Pancreatitis and chronic abdominal pain in a patient with AIDS

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A 37-year-old white woman was infected with the human immunodeficiency virus (HIV) through a blood transfusion which she received during a complicated labour in the Ivory Coast. Three years later, due to a decline in the CD4⁺ cell counts to 200/ml, zidovudine (AZT) and trimethoprim-cotrimoxazole were administered. A few months later, zalcitabine (ddC) was added, due to the appearance of fever, abdominal pain and weight loss, and a further decline in the CD4⁺ cell counts down to 15/ml. Despite these measures the patient continued to complain of abdominal pain, which was often exacerbated by food intake. Laboratory studies then showed normal serum amylase and liver enzyme levels. Abdominal ultrasonography (US) and gastroscopy were normal. Due to a suspected role of the antiretroviral drug therapy in inducing the abdominal pain, AZT and ddC were discontinued.

Three months later, the patient was admitted because of severe abdominal pain, vomiting and a fever of 38.5°C. On examination, marked epigastric tenderness was noted. Investigation results were as follows: amylase 1120 IU/l, hypocalcaemia (1.52 mmol/l), alkaline phosphate 219 IU/l, and gamma-glutamyl transpeptidase 478 IU/l. US and computed tomography (CT) revealed gall bladder wall thickening, with a dilated common bile duct and no evidence of stones. The pancreas was mildly enlarged and oedematous.

A diagnosis of pancreatitis was made, a nasogastric tube was inserted and fluids were administered with marked improvement. Blood and urine cultures for cytomegalovirus (CMV) were negative, and fundoscopic examination did not reveal the presence of CMV retinitis. Blood cultures were negative for *Mycobacterium avium-intracellulare* (MAI), and *Cryptococcus neformans* antigens were not detected.

A few weeks later, epigastric pain recurred. Amylase levels remained normal. An endoscopic retrograde cholangiopancreatography (ERCP) was performed (figure). Brush cultures from the mucosa and the biliary fluid grew CMV. Ganciclovir was administered at a dose of 10 mg/kg daily for 3 weeks, followed by 5 mg/kg daily, with improvement in her general condition and a gradual decrease of the pain.

Three months later, parenteral nutrition was started due to intractable abdominal pain which was related to food intake. On this therapy the patient developed severe abdominal pain accompanied by deterioration of liver function tests. A repeat ERCP was performed.

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Figure ERCP with contrast material within the common bile duct, showing mild dilatation without any filling defects. There was no dilatation of the pancreatic duct

Questions

- 1 What diagnosis is suggested by the findings on ERCP?
- 2 Which other organism besides CMV is likely to be found in the biliary tract in this patient?
- 3 What is the optimal management of this patient's condition?

Answers

QUESTION 1

The initial ERCP revealed marked diffuse inflammation around the area of the papilla of Vater, biliary tract narrowing with mild dilatation of the common bile duct without dilatation of the pancreatic duct. The changes in the biliary ducts were consistent with acquired immune deficiency syndrome (AIDS). Biopsies taken from the duodenal mucosa and the papilla of Vater during papillotomy, revealed a lymphocytic infiltration with inclusion bodies which reacted to monoclonal antibodies specific to CMV. The repeat ERCP showed, again, a dilated common bile duct with irregular borders with no filling defects. The papilla of Vater was draining bile adequately and the pancreatic duct appeared normal. Papillotomy was repeated. CMV inclusion bodies could not be found.

QUESTION 2

Histologic examination of the small intestine mucosa from the repeated ERCP, revealed *Cryptosporidium*. Both CMV and *Cryptosporidium* have been found, often simultaneously, within the biliary epithelium of patients with AIDS cholangiopathy. However, their role in the pathogenesis of this cholangiopathy has not been well defined. Azithromycin and oral narcotics were administered with mild improvement. Six weeks later the patient was hospitalized again due to high fever. *Candida albicans* grew in blood culture, and amphotericin B therapy was initiated. The patient died few days later.

QUESTION 3

AIDS cholangiopathy is best treated by sphincterotomy or surgical drainage of the common bile duct. This is the most effective method that leads to a rapid relief of pain which may last. Although it is legitimate to attempt eradicating any pathogens found within the biliary epithelia such as CMV or *Cryptosporidium*, these actions do not seem to affect the general biliary process or the outcome of these patients, as the primary pathological process is not affected.

Discussion

We have described an HIV-positive patient who presented with CMV-related acute pancreatitis, as the initial manifestation of AIDS cholangiopathy. AIDS-related cholangiopathy is a well described entity which presents in advanced stages of AIDS. CMV and *Cryptosporidium* are frequently found within the biliary epithelium, although their role in inducing AIDS cholangiopathy is not clear.

Pancreatitis occurs in about 5% of HIV-infected individuals,¹ and is mostly related to drugs, such as dideoxyinosine (ddI), zalcitabine (ddC), pentamidine, and trimethoprim-sulfamethoxazole.² In addition to common aetiologies of acute pancreatitis, such as chole-

Learning points

- sclerosing cholangitis may be the only manifestation of AIDS
- CMV infection plays a limited role in the induction and propagation of AIDS cholangiopathy
- acute pancreatitis can be a presenting symptom of AIDS cholangiopathy
- endoscopic sphincterotomy relieves the patient's symptoms; however, it does not change the outcome of AIDS cholangiopathy

lithiasis and alcoholism, opportunistic pathogens such as CMV, *Cryptococcus neoformans* and *Toxoplasma gondii*³ are also important causes of pancreatitis in patients with HIV infection. CMV infection is very common in advanced stages of AIDS. The gastrointestinal tract is the most involved organ in CMV infection, except for the retina.⁴ Autopsy studies have shown that CMV is the most common pathogen that involves the pancreas in AIDS patients.⁵ Antemortem diagnosis of CMV pancreatitis requires a high index of suspicion, and may be achieved by demonstrating inclusion bodies within the pancreatic parenchyma and viral culture of the pancreatic tissue. Epithelial cells from the ampulla of Vater harbouring CMV inclusion bodies, suggests strongly that CMV was the causative agent of pancreatitis in our patient.⁶

Despite the eradication of CMV from the pancreas, our patient continued to suffer from intermittent abdominal pain with cholestasis, typical of AIDS cholangiopathy.⁷ Usually, patients with AIDS cholangiopathy are well advanced in their disease, with CD4 counts below 100/ml. AIDS cholangiopathy comprises biliary tract narrowing, which may be either a result of papillary stenosis, sclerosing cholangitis, or a combination of the two processes, and is well recognized by ERCP.⁸ CMV and *Cryptosporidium* are common, and the presence of MAI has also been reported.⁷ Treatment to eradicate CMV may contribute to improvement in the patient's condition.⁷ With the lack of diarrhoea and signs of malabsorption, *Cryptosporidium* was unlikely to have played a significant role in causing the patient's symptoms.

Despite the suggested role of CMV in the pathogenesis of AIDS cholangiopathy, eradication of CMV does not seem to change the outcome or the long-term prognosis, probably because of the advanced stage of their HIV infection.

Final diagnosis

AIDS cholangiopathy.

Keywords: AIDS cholangiopathy; pancreatitis; cytomegalovirus; cryptosporidium

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Dysphagia and hypercalcaemia

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A 68-year-old man presented with a 3-month history of progressive dysphagia, anorexia, weight loss, fatigue and malaise. Two years previously, he had received palliative radiotherapy for squamous cell carcinoma of the right bronchus. There was no medical history of gastrointestinal disease and, apart from difficulty swallowing, the patient did not complain of any other gastrointestinal symptoms, urinary symptoms, or visual disturbance. On examination, the patient was alert, but cachectic. There were no signs of cognitive impairment. There was no palpable lymphadenopathy or other mass in the neck. Examination of the mouth and pharynx revealed no abnormalities. Respiratory examination revealed collapse of the right lower lobe. Abdominal examination revealed a hard, irregular, non-tender, non-pulsatile liver edge, palpable 4 cm below the right costal margin. There were no signs of chronic liver disease. Rectal, cardiovascular and neurological examinations were normal. Investigations showed haemoglobin 10.3 g/dl, mean corpuscular volume 78.2 fl, total white blood cell count $8.45 \times 10^9/l$ (normal differential count) and erythrocyte sedimentation rate 91 mm in the first hour. Renal and thyroid function were normal. Random blood glucose was 6.3 mmol/l. Alkaline phosphatase 487 IU/l (normal range 70-250 IU/l), serum calcium 3.71 mmol/l, serum phosphate 1.17 mmol/l (0.75-1.40 mmol/l) and serum albumin 25 g/l (34-48 g/l). Corrected serum calcium was 4.01 mmol/l (2.22-2.56 mmol/l). Other liver function tests were normal. Serum parathyroid hormone, as measured by radio-immunoassay, was 80 ng/l (< 100 ng/l) and angiotensin-converting enzyme levels were normal. Chest X-ray confirmed collapse of the right lower lobe, due to a carcinoma obstructing the right bronchus. Abdominal ultrasound showed multiple small echogenic lesions throughout the liver, consistent with metastatic deposits from the bronchial carcinoma. An electrocardiogram was normal. An oesophago-gastro-duodenoscopy was normal. In particular, there was no evidence of extrinsic oesophageal compression or oesophageal infiltration by the bronchial carcinoma.

Questions

- 1 What is the cause of dysphagia?
- 2 What other clinical features may be present?

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