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Arterio-Pancreatic Syndrome

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Key Words
Acute limb ischemia · Acute pancreatitis · Arterio-pancreatic syndrome

Abstract
Acute pancreatitis is a single-organ disorder that has multi-organ sequelae. As a result, it can have varied presentations. Acute pancreatitis presenting as acute limb ischemia is rare. We present a patient with acute pancreatitis presenting with bilateral lower limb ischemia. The episode of acute pancreatitis resolved but the acute lower limb ischemia precipitated as the pancreatitis progressed, and necessitated bilateral above-knee amputations. We review the literature and discuss the pathogenesis of such a phenomenon.

Case Report

The patient was an 82-year-old man with a past medical history of tuberculosis of the spine, treated 50 years earlier. He had an episode of acute gallstone pancreatitis in 2004 that was treated conservatively, and subsequently refused surgical intervention for his gallstone disease. He had no other significant medical history and did not consume alcohol or smoke. He presented with an acute onset of severe bilateral lower limb pain associated with paresthesia for one day's duration. He also complained of mild epigastric pain, abdominal distension and nausea for two days prior to the onset of lower limb pain. There was no previous history of claudication or cardiovascular risk factors such as family history, hyperlipidemia, or diabetes mellitus.

Physical examination revealed pale and cold lower limbs up to the level of mid thigh bilaterally with pulses absent in the posterior tibia, dorsalis pedis and the popliteal arteries bilaterally. Capillary refill was delayed to 5 s bilaterally. There was tenderness on deep palpation and mild guarding over his epigastrium associated with some abdominal distension with sluggish bowel sounds.

Laboratory investigation revealed leukocytosis (23.6×10^9/l), markedly elevated serum amylase levels (2,450 U/l) and lipase levels (5,265 U/l), high creatine kinase levels (8,556 U/l), and the arterial blood gas picture showed metabolic acidosis. Liver function revealed mild transaminitis and raised alkaline phosphatase (229 U/l) and a bilirubin level of 38 U/l. C-reactive protein was also elevated (45.6 mg/l). Ranson score was 5 on admission. In view of his findings, the diagnosis of acute pancreatitis and bilateral lower limb ischemia complicated by rhabdomyolysis was made.

Computed tomography of the abdomen revealed findings consistent with acute severe pancreatitis associated with choledocholithiasis and cholelithiasis. Computed tomographic angiography revealed

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occlusion of the left superficial femoral artery as well as the bilateral popliteal, tibial and peroneal arteries (fig. 1).

He was admitted to the surgical intensive care unit for management and started on intravenous fluids, antibiotics, and heparin, and was kept on a nil-by-mouth regime. The patient was offered bilateral above-knee amputations, which he initially refused. He improved clinically with these supportive measures, and the ileus resolved. Laboratory indicators also improved with normalization of liver enzymes, amylase levels, creatine kinase levels and blood gases (fig. 2). Ranson score at 48 h was 7. However, the ischemia of his lower limbs worsened and necessitated bilateral above-knee amputation during the same hospital admission. He recovered uneventfully post-operatively and was discharged well.

Discussion

Acute pancreatitis is a common and important surgical condition with significant morbidity and mortality. Acute pancreatitis presenting with acute bilateral lower ischemia is rarely reported [1]. Regardless of its etiology, acute pancreatitis, with its liberation of proteolytic enzymes, lipase, kinins and other active peptides, converts a single-organ disease to a multi-systemic one by generating a cascade of immunological events via these inflammatory mediators if the initiating insult is sufficiently extensive. It constitutes a systemic inflammatory response syndrome with local complications, including pancreatic necrosis with pseudocyst or abscess formation as well as extra-pancreatic complications such as pulmonary, renal, hepatic, endocrine and coagulation abnormalities. Coagulation disorders associated with acute pancreatitis are well documented and are related to the severity of disease in both experimental animal and human studies [2]. Vascular disturbances are not limited to local pancreatic microcirculatory impairment but also involve distant micro- and macro-vascular circulation [3, 4]. The activation of the complement system can account for many of its hematological acute disorders due to leukocyte emboli or other complement-mediated aggregates. It has varied presentations, ranging from isolated intravascular thrombosis to disseminated intravascular coagulation. Rarely, microemboli can result in occlusion of the retinal arterioles with subsequent blindness [2, 5]. Acute pancreatitis has also been reported in causative association with thrombotic thrombocytopenic purpura-hemolytic uremic syndromes and thrombotic microangiopathy, resulting in acute renal failure [6, 7]. In autopsy studies, it has been shown that the percentage of ischemic enterocolitis in patients with acute pancreatitis is higher than previously reported, with diffuse intestinal involvement, consistent with the findings of fibrin thrombi in the mucosal and submucosal small vessels [4]. Causative factors for these thrombotic and ischemic events include poor blood fluidity from hemoconcentration, intravascular hypercoagulability, impairment of arteriolar inflow due to vasospam, disturbance of capillary flow due to direct endothelial injury and edema, obstruction of venous outflow by thrombosis, leukocyte-endothelium interaction and direct toxic injury by activated enzymes, kinins and other mediators. These inflammatory mediators include tumor necrosis factor α, intercellular adhesion molecule 1, interleukin 1β, interleukin 6, interleukin 8, platelet-activating factor, amongst many others. It has been established that inflammation plays a central role in the pathophysiology of peripheral arterial disease and contributes to all stages of the atherosclerotic process. Many of these pro-inflammatory mediators such as intercellular adhesion molecule 1, interleukin 6 and tumor necrosis factor α are pivotal in the development of peripheral vascular disease [8].

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Acute lower limb ischemia is a rare manifestation and complication of acute pancreatitis. In this patient, the acute pain resulting from bilateral limb ischemia was so severe as to mask the pain of acute pancreatitis. The acute limb ischemia was likely triggered by the coagulation disorders as a sequelae of acute pancreatitis, rather than being a primary event, as it is uncommon for acute limb ischemia to present bilaterally, especially in the absence of a history of claudication and cardiovascular or vasculopathic risk factors such as hyperlipidemia, hypertension, diabetes mellitus, family history, or smoking. The episode of acute pancreatitis was precipitated by gallstone disease, which in turn triggered a cascade of events including hypercoagulability, causing intravascular thrombosis coupled with microemboli formation, which affected this patient's bilateral lower limb arteries.

This case illustrates several interesting points. Despite the pain of acute pancreatitis classically being described as severe and piercing, in this patient, the acute ischemia of his legs caused him significantly more distress than his pancreatitis. We predict that in many patients who might present similarly, the diagnosis of acute pancreatitis might be delayed or even missed, resulting in greater morbidity and mortality if the acute limb ischemia is managed in isolation. Clinicians involved in the care of such patients should be aware of this possibility, particularly when dealing with atypical cases of limb ischemia. The acute limb ischemia was extensive and severe as demonstrated by the rhabdomyolysis in this patient; this was consistent with the pathogenesis of acute pancreatitis causing microembolization and widespread intravascular thrombosis, thus rendering significant muscle bulk to undergo ischemic changes and subsequently lysis. It is important to treat the pancreatitis aggressively so that the patient can be optimized medically prior to definitive treatment for the acute limb ischemia to prevent further complications.

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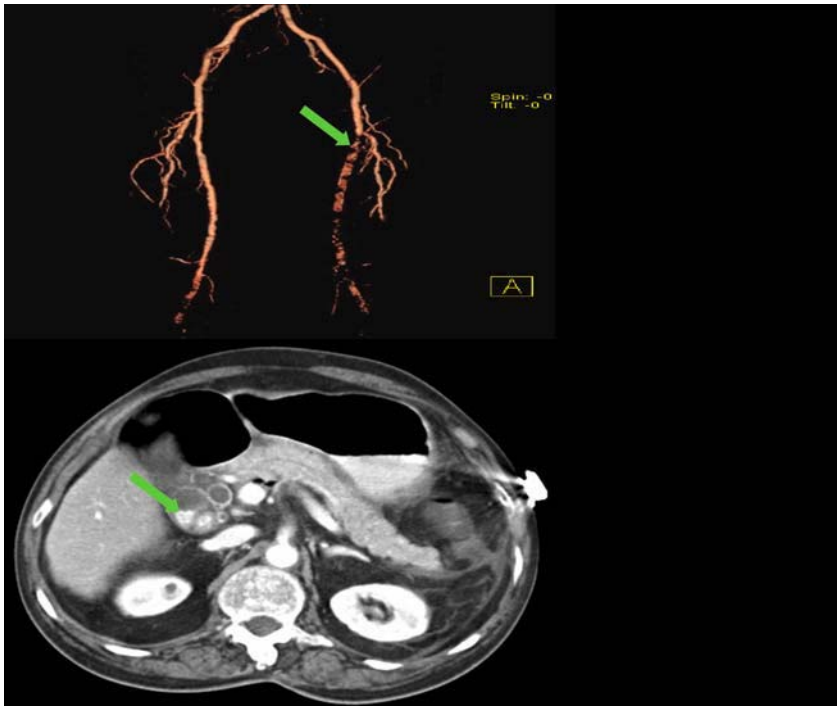

Fig. 1. Upper part: CT angiography revealing the filling defects in the left superficial femoral artery (arrow); the bilateral popliteal, anterior and posterior tibial and the peroneal arteries are all occluded. Lower part: CT of the abdomen revealing the presence of fluid in the bilateral perinephric and paracolic spaces with thickening of the left anterior renal fascia and left lateral conal fascia in keeping with acute severe pancreatitis; several gallstones are seen in the gallbladder (arrow).

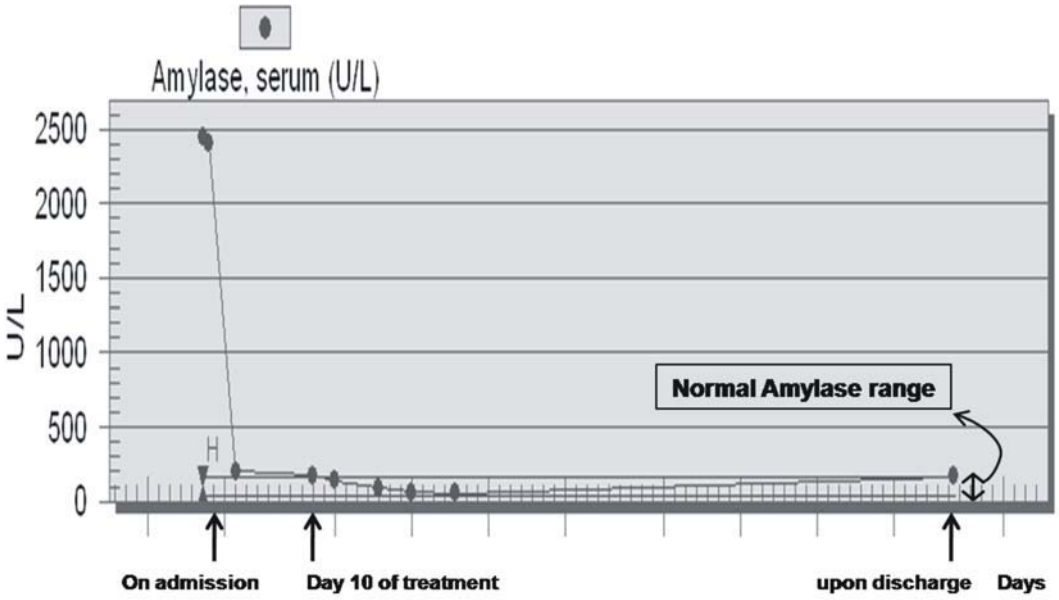

Fig. 2. Serum amylase levels on admission and subsequent improvement with management. The normal amylase range is 44–160 U/l, as shown in the graph.

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