

CASE REPORT

PANCREATITIS IN A CHILD ON ANTI-RETROVIRAL THERAPY

A 5-year-old HIV-infected child on antiretroviral therapy (ART) (stavudine, lamivudine and efavirenz) for the preceding 2 years presented to the outpatients' department at Red Cross War Memorial Children's Hospital with a history of vomiting and epigastric pain. These symptoms had been present intermittently for the previous 2 - 3 months after the ingestion of food. Weight loss of 1 - 2 kg over the preceding 3 months was noted. There was no associated fever, diarrhoea, cough or headache. The child was not receiving any other medication and there was no history of trauma.

On physical examination, there was no jaundice and no features of respiratory tract infection or meningitis. The abdomen was non-distended but the epigastrium was tender to palpation. No masses or hepatosplenomegaly was palpable and bowel sounds were present. The remainder of the examination was normal.

Urine dipstick examination showed protein (1+) and ketones (2+). Blood investigations revealed the amylase to be 3 861 U/l (normal range 25 - 125 U/l), and lipase 2 826 U/l (normal range 0 - 60 U/l). Alanine transferase (ALT) was 17 U/l (normal range 5 - 25 U/l) and other electrolytes, including calcium, magnesium and inorganic phosphorus, were within the normal range. The venous plasma lactate was 1.3 mmol/l (normal range 0.5 - 2.2 mmol/l) and the venous blood gas was normal. Triglycerides were 1.0 mmol/l (normal range 0.4 - 1.2 mmol/l).

The child was diagnosed with acute pancreatitis most likely due to ART, in particular the nucleoside reverse transcriptase inhibitors (NRTIs) stavudine or lamivudine. Symptomatic lactic acidosis was excluded by a normal plasma lactate and venous blood gas. ART was discontinued and the child was admitted for further investigations and management.

Abdominal ultrasound revealed a morphologically normal pancreas, with a worm occupying the entire length of the pancreatic duct (Fig. 1). There were no peri-pancreatic fluid collections and no biliary dilatation. The liver and gall bladder were normal.

The child's symptoms improved over the next 24 - 48 hours and the amylase level gradually decreased over the following week. Repeat abdominal ultrasound after one week showed the worm still present within the pancreatic duct.

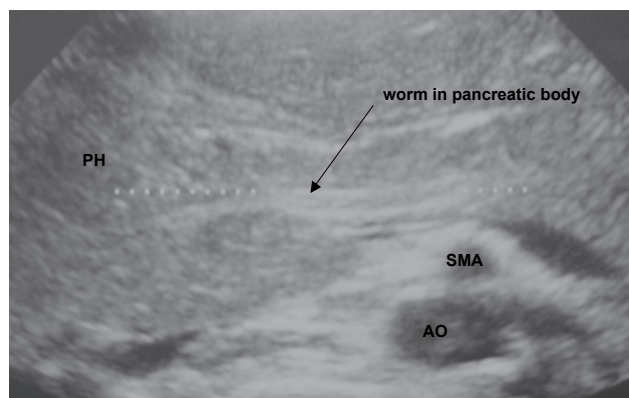


Fig. 1. Transverse ultrasound scan through epigastrium demonstrating pancreatic head and body with two parallel echogenic lines consistent with a worm in the pancreatic duct (PH = pancreatic head; SMA = superior mesenteric artery; AO = aorta).

Ascaris-induced pancreatitis rather than NRTI-induced pancreatitis became the most likely diagnosis, and ART was re-started with no alteration of the drug regimen. The child remained asymptomatic and was followed up at a regional ART clinic. The patient did not attend follow-up ultrasound appointments but a repeat ultrasound 3 months later showed no worm present in the pancreas, although worms were visualised in the small bowel. The child was treated with albendazole 400 mg daily for 3 days.

Discussion

Pancreatitis should always be considered in the diagnostic evaluation of children presenting with abdominal pain and vomiting. There are a number of well-recognised causes in HIV-infected individuals, including HIV itself, but of particular importance are antiretroviral drugs.

NRTI-associated pancreatitis may occur as an isolated event or in the context of systemic lactic acidosis as a result of mitochondrial toxicity. Didanosine, stavudine, lamivudine and abacavir have all been implicated, although didanosine is the most frequently reported agent. Didanosine-related adverse effects occur more frequently when the mean daily dose exceeds 360 mg/m² and are usually reversible after discontinuation of treatment. Administration of didanosine in combination with hydroxyurea or ribavirin appears to increase the risk of pancreatitis although neither of these agents is in widespread use.

Protease inhibitors (PIs) that have been implicated include lopinavir/ritonavir (Kaletra) and ritonavir. In addition, long-term PI therapy may result in moderate to severe hypertriglyceridaemia – a risk factor for pancreatitis. Other drug-

related causes include pentamidine isethionate used as a second-line agent for prophylaxis or treatment of *Pneumocystis jiroveci* pneumonia.

Pancreatic involvement by opportunistic infections including cytomegalovirus, cryptosporidium, *Mycobacterium avium intracellulare* and candida has been described in autopsy studies on HIV-infected children.

High rates of helminthic infestation with *Ascaris* have been documented in children living in poor communities in South Africa. *Ascaris*-induced pancreatitis due to a worm either in the ampulla of Vater or the pancreatic duct itself is a far less common complication than biliary or intestinal obstruction. However, a number of case reports have appeared in the medical literature, including that of a 4-year-old with a fatal outcome. Ultrasonography is the diagnostic and follow-up imaging modality of choice and is able to demonstrate the presence of *Ascaris lumbricoides* in the biliary and the pancreatic ducts, as well as signs of pancreatitis, biliary obstruction, cholecystitis, and hepatic abscess. Endoscopic retrograde cholangiopancreatography (ERCP) can be used to confirm the diagnosis and allows removal of worms from the biliary duct if symptoms fail to resolve or if the worms are still present after four weeks. If ERCP fails or is not available, surgical exploration may be required.

Acute pancreatitis, diagnosed on the basis of an elevated lipase measurement (elevated amylase may be caused by parotid gland inflammation associated with HIV infection itself or mumps) and suggestive symptomatology (epigastric pain, vomiting), is a potentially life-threatening condition.

The medical management of acute pancreatitis entails supportive measures. This includes bed-rest, intravenous fluids,

drainage of gastric secretions by nasogastric tube, analgesics, and antispasmodics, e.g. hyoscine butylbromide. Some authors recommend that in *Ascaris*-induced pancreatitis, antihelminthic medication should only be administered once the patient is no longer symptomatic. The majority of cases resolve within 24 - 48 hours. Indications for surgery include pancreatic necrosis and pseudocyst formation.

Non-nucleoside reverse transcriptase inhibitor (NNRTI) drugs have a much longer half-life than NRTIs. Stopping all antiretroviral drugs simultaneously may potentially lead to the development of viral resistance to the NNRTI class of drugs as a result of ongoing exposure to NNRTI levels for some days after stopping ART. However, in the setting of suspected serious drug toxicity it is recommended that all antiretroviral drugs are stopped simultaneously until the patient is stabilised and the toxicity resolved. In cases where pancreatitis is most likely attributable to a specific drug(s) in the ART regimen, ART may be re-started after substitution of the relevant drug(s) for other drug(s) in the same class. Consultation with an HIV expert is recommended in this situation.

References available on request.

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SINGLE SUTURE

HEALTHY AGEING

Governments tend to think that it is the provision of hospitals and health care that leads to healthy ageing, but a study from Canada suggests that there is more to a healthy old age than having access to medication. Naturally occurring retirement communities are areas to which the elderly either retire or where they remain once retired. This study showed that people tend to be healthier in communities where the physical and social environment encourages activity and promotes a feeling of wellbeing and, what is more, it is cost effective. Happy, physically active people tend to be healthier and so make fewer calls on health care facilities.

Masotti PJ, et al. *Am J Public Health* 2006; **96**: 1164-1170.