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CASE REPORT

Gallstone pancreatitis masking malignancy: when is additional imaging warranted?

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Summary
Gallstones are common and they are a common cause of acute pancreatitis. Gallstones are themselves also a recognised risk factor for biliary malignancy, along with advancing age and female sex. We report two cases that highlight how presumed gallstone pancreatitis can mask coexisting malignancy. They illustrate that when patients present with gallstone pancreatitis in the presence of additional risk factors or constitutional features such as unintentional weight loss or anaemia, clinicians should maintain a high index of suspicion and pursue further diagnostic work-up to detect and stage any underlying malignancy.
Keywords: pancreatitis, synchronous malignancy, cholecystectomy, distal cholangiocarcinoma, gastric cancer, gallstone related pancreatitis

Case report

Patient one

A 57-year-old woman with hypertension and hypercholesterolaemia presented with a three-day history of epigastric and right upper quadrant pain, nausea, postprandial vomiting and dark urine. She also reported two years of unintentional weight loss with normal bowel habits. Examination revealed diffuse upper abdominal tenderness but no palpable masses and a negative Murphy's sign. There was no scleral icterus or conjunctival pallor present. The respiratory, cardiovascular and neurological exam was all within normal limits. Laboratory tests showed diffusely deranged liver functions with an elevated total bilirubin of 32 µmol/l (5–21) with a conjugated fraction of 25 µmol/l (0–3), ALP 405 U/l (42–98), GGT 461 U/l (< 40), ALT 223 U/l (7–35), AST 89 U/l (13–35). Lipase was markedly elevated at 1319 U/l (13–60) with normal white cell count (4.66 × 10^9/l) and haemoglobin 12.4 g/dl (12.0–15.0).

Ultrasound demonstrated cholelithiasis without biliary dilatation.

A diagnosis of acute gallstone pancreatitis was made, with the weight loss attributed to "food insecurity" and was not investigated further. She underwent laparoscopic cholecystectomy with intraoperative cholangiogram (IOC) which revealed a mid-common bile duct filling defect and a gallbladder fundal mass with local invasion into the adjacent liver. Cholecystectomy and resection of the adjacent liver and regional lymph nodes were performed. Histology confirmed a moderately differentiated biliary-type adenocarcinoma with metastases to regional lymph nodes and adjacent liver (T3N1M0). Postoperative magnetic resonance cholangiopancreatography (MRCP) demonstrated a common bile duct calculus, a segment IVb liver lesion suggestive of metastasis, and coeliac axis and portocaval lymphadenopathy.

During admission, she developed a pulmonary embolism, confirmed on computed tomography pulmonary angiography (CTPA), and was treated with unfractionated heparin followed by enoxaparin. She was referred to the oncology multidisciplinary team and commenced chemotherapy. At six-month follow-up, she remained clinically well with no evidence of local recurrence or metastases on computed tomography (CT) imaging.

Patient two

A 58-year-old woman with a history of gastroesophageal reflux disease and diabetes mellitus presented with a two-day history of worsening epigastric and right upper quadrant pain, diarrhoea, vomiting, and dark urine.

On examination, she was jaundiced with mild epigastric and right upper quadrant tenderness, a negative Murphy's sign, and no palpable masses. She also had mild conjunctival pallor. Laboratory results showed diffusely deranged liver function tests with elevated total bilirubin 85 µmol/l (5–21) with a conjugated fraction of 60 µmol/l (0–3), ALP 203 U/l (42–98), GGT 154 U/l (< 40), ALT 238 U/l (7–35) and AST 129 U/l (13–35). Lipase was markedly elevated at 1200 U/l (13–60). White cell count was mildly elevated at 12.75 × 10^9/L (3.90–12.60), and haemoglobin was 10.5 g/dl (12–15) with a normocytic anaemia. Ultrasound demonstrated cholelithiasis, common bile duct dilatation, and hepatic steatosis, with no intraductal calculi visualised.

A diagnosis of acute gallstone pancreatitis was made, however, in light of the anaemia and biliary dilatation, a contrast-enhanced CT scan was performed which revealed a large fundal gastric mass with local lymphadenopathy and a calculus in the head of the pancreas (Figure 1). Upper gastrointestinal endoscopy confirmed a fundal gastric mass, and histology demonstrated a moderately differentiated

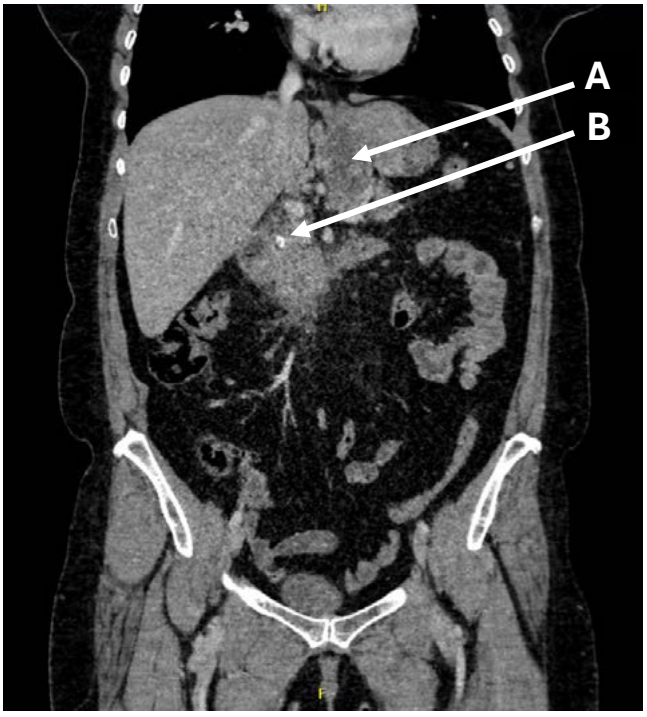

Figure 1: Coronal computed tomography scan of patient 2 demonstrating a gastric fundal mass (A) and a calculus in the common bile duct (B)

gastric adenocarcinoma. The patient declined further intervention and elected to be discharged home to her family.

Discussion

Gallstones and alcohol remain the leading cause of acute pancreatitis (AP) worldwide with gallstones being the most common cause in many adult populations, typically accounting for roughly 35% of cases and occurring more often in older women (30.2% of cases compared to 19.3% of cases in men for all-cause AP).[1] In contrast South African data has historically shown alcohol to predominate, with a regional KwaZulu-Natal cohort study finding that gallstones accounted for only 14% of episodes versus 62% due to alcohol (median age 37 years; male preponderance).[2] However, local epidemiology is shifting with longitudinal work from Pretoria documenting a rise in gallstone-related AP between 1988 and 2007, paralleling an increasing proportion of female and older patients.[3] This shift in epidemiology is further confirmed with national surgical pathology data demonstrating a 92% increase in cholecystectomies for gallstone disease between 2004 and 2014, with a marked female predominance across South Africa.[4] Our two cases of older females fit the typical patient profile for gallstone pancreatitis, and the diagnosis is in keeping with the Atlanta criteria, having elevated lipase levels more than three times the upper limit of normal and typical pain.[5] However, these cases also raise concerns regarding potentially missing concurrent malignancy, especially considering that it is well established that besides advancing age predisposing to gallstones and gallstone pancreatitis, it also increases the risk of malignancy overall.[6] Furthermore, it has been established that the presence of gallstones in itself increases the risk of biliary malignancy.[6] A temporal association where AP can occasionally accompany or precede a cancer diagnosis should be considered. Large cohort data indicate that AP is associated with an elevated short- and medium-term risk of pancreatic cancer, with risk attenuating over time but persisting for years.[7] This supports a cautious stance toward persistent "constitutional" symptoms after an apparent biliary AP, particularly in older adults, prompting re-imaging and directed investigation rather than attributing weight loss or anaemia solely to socioeconomic factors or intercurrent illness.

The practice of careful intraoperative assessment and routine histopathological gallbladder analysis after laparoscopic cholecystectomy, ensures that incidental gallbladder carcinoma (IGBC) will be detected when present.[8] The pooled global incidence of IGBC at cholecystectomy is 0.7%, with a sizeable share ≥ T2 at diagnosis.[8] A South African study measuring IGBC from 2003 to 2015 found the South African incidence to be 0.39% with most tumours also being ≥ T2.[9] Thus, in South Africa the ideal practice would be for all gallbladder specimens to undergo histopathological analysis, although cost constraints may impede this practice.

Careful interrogation of constitutional or otherwise "atypical" symptoms and features in presumed gallstone pancreatitis should lower the threshold for early cross-sectional imaging to look beyond biliary causes. Unintentional weight loss and anaemia, as in our two cases proved herald sinister co-existing pathology. Although biliary and pancreatic malignancies are the most well-described malignancies detected in cases of gallstone pancreatitis,[6-7] our second case illustrates that this principle is true even for non-hepatobiliary malignancies. Risk stratification such as with the NICE NG12 guidelines recommends urgent CT scans in adults ≥ 60 years with weight loss and upper-abdominal pain, jaundice, diarrhoea or back pain to evaluate for pancreatic or other upper GI malignancy.[10] This approach is pragmatic in South Africa where CT is generally available in referral centres.

In summary, both cases illustrate how "typical" gallstone pancreatitis can coexist with, or distract from, occult malignancy. Within South Africa, where biliary disease is rising, and older female patients are at increased risk of both gallstone pancreatitis and malignancy in general, clinicians should maintain a low threshold for cross-sectional imaging when constitutional symptoms such as unintentional weight loss or anaemia are present to reduce the risk of delayed or missed cancer diagnosis.

Conflict of interest

The authors declare no conflict of interest.

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Ethical declaration

The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

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