Familial pancreatic enzyme insufficiency

G Owen, P W Buss, H R Jenkins, A H Goodwin, M C Goodchild

Abstract

A father and son with profound reduction of exocrine pancreatic activity and little visible pancreatic tissue on ultrasound or computed tomography are described. Both have some degree of liver disease, which is more marked in the son. The disorder, apparently familial, does not correspond to any reported previously.

(*Arch Dis Child* 1992;67:1481-2)

Although there are numerous causes of pancreatic exocrine insufficiency in childhood, cystic fibrosis is responsible for the vast majority, followed by Shwachman's syndrome.^{1 2} Other causes, including those with a familial incidence, are rare. We describe a father and son who have pancreatic enzyme insufficiency and abnormal liver function. We believe this may represent a new disorder.

Case reports

CASE 1

A 3 year old boy presented with a history of steatorrhoea since birth, frequent episodes of rectal prolapse, and generalised pruritis. There were no dysmorphic features. Height and weight were just below the 97th and on the 75th centile respectively. Positive findings were excoriation marks, slight abdominal distension, and a reducible rectal prolapse. Stools were cream coloured and loose. Faecal fat was raised at 12.3 g/day. Sweat electrolytes were normal, as were repeated full blood counts, including differential white cells counts. Neutrophil function tests and a comprehensive immunological screen were normal. Serum amylase and immunoreactive trypsin were low. The tocopherol:cholesterol ratio was low, while fasting liver enzymes and total serum bile acid concentrations (TSBA) were high (table 1). The

bilirubin concentration was normal. Pancreatic function testing revealed very low or absent values for lipase, trypsin, and amylase, both fasting and after intravenous pancreozymin and secretin (2U/kg each).

A jejunal biopsy specimen and skeletal survey were normal. Ultrasound scan and computed tomography of the pancreas revealed only a small amount of normal tissue located in the head and tail.

He was given daily vitamin supplements and pancreatic replacement treatment that produced a decrease in faecal fat excretion to 5.7 g/day and gradual disappearance of the rectal prolapse. However results of liver function tests remained abnormal (table 1). Further investigations for possible causes of liver disease, both infective and metabolic, including a liver biopsy with examination by light and electron microscopy, were all normal. An endoscopic retrograde cholecystopancreatogram (ERCP) showed normal pancreatic and common bile ducts but little contrast medium passed into the common hepatic and intrahepatic ducts—possibly due to a stricture of the common hepatic duct, but it was impossible to exclude compression by the endoscope. The small amount of contrast within the intrahepatic ducts showed normal ducts.

The boy has been followed up to age 8 and has remained clinically well and the pruritis and scratching have ceased. Results of liver function tests continue to show an improvement but remain abnormal (table 1).

CASE 2

The father of case 1, born in 1955, also gave a lifelong history of loose fatty stools and pruritis. He had been investigated at ages 5 and 18 years and found to have a raised faecal fat excretion, a low serum calcium and normal full blood count, though γ -glutamyltransferase was not measured. A Lundh test meal had shown a marked

Table 1 Results of blood tests in case 1. Normal values are given in square brackets

Date	Aspartate transaminase [5-45] (IU/l)	γ -Glutamyl- transferase [0-45] (IU/l)	Alkaline phosphatase [30-350] (IU/l)	Calcium [2.26-2.6] (mmol/l)	Vitamin A [0.7-1.5] (μ mol/l)	α -Tocopherol: cholesterol ratio [>2.2] (μ mol/mmol)	TSBA [<15] (μ mol/l)
4/8/87	225		656	2.1	0.94	1	
Started pancreatin*							
28/9/87	406	302	787	2.38	1.8	2.4	34
Started vitamins A, B, C, and E†							
9/12/87	374	260	774	2.23			129
23/6/89	140	153	534	2.08	1.06	4	
Started alfalcidol							
12/6/90	145	137	445	2.25	0.94	2.2	
12/5/92	109	89	354	2.25	1.02	3.8	55

*Creon (Duphar); †vitamins A, B, and C given as Abidec (W-L).

Department of
Child Health,
University of Wales
College of Medicine
G Owen
P W Buss
H R Jenkins
M C Goodchild

Department of
Paediatrics,
West Wales
General Hospital
A H Goodwin

Correspondence to:
Dr G Owen,
Department of Child Health,
University of Wales College
of Medicine,
Heath Park,
Cardiff CF4 4XW.

Accepted 2 September 1992

Table 2 Results of blood tests in case 2. Normal values are given in square brackets

Date	Aspartate transaminase [5-45] (IU/l)	γ -Glutamyl- transferase [0-45] (IU/l)	Alkaline phosphatase [30-110] (IU/l)	Calcium [2.26-2.6] (mmol/l)	Vitamin A [0.9-2.5] (μ mol/l)	α -Tocopherol: cholesterol ratio [>2.2] (μ mol/mmol)	TSBA [<15] (μ mol/l)
28/9/87	40	90	125	2.5	2.7	1.3	13
Changed to pancreatin as Creon 22/11/88	40	109	103		2	0.7	
Started vitamin E							
16/5/89	42	62	137	2.15	2.08	4.0	21
7/5/91	81	119	97		2.0	5.2	40
12/5/92	36	60	75	2.08	1.63	4.3	16

reduction of all three major pancreatic enzymes; pancreatic scan revealed no normal pancreatic tissue and the diagnosis was exocrine pancreatic insufficiency. He was treated with pancreatin as Nutrizym (Merck) tablets, vitamins A and D, and calcium supplements; alfalcidol had been added later. He improved and at the time of his son's presentation he had no specific complaints. Bowel actions were 1-2 times daily, usually formed but somewhat bulky and pale in colour. General examination was normal with height and weight on the 75th centile. There was no visible pancreatic tissue on ultrasound or computed tomography. Repeated full blood counts and tests of neutrophil function were normal. A glucose tolerance test showed normal insulin concentrations, but the two hour blood glucose concentration was raised at 7.6 mmol/l. Values for serum amylase and immunoreactive trypsin were low. Serial tests of liver function (abstaining from alcohol) with measurements of fasting TSBA and vitamin concentrations are shown in table 2. Detailed investigations for possible causes of liver disease were normal, though an ERCP and liver biopsy were not performed. Pancreatic enzyme replacement treatment was changed to Creon (Duphar) with further improvement in stool character, and vitamin E supplementation was given.

A paternal uncle of case 2, who had died at the age of 62 had been underweight, suffered diarrhoea all his life, and scratched excessively. No hospital tests or biochemical measurements had been performed.

Discussion

Investigations of this father and son with exocrine pancreatic insufficiency and abnormal liver function tests have excluded cystic fibrosis, Shwachman's syndrome, isolated pancreatic enzyme deficiencies, malnutrition, and congenital pancreatic hypoplasia.¹⁻³ Partial exocrine pancreatic insufficiency has been described in association with paucity of interlobular bile ducts,⁴ but severe failure to thrive is an important feature of children with this disorder; in addition,

there are characteristic changes on a liver biopsy specimen that were not seen in case 1.

There may be an association between sclerosing cholangitis and chronic pancreatitis in adults⁵ and between sclerosing cholangitis and inflammatory bowel disease in childhood.⁶ Neither of our patients has evidence of inflammatory bowel disease and sclerosing cholangitis with chronic pancreatitis has not been reported in childhood. An attempt to confirm or refute such an association by performing an ERCP in case 1 was only partially successful due to technical problems and it was felt unethical to repeat this.

Both patients have raised TSBA in the fasting state, a finding more marked in the son. The meaning of this is unclear, but it may be a reflection of the underlying liver disease.

Follow up over five years has shown a considerable improvement in liver function test status, especially in the son, since the introduction of pancreatic enzyme and vitamin supplements; which suggests that this may be associated with correction of malabsorption. The son's present results are not dissimilar from those of his father, allowing for normal age related variation, and we conclude that both patients have the same disorder.

We thank Professor J Rhodes and Dr R Lewis for permission to report the findings of case 2 and Mr Y Qureshi for measurement of total serum bile acid concentrations.

- 1 Hadorn HB, Munch G. The exocrine pancreas: development, physiology and disease. In: Anderson CM, Burke V, Gracey M, eds. *Paediatric gastroenterology*. Oxford: Blackwell, 1987:456-502.
- 2 Aggett PJ, Cavanagh NPC, Matthew DJ, Pincott JR, Sutcliffe J, Harries JT. Shwachman's syndrome. *Arch Dis Child* 1980;55:331-47.
- 3 Winter WE, Maclaren NK, Riley WJ, Toskes PP, Andres J, Rosenbloom AL. Congenital pancreatic hypoplasia: a syndrome of exocrine and endocrine pancreatic insufficiency. *J Pediatr* 1986;109:465-8.
- 4 Chong SKF, Lindridge J, Moniz C, Mowat AP. Exocrine pancreatic insufficiency in syndromic paucity of interlobular bile ducts. *J Pediatr Gastroenterol Nutr* 1989;9:445-9.
- 5 Benett I, Salh B, Haboubi NY, Braganza JM. Sclerosing cholangitis with hepatic steatosis in cystic fibrosis and chronic pancreatitis. *J Clin Pathol* 1989;42:466-9.
- 6 Classen M, Gotze H, Richter HJ, Bender S. Primary sclerosing cholangitis in children. *J Pediatr Gastroenterol Nutr* 1987;6:197-202.