High fever and high lipids

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A 41-year-old-man was admitted through the Accident and Emergency department with a four day history of high fever, vomiting and mild generalised abdominal pain. He smoked 20 cigarettes a day and drank half a bottle of spirits on most days. On examination he was sweating profusely with a temperature of 40°C and a pulse rate of 120 beats/min. His abdomen was soft and non-tender with normal bowel sounds. The investigations performed are summarised in the table (third admission). His serum was noted to be lipaemic and fasting lipids showed combined hyperlipidaemia with a serum triglyceride concentration of 35 mmol/l and cholesterol of 17.6 mmol/l. Arterial blood gases showed a pH of 7.42, pO₂ of 8.4 kPa and pCO₂ of 5.15 kPa.

He had been admitted to our hospital on two previous occasions with similar symptoms but his medical history was otherwise unremarkable. The first admission was 16 months previously when he presented with a five-hour history of fever and vomiting but without abdominal pain. Abnormal findings on examination were a tachycardia and a temperature of 39.3°C. The investigations are summarised in the table. In addition, three sets of blood cultures, an echocardiogram, urine culture and abdominal ultrasound were all normal. His temperature settled and he was discharged after four days in hospital with no cause found for his symptoms. Seven months after this admission he was re-admitted with a similar history of a pyrexia for three days and mild upper abdominal pain. On examination his temperature was 38.5°C and there were no abnormal findings in his abdomen. Blood cultures, abdominal ultrasound and urine culture were again all negative. His temperature settled and he was discharged from hospital after five days. He remained well until the most recent admission.

In view of the recurrent episodes of unexplained fever and abdominal pain, a computed tomography (CT) scan was carried out on his abdomen (figure).

Table Laboratory and radiological investigations performed on the three admissions to hospital. Abdominal X-ray and ultrasound were normal on all three occasions

Admission	Blood white cell count (× 10 ⁹ /l)	ESR (mm in 1 st h)	C-reactive protein (mg/l)	Serum liver biochemistry urea and electrolytes	Serum amylase (U/l) (normal<220)
1	18.0 (91% neutrophils)	17	not done	normal	117
2	18.7 (87% neutrophils)	not done	>150	normal	97
3	12.7 (91% neutrophils)	104	>150	normal	49

Figure Contrast-enhanced CT scan of abdomen

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Question

What does the CT scan show and what are the most probable causes in this patient?

Answer

The contrast-enhanced CT scan of the abdomen shows typical appearances of distal pancreatitis with peripancreatic inflammation. There was no evidence of abscess formation but there are areas of reduced enhancement suggesting pancreatic necrosis. His pancreatitis is thought to be secondary to hypertriglyceridaemia or alcohol abuse or a combination of the two. Gallstones are the commonest cause of pancreatitis (box 1) but in this case none were seen on ultrasound examination.

Discussion

Acute pancreatitis is a common condition with a mortality of about 7%. The principal symptom is abdominal pain which is present in almost all patients and may be generalised or confined to the epigastrium. The diagnosis is usually made by finding a raised serum amylase (box 2) which is a highly sensitive test if the patient presents within hours of the onset of abdominal pain.¹ Our patient presumably had recurrent episodes of acute pancreatitis which presented on each occasion with high fever as the only, or predominant symptom. Abdominal pain was mild or absent and serum amylase was always within the normal range.

Abdominal pain is cited as the major presenting complaint in 95–100% of patients with acute pancreatitis.² Such a high frequency may merely reflect the fact that the standard criteria for the diagnosis of pancreatitis are the 'typical' symptoms (ie, abdominal pain) plus

an amylase elevation. In a retrospective survey by Read *et al*, pain was absent in seven of 47 (15%) cases of acute pancreatitis.³ However, in all but one of these cases, the patients were receiving postoperative analgesia or had other severe medical conditions (eg, hepatic coma, staphylococcal pneumonia with disseminated intravascular coagulation) and thus any pain may have been masked. Therefore, painless acute pancreatitis remains an unusual presentation.

A second unusual feature of this case was the high fever (38–40°C) and white cell count which often indicates infection of necrotic pancreatic tissue when it occurs early in the course (less than two weeks). An abscess, which may also cause a high fever and white cell count, usually does not occur until after the first month of illness. A low-grade fever (<38°C) and moderate leucocytosis may occur in uncomplicated acute pancreatitis. However, a high temperature and white cell count in the presence of pancreatic necrosis often indicates pancreatic infection. Pancreatic necrosis is best demonstrated by CT scan with intravenous contrast which shows areas of reduced enhancement where the microcirculation is disrupted, in contrast to interstitial pancreatitis which shows uniform enhancement. In general, patients with pancreatic necrosis have a higher mortality than those with interstitial pancreatitis; mortality is greatest in those with infected necrosis. CT guided percutaneous aspiration of a pancreatic mass with Gram's stain and culture is a safe and reliable method of distinguishing infected from sterile necrosis. Surgical debridement is indicated in patients with infected necrosis and in some severely ill patients with sterile necrosis. Antibiotics alone are not effective in treating infected necrosis. Although direct evidence of pancreatic infection was not sought in our patient, the rapid recovery within four days of presentation makes this highly unlikely.

Perhaps the most surprising aspect of this case is the repeatedly normal serum amylase. The amylase is thought to rise within 24 hours after onset of the disease and return to normal, in uncomplicated cases, within about five days.⁴ Clavien *et al* found that the amylase was within the normal range in 19% of cases diagnosed on contrast-enhanced CT scan.⁵ However, in 40% of these cases the amylase did rise to above the normal range on at least one occasion during the hospital admission. In the case described here, amylase was always normal, despite being measured within five hours of the onset of symptoms on the first admission, and was repeatedly normal on the last admission to hospital. In patients with acute pancreatitis and hypertriglyceridaemia the serum amylase is reported to be normal more often than in patients with normal lipids. The mechanism of this is uncertain, but experimental work suggests a true reduction in the serum amylase activity rather than simply interference with the assay.² In this patient, serum amylase was measured by an enzymatic colorimetric test assayed on an Hitachi 717 analyser; a serum triglyceride

Acute pancreatitis: aetiology

- biliary tract stones
 - alcohol
 - idiopathic
 - drugs, eg, thiazide diuretics, frusemide, azathioprine
 - postoperative
 - metabolic abnormalities
 - infections, eg, mumps
 - trauma
 - miscellaneous
- } 90% of cases

Box 1

Acute pancreatitis: diagnostic tests

- elevated serum amylase: sensitive test in the early stages, but not specific; other abdominal conditions may cause a mild/moderate rise
- elevated serum lipase: greater specificity than the serum amylase
- urinary amylase: may remain raised longer than serum amylase
- ultrasound: 70% sensitive and highly specific
- CT scan with intravenous contrast: very sensitive; imaging method of choice in determining severity and complications of pancreatitis
- measurement of serum trypsinogen and pancreatic isoamylase adds little to other laboratory investigations

Box 2

concentration of up to 28 mmol/l has been shown not to interfere with measurement of serum amylase with this technique (personal communication, Boehringer Mannheim).

In view of his heavy alcohol intake, we considered that our patient may have chronic relapsing pancreatitis in which a normal serum amylase is seen more commonly. This is unlikely, however, as the patient was well between acute episodes, with no abdominal pain. In addition, there is no evidence of pancreatic exocrine insufficiency and no pancreatic calcification or other features of chronic

pancreatitis on plain abdominal radiograph or abdominal CT scan. Finally, our patient has had no further episodes of pancreatitis since effective treatment of his hyperlipidaemia.

Final diagnosis

Recurrent acute pancreatitis with normal serum amylase concentration.

Keywords: pancreatitis, hyperlipidaemia

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- 4 Moosa AR. Diagnostic tests and procedures in acute pancreatitis. *N Engl J Med* 1984; 311: 639–43.
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Recurrent dehydration in a young girl

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A 50-day-old girl was admitted to hospital because of fever, vomiting and refusal of feeding of four days duration. She was born normally at term to healthy parents who were first cousins. On admission she was dehydrated and weak. Basic blood biochemical investigations were normal apart from a serum sodium of 159 mmol/l. She was given parenteral therapy with subsequent improvement of her condition and she was discharged in good health after a few days. She was re-admitted again the following week with fever, lethargy and marked dehydration without an associated history of vomiting or diarrhoea. Investigations showed a serum sodium of 165 mmol/l, potassium 5 mmol/l, chloride 117 mmol/l, bicarbonate 21 mmol/l, urea 5.5 mmol/l, creatinine 52 μ mol/l, blood sugar 5.2 mmol/l and serum calcium was 2.2 mmol/l. Complete blood count was normal. Urine was negative for sugar, protein and abnormal sediments with an osmolality of 17 mmol/kg while that of the serum was 294. Urine volume passed over a 12-hour period was 700 ml. Administration of intranasal ADDVP did not result in any change in the biochemical values and osmolality of blood or urine. After an initial period of normal psychomotor development it was observed that her progress had begun to lag behind that expected for her age. At the age of seven years her psychomotor development was 12-months retarded and her weight and height were below the third centile for her age. Non-contrast computed tomography (CT) of the head was performed at that age (figures 1 and 2).

Figure 1 Brain CT scan

Figure 2 Brain CT scan

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Questions

- 1 What is the diagnosis?
- 2 What do the figures show?