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CASE REPORT

Infected necrotising pancreatitis with associated emphysematous cholecystitis and pneumobilia

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Abstract

We present a case of infected necrotising pancreatitis with associated emphysematous cholecystitis and pneumobilia. Terminology, pathophysiology and treatment strategies are reviewed based on recent international evidence-based guidelines.

Introduction

During the last years our understanding of pathophysiology and treatment of necrotising pancreatitis and its complications has improved.[1] Terminology has been redefined[2] and several randomised trials have added evidence to the current consensus of treating acute pancreatitis.[3] In general, treatment of necrotising pancreatitis nowadays puts the emphasis on a conservative treatment with minimally invasive intervention.[1,4] We present a rare case of infected necrotising pancreatitis with associated emphysematous cholecystitis and pneumobilia. Pathophysiology and treatment strategies for infected necrotising pancreatitis are reviewed based on recent international evidence-based guidelines.

Case history

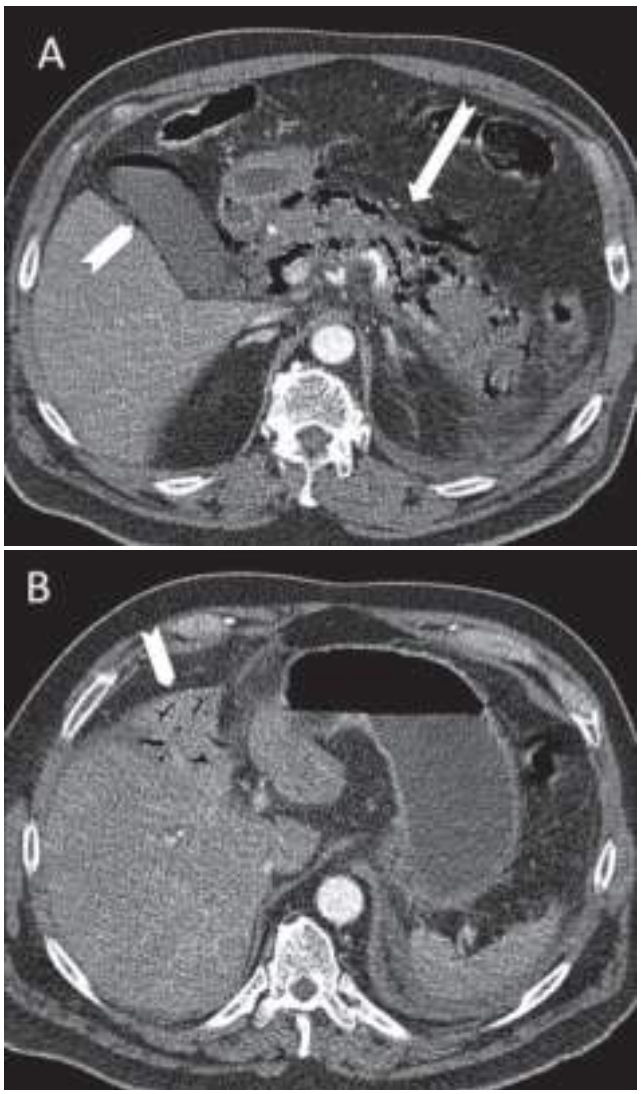
A 63-year-old man with a history of myocardial infarction and no evidence of residual ischaemia on recent exercise testing was admitted in a regional hospital with a one-day history of vomiting and pain in the epigastric region. Vital signs on admission: respiratory rate 38 per minute, blood pressure 60/40 mmHg, increasing to 90/60 after fluid resuscitation, heart rate 160 beats/minute, decreased capillary refill, temperature 38.3 °C. Laboratory testing revealed haemoglobin 12.7 mmol/l, leucocytes 8.6 × 10^9 /l, C-reactive protein 82 mg/l, creatinine 207 µmol/l, glucose 20.6 mmol/l, ASAT 403 U/l, ALAT 328 U/l, γGT 627 U/l, LDH, 705 U/l, total bilirubin 137 µmol/l, CK 384 U/L, CK-MB 4.6 µg/l, troponin T 0.07 µg/l, p-amylase 1197 U/l, lactate 14.4 mmol/l. Blood gases: pH 7.28, pO_2 24 kPa (with oxygen therapy), pCO_2 2.6 kPa, base excess -15.2 mmol/l. Contrast-enhanced computed tomography revealed emphysematous cholecystitis, pneumobilia and infected necrotising pancreatitis with intra-abdominal collections (*figure 1A and B*). Antimicrobial therapy (amoxicillin, clavulanic acid and gentamicin) was prescribed within one hour after presentation and the patient was transferred to the intensive care unit.

The same day, after intubation and initiation of vasopressive support, a mobile intensive care unit transported the patient to an intensive care unit in a tertiary hospital. There, percutaneous cholecystostomy and drainage of fluid in the subhepatic region was performed and according to the local protocol, antimicrobial therapy was modified into cefotaxime, gentamicin and metronidazole. The peripancreatic region was not drained given the fact that no or little drainable fluid was seen. The APACHE IV score was 124, corresponding to a predicted hospital mortality of approximately 70%. Forty hours after the initial presentation to the regional hospital the patient died of severe refractory septic shock and multi-organ failure. Culture of blood samples and cholecystic drain fluid showed *E. coli*, sensitive to both antibiotic regimens. No autopsy was performed.

Discussion

According to the recently updated Atlanta classification of acute pancreatitis,[2] necrotising pancreatitis is defined as inflammation associated with pancreatic parenchymal necrosis or peripancreatic necrosis. Imaging criteria for necrotising pancreatitis are lack of pancreatic parenchymal enhancement by intravenous contrast agent or presence of findings of peripancreatic fat necrosis.[2] In a recent large Dutch multicentre series, mortality of infected necrotising pancreatitis was 20%.[4]

Figure 1. (A) emphysematous cholecystitis (arrowhead) and infected necrotising pancreatitis (arrow) (B) hepatic pneumobilia (arrowhead)



Gas bubbles or gas-fluid level in a peripancreatic collection in necrotising pancreatitis is considered pathognomonic of infected necrotising pancreatitis.[2,4] The source of gas is presumably gas-forming bacteria, but even if the gas were to be introduced by a pancreatic enteric fistula, infection would still be very likely.[1,5,6] Infected necrotising pancreatitis is considered probable when symptoms of sepsis or organ failure arise, typically 3-4 weeks after the onset of necrotising pancreatitis.[1,7] A positive culture or Gram stain of pancreatic or peripancreatic tissue or fluid confirms the presence of infected necrotising pancreatitis but false negatives have been described.[1,2] However, in a strategy of postponed intervention, fine needle aspiration is no longer considered mandatory because a positive culture does not automatically imply minimally invasive or surgical intervention. Currently, initial antibiotic treatment is the treatment of choice in all patients.[1,3,4,8-12] The timing of bacterial cultures is therefore postponed to either during invasive intervention, which is indicated when symptoms of sepsis persist for several weeks, or to the moment when combination antibiotic therapy appears ineffective.[1] When intervention is indicated because of infected necrosis, early open surgery should be avoided because of its association with high mortality.[4] Minimally invasive catheter drainage, either percutaneous or endoscopic transluminal, is the treatment of choice.[13-15] If patients do not recover with percutaneous drainage, additional necrosectomy is indicated; the preferred techniques are video-assisted retroperitoneal debridement or endoscopic transluminal necrosectomy.[13,14] Necrosectomy is preferably performed when the stage of 'walled-off necrosis' has been reached, a process which usually takes about four weeks.[16] At this stage, the risk of bleeding and iatrogenic damage is less.[4]

Emphysematous cholecystitis (EC) has mainly been described in case series[17] and pooled case series.[18,19] The largest series is a retrospective study comparing 164 cases of EC with 4303 cases of acute cholecystitis.[19] The results of this paper suggest that EC is not just an indicator of severity of acute cholecystitis: first, EC affected more men (71%) as opposed to acute cholecystitis (27%).[19] Second, the appearance of acalculous cholecystitis was three times higher in EC, 28 vs. 10%.[19] Third, the occurrence of gangrene and perforation was 30- and 5-fold higher in EC, respectively,[19] which probably accounts for another difference: the overall mortality of EC reached 15% compared with 4% in the acute cholecystitis group.[19] Of the patients with EC, 38% suffered from diabetes,[19] while no data on the occurrence of diabetes in the acute cholecystitis group were available. The proposed theory, which is strengthened by several case reports, is that vascular compromise within the gall bladder wall is a predisposing factor of EC in a way that, in a state of additional hypoperfusion, growth of gas-forming bacteria is facilitated.[19-22] A microbiological study reported that 95 out of 109 bacterial cultures of gall bladder fluid in EC cases were positive, revealing *Clostridium* species in 46% and *E. coli* in 33%.[19] Another case series of bile cultures of 20 patients with EC showed *E. coli* (40%), *Bacteroides* (30%), *Clostridium* (25%) and *P. vulgaris, A. aerogenes, Klebsiella, Streptococcus, Staphylococcus* and *Enterococcus* (40%).[17] Despite the correlation with increased mortality, gangrene and perforation of the gallbladder, patients with EC may present with low-grade fever or even be afebrile, and severe localised abdominal tenderness may not be present.[19] The treatment of choice for EC is surgery; however, when deemed contraindicated, for example during severe sepsis, percutaneous gallbladder drainage may be a temporary alternative.[17,23-25]

To our knowledge, the simultaneous occurrence of EC and infected necrotising pancreatitis has been scarcely described.[24,26,27] Reconstructing the pathophysiological

sequellae in this particular case is speculative, but it seems rational to think of EC and pneumobilia secondary to infected necrotising pancreatitis. The pancreatitis in this case represents the extremes of the spectrum of disease given the rapid onset of infection with large amounts of gas and necrosis. No obvious cause of the pancreatitis could be identified. The present cholestasis may have been induced by biliary obstruction in the pancreatic head due to inflammation. This might have caused cholestasis and subsequent ascending infection into the bile tract and gallbladder, causing cholecystitis and pneumobilia. Pneumatosis of the gall bladder may be the result of presence of gas-forming bacteria, facilitated by the low perfusion state and vascular disease of which the patient's history of myocardial infarction is proof.

In this particular case, minimal invasive intervention was considered necessary because of the severe sepsis and rapid progression into septic shock under antimicrobial therapy. When multi-organ failure in the context of necrotising pancreatitis occurs in the first week after admission, mortality is reported to be 47%.[4] For that, and because of the high APACHE score and high lactate level on admission,[28] the unfavourable outcome in this case was not unexpected.

Finally, where should a patient with severe pancreatitis be treated? There is expert agreement on referral to a specialist centre in case of 'patients with severe acute pancreatitis and for those who may need interventional radiological, endoscopic, or surgical intervention'.[3] However the available evidence supporting the agreement is a matter of debate.[29,30] In this case the reason for referral was local expertise.

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