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RAPID METASTATIC GROWTH OF A PANCREATIC SIGNET RING CELL CARCINOMA WITHIN 6 WEEKS OF A NEGATIVE CT

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ABSTRACT

Pancreatic signet ring cell carcinoma (PSRCC) is a rare and aggressive subtype of pancreatic cancer with a dismal prognosis. We present the case of a 50-year-old male who, within six weeks, developed a pancreatic mass with liver metastases. Endoscopic ultrasound-guided biopsy confirmed PSRCC. The presentation of this tumour with distant metastasis after a negative computed tomography (CT) of the abdomen and pelvis six weeks prior underscores the highly aggressive nature of PSRCC and the crucial need for heightened clinical suspicion, especially in cases with persistent or atypical abdominal pain. This case highlights the limitations of current diagnostic modalities and emphasises the urgent need for further research into improved early detection methods, molecular characterisation and effective treatment strategies for this rare and lethal subtype of pancreatic cancer.

KEYWORDS

Pancreatic cancer, signet ring cell-like, metastatic disease

LEARNING POINTS

- Aggressive malignancy can become metastatic within six weeks of a negative CT scan.
- A CT scan may not detect a small pancreatic lesion <2 cm.

INTRODUCTION/BACKGROUND

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies worldwide, with a five-year survival rate of approximately 12%, despite advancements in early detection and systematic treatment[1]. It represents the fourth leading cause of cancer-related deaths in the United States and is projected to become the second by 2030[2]. Nine histopathologic variants have been identified, with pancreatic adenocarcinoma representing 85.8% of cases[3]. The majority of PDAC cases exhibit typical gland-forming histology although rare variants such as signet ring cell carcinoma (SRCC) have been identified and are

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associated with an even more aggressive clinical course[4].

SRCC is a mucin-producing neoplasm defined by the presence of malignant cells with prominent intracytoplasmic mucin that compresses the nucleus to the periphery, yielding the characteristic 'signet ring' morphology. While SRCC most commonly arises in the stomach, isolated cases have been documented in the colon, breast, bladder and pancreas[5]. Pancreatic signet ring cell carcinoma (PSRCC) is extremely rare, comprising less than 1% of pancreatic cancers. Recent studies indicate that PSRCC patients often present with advanced disease and have a median survival of 3–6 months[4,6]. Most available data derive from case reports and limited retrospective series. In a population-based study using the SEER database, Nie et al. (2023) reported that PSRCC is associated with a significantly worse prognosis than conventional PDAC, often presenting at a higher stage with a poorer histological grade, more frequent lymph nodes and distant metastases[5].

We present a case of a 50-year-old male diagnosed with metastatic signet ring cell-like pancreatic adenocarcinoma after six weeks of a negative computed tomography (CT) of the abdomen and pelvis. This case underscores the importance for heightened awareness and developing diagnostic interventions that help in early recognition of this highly aggressive type of pancreatic adenocarcinoma. Given the lack of definitive treatment protocols, further investigation into effective treatment approaches, the pathogenesis, molecular characteristics and optimal management strategies for this rare subtype is warranted.

CASE DESCRIPTION

A 50-year-old male with a past medical history of hypertension, hyperlipidaemia and gastroesophageal reflux disease (GERD) presented to the emergency department (ED) with a three-day history of left and right lower quadrant abdominal pain. Associated symptoms included one episode of non-bloody vomiting, intermittent nausea, chills and decreased oral intake. He denied diarrhoea, melaena, haematochezia, sick contacts or recent travel. The abdominal pain was constant without any alleviating or exacerbating factors. The patient's social history was significant for prior tobacco and social alcohol use. His family history included colon cancer in his father; however, the patient had not yet undergone colorectal cancer screening.

On examination, he was febrile (39.1°C F rectal) and tachycardic (heart rate 120 bpm), consistent with sepsis. Laboratory findings revealed leucocytosis (white blood cell count 12,000/µl), elevated bilirubin (1.3 mg/dl) and lactate of 1.7 mmol/l. Urinalysis was negative. A CT of the abdomen and pelvis with intravenous contrast demonstrated sigmoid colitis without evidence of a drainable fluid collection or pneumoperitoneum, and CT was negative for any pancreatic or liver lesions *(Fig. 1)*. He was discharged on a course of ciprofloxacin with planned outpatient gastroenterology follow-up. Given the colitis picture noted on the initial CT abdomen and pelvis, an outpatient diagnostic colonoscopy was performed and was negative for colonic malignancy.

Six weeks later, the patient returned to the ED with persistent, nagging abdominal pain, but this time it was in the epigastric region and radiating to his back for the preceding two weeks. This pain was described as different from his initial presentation, with a severity of 6/10. He denied any association with meals, nausea or vomiting, and reported normal food intake. Vital signs and physical examination were unremarkable. Laboratory studies showed a normal white blood cell count and a mildly elevated lipase (137 U/l) with otherwise normal liver function tests. Abdominal ultrasound was performed and was unremarkable, with a normal common bile duct diameter (4 mm). A repeat CT scan of the abdomen revealed acute pancreatitis with an ill-defined hypoattenuating focus in the body of the pancreas, suggestive of necrosis. Of concern, the CT also showed a possible soft tissue component adjacent to the splenic artery and celiac axis, raising suspicion for a tumour. Furthermore, numerous new bilobar hypoattenuating hepatic lesions, measuring up to 1.3 cm, were identified compared to the prior CT scan *(Fig. 2 and 3)*.

An endoscopic ultrasound was performed and revealed a 24 × 22 mm ill-defined, subtle, irregular, heterogenous and predominantly hypoechoic mass at the junction between the body and the tail of pancreas *(Fig. 4)*. In addition, two other well circumscribed hypoechoic lesions were noted in the left lobe of the liver, suggestive of metastasis. EUS-guided fine needle biopsies were performed from the pancreatic mass and one of the liver lesions, using two different 22-gauge needles. Magnetic resonance imaging of the abdomen confirmed multiple small rim-enhancing hepatic lesions



Figure 1. Initial CT showing normal pancreatic body and tail junction.

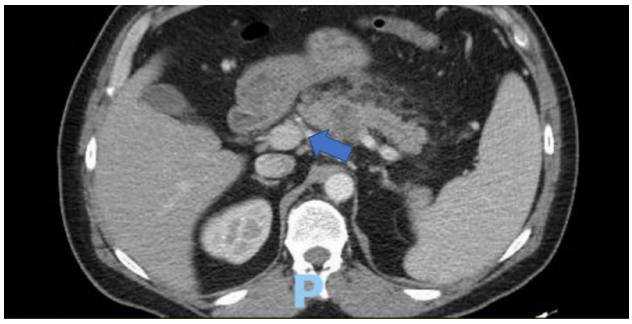


Figure 2. Repeat CT 6 weeks later showing pancreatic mass at the body and tail junction.

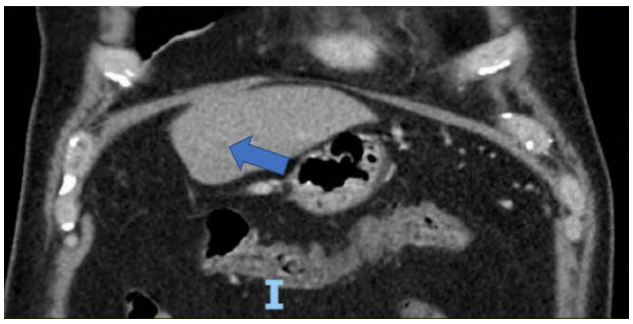


Figure 3. Repeat CT 6 weeks later showing liver metastasis.



Figure 4. Pancreatic mass at the body and tail junction.

measuring up to 1.5 cm, suspicious for metastatic disease. The previously identified hypoattenuating focus on CT now appeared as a 3 × 1.8 cm cystic mass-like process, potentially representing a cystic pancreatic neoplasm or an area of pancreatic necrosis. Soft tissue nodularity around the celiac artery, measuring 3 × 1.8 cm, was suspicious for tumour involvement. Attenuation at the portal splenic confluence and splenomegaly were also observed.

Pathology results from the EUS-guided biopsies confirmed the diagnosis of infiltrating adenocarcinoma of the pancreatic tail with focal signet ring cell-like features. The patient was subsequently referred to medical and surgical oncology for further management.

DISCUSSION

Our report describes a 50-year-old white male who initially presented with abdominal pain. An initial CT showed no evidence of intra-abdominal malignancy. However, the patient was readmitted six weeks later due to persistent epigastric pain, and a repeat CT revealed findings suggestive of a pancreatic mass with hepatic metastasis. An endoscopic ultrasound-guided fine needle biopsy confirmed the diagnosis of metastatic pancreatic signet ring cell adenocarcinoma. As the CT with contrast did not detect malignancy or metastasis on the initial presentation, this case emphasises both the aggressive nature of pancreatic signet ring cell adenocarcinoma and the diagnostic limitations of CT imaging in detecting early-stage pancreatic cancer.

Although our patient was relatively young and of white ethnicity, PSRCC predominantly affects elderly, male and Black patients, with the incidence peaking at around 80 years of age, making this case even more unique[7]. The median survival time for patients with PSRCC is approximately 12.6 months, with 1-, 2- and 5-year survival rates being 20.1, 8.3 and 3.4%, respectively[4,5]. The rapid progression is attributed to the tumour's aggressive nature, high metastatic potential and the frequent presence of advanced disease at diagnosis[4].

Recent studies have shown that pancreatic cancer cells can disseminate early in the disease process, even before the primary tumour is fully developed. This phenomenon is supported by evidence of circulating tumour cells in patients with localised pancreatic cancer and the presence of metastatic cells in distant organs before the primary tumour is clinically detectable[8]. Factors such as early stage at diagnosis, surgical intervention and chemotherapy have been shown to improve survival outcomes[5,6].

Multi-detector computed tomography is currently one of the most useful tools in pancreatic adenocarcinoma imaging[9]. Overall, the sensitivity of contrast-enhanced CT for detecting pancreatic ductal adenocarcinoma (PDAC) is approximately 83.9%[10]. The American Gastroenterological Association highlights that CT is less sensitive for pancreatic lesions <2 cm, which can be a significant limitation in early-stage disease[11]. Endoscopic ultrasound has a sensitivity ranging between 91 and 100% in detection of PDAC, particularly when lesions are equivocal by or are less than 2 cm in size[11].

Although pancreatic cancer often presents with advanced disease at diagnosis, we believe our report is the first to present this pattern of tumour progression within six weeks. More studies are needed to establish proper screening for pancreatic cancer and to promote early detection with advancements in imaging modalities, especially in patients with unexplained symptoms or in the context of concurrent pancreatitis on imaging.

Given the rarity of this case, our findings may not be generalisable to a broader patient population, thereby making it challenging to determine definitive patterns of behaviour, treatment efficacy or long-term outcomes of PSRCC. Further research is crucial to improve diagnostic accuracy, therapeutic strategies and patient outcomes. Comprehensive molecular and genomic profiling of PSRCC is needed to help identify potential driver mutations or biomarkers, tumour suppressor losses or actionable pathways that may inform scientists of target therapies and prognostic assessment. Insights from gastric signet ring cell carcinoma, a more extensively studied entity, may offer valuable direction. As individual case reports remain the primary sources of clinical data, the establishment of a multi-centre collaboration would greatly enhance our understanding of its epidemiology, treatment responses and clinical behaviour. These collective efforts could ultimately lead to the development of tailored treatment algorithms and inform future clinical trials targeting this rare and aggressive pancreatic cancer subtype.

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