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CASE STUDY

Pancreatitis, complicated by a pancreatic pseudocyst associated with the use of valproic acid

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Summary A 12-year-old boy developed pancreatitis, complicated by a pancreatic pseudocyst, as an adverse reaction to valproic acid (VPA) treatment for epilepsy. Pancreatitis subsided within three weeks after discontinuation of VPA. The pancreatic pseudocyst was managed without surgery and resolved spontaneously in four weeks. Valproic acid was concluded to be the most probable cause, since no other explanation was found. According to the literature VPA is a rare but known cause of pancreatitis.

A computer-assisted literature search revealed seven previously reported cases of VPA-induced pancreatitis complicated by a pancreatic pseudocyst. Six of these patients were under 20 years of age. Four patients were treated conservatively; three needed cystostomy or external drainage. All patients recovered.

Patients using VPA, especially children, presenting with acute abdominal pain should be suspected of valproic acid-induced pancreatitis. If VPA induced pancreatitis is complicated by a pseudocyst, conservative treatment should be the first line of treatment.

Case

A 12-year-old boy presented at the pediatric ward of our hospital with intermittent upper abdominal pain that started two weeks before. The pain attacks lasted for several minutes, and were less painful when the boy was lying still with his legs flexed. The attacks occurred 4–8 times a day. On examination the boy appeared moderately ill. His body weight was 45 kg and his temperature was 38 °C. He had no signs of jaundice nor did the skin reveal any haematomas. The bowel sounds were normal but there was some left upper abdominal tenderness. The liver and spleen were not enlarged, nor were any abnormal masses felt.

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The boy was known with cryptogenic localisation-related epilepsy with secondarily generalised seizures for which two years before valproic acid (VPA)-therapy was titrated up to 1500 mg a day (33 mg/kg). Since then the boy was free of seizures. VPA serum levels were compatible with a good compliance. The boy did not use any co-medication. There was no history of abdominal trauma.

Laboratory investigations showed a haemoglobin of 8.1 mmol/l (normal: 8.5–11.0 mmol/l), leukocytes 4.9×10^9/l (normal: $3.5\text{–}11.0\times10^9$/l) and thrombocytes 161×10^9/l (normal: 150–400×. 10^9/l). The ESR was 12 mm in the first hour. Serum amylase was 103 U/l (15–110 U/l). The serum lipase 278 U/l level was elevated (normal: 7–75 U/l). The urine amylase was 375 U/l (normal: <650 U/l). An abdominal ultrasound showed an enlarged pancreas with a homogeneous aspect. Based on clinical presentation, abdominal ultrasound and elevated serum lipase, the diagnosis pancreatitis was made. There were no other causes (infection, trauma, obstruction, hypercalcemia, elevated triglycerides nor medication (co-trimoxazol, metronidazol e.g.)) of pancreatitis found than the use of VPA. Furthermore the pancreatitis developed during VPA treatment. VPA is a known cause of pancreatitis.[1]

In the absence of other obvious causes, VPA was considered the most probable explanation and was therefore discontinued.

Three weeks later and 14 days after the last dose of VPA, abdominal pain returned in increased intensity and frequency. The boy had become anorexic and had lost 3 kg body weight. Upon presentation he was nauseous, but did not vomit. His stools were normal. The serum amylase and lipase values had decreased (amylase 76 U/l, lipase 89 U/l). The urine amylase had decreased to 116 U/l. Ultrasound examination showed a left-sided upper abdominal cyst originating from the tail of the pancreas. Computed tomography confirmed the presence of a pancreatic pseudocyst with a diameter of 10 cm (Fig. 1). It was concluded that the pancreatitis had subsided, but the situation was now complicated by the development of a pseudocyst. For the pancreatic pseudocyst conservative treatment with analgesics and a low fat diet was instituted. The abdominal complaints gradually resolved and an ultrasound four weeks later showed complete resolution of the pancreatic pseudocyst. After discontinuation of VPA, the epilepsy was treated with subsequently levetiracetam, lamotrigine and clobazam without success. A rechallenge with VPA was considered. Because of the severity of a pancreatitis (20% leads to multi-organ failure and 5–10% results in death) and the high risk of recurrence,[1–3] a rechallenge was not performed. Finally, after the introduction of topiramate, the boy only experienced auras, but no generalised seizures anymore.

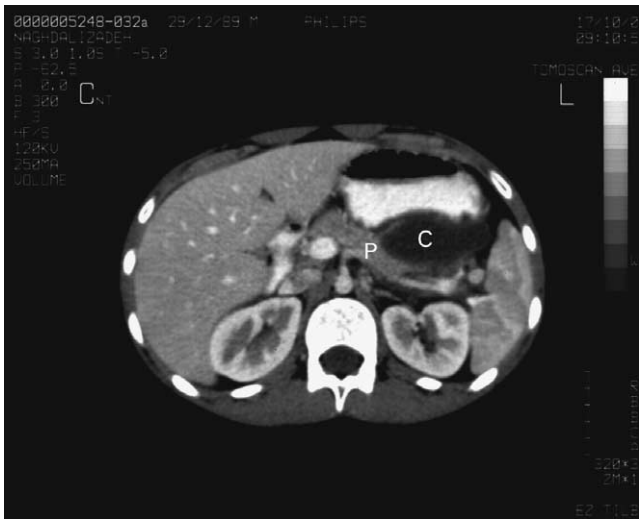

Figure 1 Abdominal computed tomography showing a pancreatic pseudocyst (C) originating from the tail of the pancreas (P).

Discussion

We describe the history of a 12-year-old boy in whom a pancreatitis, complicated by a pancreatic pseudocyst, developed after two years of monotherapy with VPA. Discontinuation of VPA led to a quick disappearance of complaints and normalisation of laboratory parameters. The boy did not use other medication, nor were any other causes of pancreatitis found. The prompt recovery, upon discontinuation of VPA, and the absence of other known causes of the pancreatitis led to the conclusion that VPA was the causal factor for the pancreatitis in our patient.

VPA is an agent used for the treatment of epilepsy, bipolar disorders and migraine. The drug is well tolerated by most people. Therapy may, however, be complicated by several adverse reactions. Common adverse reactions include weight gain, tremor, hair loss and thrombocytopathy. Rare but possibly very serious adverse reactions include hepatotoxicity, especially in very young retarded children, and pancreatitis, as observed in our patient.[1,4,5]

The incidence of acute pancreatitis in childhood, in general, is estimated at 2.0–2.7 per 100,000 per year.[2] Pancreatitis complicated by pancreatic pseudocysts (a collection of amylase-rich, lipase-rich, and enterokinase-rich fluid) in childhood is