasmic deposits of mucin accumulate that force the nucleus against the periphery to give its characteristic appearance. While more than 90% of all SRCC originate within the stomach, a small subset is also found within the colon, ovaries, and pancreas. Gastrointestinal signet-ring cell carcinoma has been known to present with significant phenotypic variability, including cutaneous metastases [7], though primary symptoms involving the pancreas are rare. While the vast majority of patients presenting with acute pancreatitis can be attributed to cholelithiasis and chronic alcohol abuse, in the setting of concurrent, pathologic intra-abdominal lymphadenopathy, malignant etiologies must be aggressively explored.

## CONCLUSION

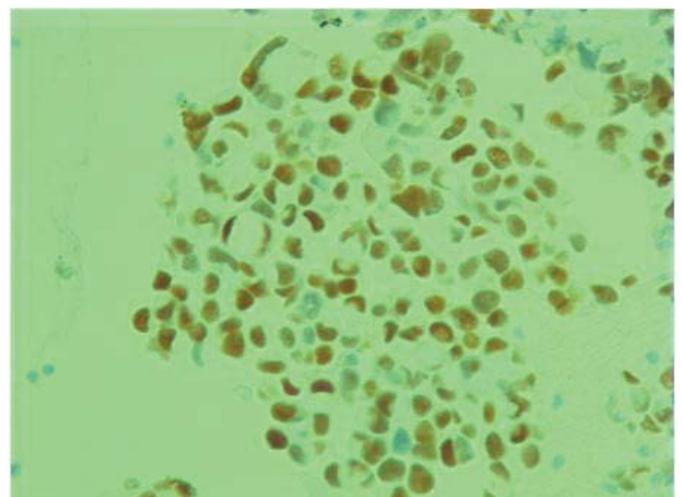
We present a rare case of signet-ring cell carcinoma (SNCC) of unknown primary origin presenting initially as acute pancreatitis. Based on the literature, the majority of patients presenting with metastatic SRCC have a primary tumor of gastric origin (>90%). Our case had an



**Figure 1.** Signet-ring cell adenocarcinoma.

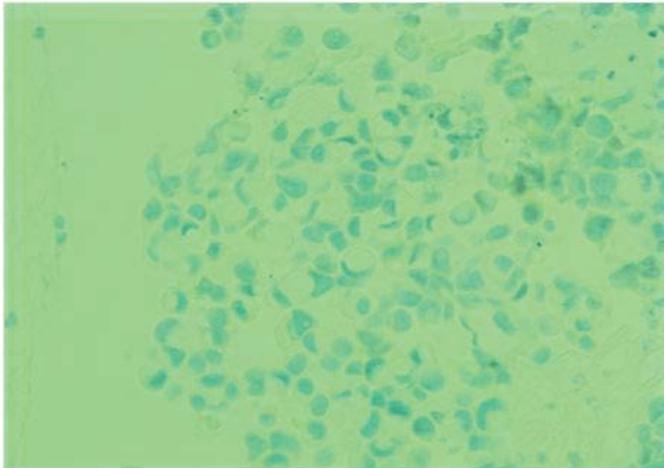


**Figure 2.** Immunophenotype staining was positive for pankeratin, keratin 20.



**Figure 3.** CDX2.

EGD with negative biopsies along with imaging that was unremarkable for any gastric primary. While there are few case reports that have had pancreatitis associated with SRCC, nearly all reported cases have been from Ampulla of Vater metastasis which was not observed in our case. In conclusion we hope that by presenting our case of SRCC presenting initially as pancreatitis we can broaden our breadth of knowledge of clinical scenarios of SRCC to hasten diagnosis and, subsequently, treatment.



**Figure 4.** Cytokeratin 7.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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