Relapsing acute and chronic pancreatitis

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SUMMARY Twenty five children with non-traumatic relapsing acute or chronic pancreatitis who had been followed up from five months to seven years were studied. Seven had congenital anomalies, including two with choledochal cysts and four with pancreas divisum. Alcohol related disease was suspected in one child. The importance of diabetes in two patients and a positive family history in a further three is discussed, but in 12 children no association was found. Management was similar to that for adults. Surgical intervention was required in six patients, and percutaneous drainage of pseudocysts in a further three. Outcome has generally been good.

Pancreatitis is unusual in children and has a different aetiological spectrum from that seen in adults. Trauma, drugs, and infection are relatively more common causes; gall stone and alcohol related disease are rarely seen.¹ Most acute attacks are self limiting and do not result in permanent damage or disability. Over the past nine years we have studied 25 children with persisting problems due to relapsing acute and chronic pancreatitis.

Patients and methods

Twenty patients (11 boys, nine girls) between the ages of 3 and 15 years were investigated; the other five patients (three boys, two girls) were older when referred (age range 16 to 22 years) but had clear evidence of pancreatitis before the age of 16 (Tables 1 and 2). Assessment included a detailed family and personal enquiry searching particularly for a history of abdominal trauma, drug and alcohol consumption, mumps and other infections, and chest and metabolic diseases. Investigations included blood count (and eosinophil count), liver function tests,

fasting lipids, sugar, amylase, and calcium. Viral titres and sweat tests were performed in many patients. All patients had plain abdominal radiographs and ultrasound scans and all but one underwent endoscopy with retrograde cholangiopancreatography (ERCP).² Pancreatitis was confirmed by one or more of the following: pancreatic calcification or duct calculi; pancreatitis at laparotomy; at least one episode of typical pain requiring hospital admission with serum amylase concentrations greater than three times the upper limit of normal; or unequivocal changes on computed tomography, ultrasound scan, or endoscopic pancreatogram. Most patients fulfilled several criteria.

Follow up ranged from five months to seven years with a mean of 2.9 years since referral or last intervention, whichever was shorter.

Clinical details

The clinical features and duration of follow up are outlined in Tables 1 and 2 and aetiological factors are summarised in Table 3.

Table 1 Children with congenital anomalies who had relapsing acute and chronic pancreatitis

Case No	Anomaly	Sex	Age (years) at		Acute attacks	Chronic pancreatitis	Intervention	Outcome	Follow up (months)
			Onset	Diagnosis					
1	Choledochal cyst	M	4	4	> 5	+	—	Good	39
2	Choledochal cyst + surgery	F	13	13	0	+	See text	Fair	12
3	Anomalous pancreas	F	13	13	5	+	—	Good	48
4	Pancreas divisum	F	13	13	2	+	—	Good	57
5	Pancreas divisum	F	14	14	> 5	—	—	Good	78
6	Pancreas divisum	F	9	14	0	+	—	Good	11
7	Pancreas divisum + mumps	F	5	5	2	—	—	Good	45

Table 2 Children with pancreatitis of uncertain aetiology

Case No	Associations	Sex	Age (years) at		Acute attacks	Chronic pancreatitis	Complications	Intervention	Outcome	Follow up (months)
			Onset	Diagnosis						
8	Alcohol	M	13	13	3	+	—	—	Good	12
9	Diabetes	M	11	11	2	+	—	—	Good	6
10	Diabetes	M	14	14	>5	+	—	—	Good	68
11	Family history	F	2	7	2	+	Malabsorption + cyst	Distal pancreatectomy	Good	38
12	Family history	M	5	5	4	+	—	—	Good	29
13	Family history	F	12	12	1	+	Cyst	Percutaneous drainage	Good	5
14	None	F	5	10	1	+	—	—	Good	19
15	None	M	15	15	3	±	—	—	Good	63
16	None	M	8	15	3	+	—	—	Good	24
17	None	F	8	8	3	—	—	—	Good	43
18	None	F	6	12	>5	+	—	Sphincterotomy (elsewhere)	Fair	24
19	None	M	6	8	1	±	—	—	Good	17
20	None	M	12	12	>5	+	—	—	Fair	42
21	None	M	13	13	4	+	Malabsorption + cyst rupture	Emergency Whipple	Poor	86
22	None	M	6	11	1	+	Calcification + cyst	Puestow	Good	13
23	None	M	2	2	>5	±	Cyst	Percutaneous aspiration	Good	29
24	None	M	4	11	4	+	Cyst	Percutaneous aspiration	Fair	21
25	None	F	7	7	3	+	Cyst, calculi + stricture	Internal drainage Failed endoscopic treatment Distal pancreatectomy	Poor Good	 42

Table 3 Summary of aetiologies in patients with relapsing acute and chronic pancreatitis

<i>Congenital anomalies</i>		7
Choledochal cyst	2	
Pancreas divisum	4*	
'Anomalous pancreas'	1	
<i>Uncertain</i>		18
Alcohol related	1	
With diabetes	2	
Family history	3	
No associations	12	
Total		25

* One also had mumps.

Congenital anomalies and pancreatitis. Seven patients had pancreatobiliary anomalies. Two had cystic dilatation of the biliary tree with a long common biliary and pancreatic channel (Fig. 1). One of these has done well with conservative management but the other (case 2) required multiple operations including biliary revision and extensive distal pancreatic resection; she has since remained reasonably well on enzyme supplements and has no diabetes. Duodenostomy was performed in infancy for duodenal obstruction attributed to an abnormally shaped pancreas in one patient (case 3) who developed chronic pancreatitis in early adolescence; other aetiological factors are absent and it is concluded that the underlying

anomaly (or related surgery) are responsible. This patient is well with dietary fat restriction.

Four patients have the pancreas divisum anomaly (Fig. 2); in three of these there is no other aetiological factor but in one (case 7) the first episode of pancreatitis was associated with mumps contact, and later titres were positive. Conservative management has been effective in all four.

Idiopathic pancreatitis. No definite aetiology has been established in 18 patients, but one drank moderate amounts of alcohol, two have diabetes, and three have a family history.

One boy aged 15 had drunk an average of two pints of beer per day (approximately 40 g ethanol) for three years before presenting with chronic pancreatitis. In no other case was alcohol consumption other than trivial, but two patients had dramatic precipitation of symptoms within a few hours of minimal exposure.

In two boys aged 11 and 14 years, with poorly controlled diabetes and secondary hyperlipidaemia, pancreatic symptoms have been relieved with better diabetic control.

Three patients had positive family histories for pancreatitis (Fig. 3). One girl who presented at the age of 7 years with a five year history of abdominal pain had suffered two episodes of acute pancreatitis;

Fig. 1 Pancreatitis with choledochal cyst.

(a) Endoscopy with retrograde cholangiopancreatography showing a long common channel (large white arrow) with strictured origin of common bile duct (small white arrow), and pancreatic duct (black arrow).

(b) Air cholangiogram showing gross cystic dilatation of the common bile duct (arrow).

there was pancreatic calcification and she subsequently developed a pseudocyst. Operative management was successful and she remains well three years later. The second presented at the age of 5 years after four episodes of acute pancreatitis, with chronic pancreatitis on ultrasound and ERCP. He has done well with conservative management (apart from two mild acute attacks) during almost three years of follow up. The third patient (whose father died unexpectedly while on steroids for rheumatoid arthritis and was found to have haemorrhagic pancreatitis at necropsy) presented with a severe episode of acute pancreatitis and developed a pseudocyst which required prolonged percutaneous drainage. Despite the finding of severe abnormality at ultrasound and ERCP, she has been well over follow up of five months.

Thorough investigation showed no aetiological factors in the remaining 12 patients. Sweat tests have not been performed in three who are all now over 18 years of age and have no chest symptoms or evidence of malabsorption, making cystic fibrosis most unlikely. Ascariasis was felt to be adequately excluded by the absence of eosinophilia or identified obstructing helminths.

Seven of this group have remained well with only single acute exacerbations or minor chronic symptoms. One patient with established chronic pancreatitis subsequently developed an haemorrhagic cyst, spontaneous rupture of which necessitated an emergency Whipple's procedure; he has now been pain free over seven years' follow up but malabsorption, which was present preoperatively, remains a major problem. The ninth patient had calcific chronic pancreatitis from the age of 10 years (Fig. 4); he developed a large pancreatic pseudocyst which led to a Puestow procedure at the age of 11 years, with good results.

The remaining three patients presented to us with pseudocysts after repeated episodes of acute pancreatitis; investigations showed chronic pancreatitis in all cases. Two boys treated by percutaneous cyst aspiration were well at follow up at 21 and 29 months. A girl who had had surgical cyst drainage when aged 7 years had persistent symptoms, and ERCP at the age of 13 showed a pancreatic duct stricture. She eventually underwent distal pancreatectomy and removal of duct calculi at the age of 18 years, since when she has remained well.

Fig. 2 *Pancreas divisum.*

(a) Tiny ventral pancreatogram (arrowed), obtained after cannulating the main papilla of Vater.
 (b) Pancreatogram of the dorsal segment obtained by cannulating the accessory papilla (arrow). The endoscope has been removed. The duct shows calibre irregularity indicating chronic pancreatitis.

Discussion

Advances in imaging techniques have made it easier to investigate and document pancreatitis at all ages.² Our patients have all been secondary referrals from

general paediatricians and surgeons. The series does not include patients with uncomplicated acute pancreatitis or three children with traumatic pancreatitis seen during the same period, and thus comprises a different population from those studied by others,³⁻⁶

Fig. 3 Patients with positive family histories (index cases ringed).

perhaps explaining the relative paucity of cases where drugs or infections could be implicated.⁴ These 25 children constitute a very small proportion of some 1000 patients with chronic and relapsing pancreatitis investigated by this unit during the same period.

Aetiological aspects. Most cases of relapsing acute and chronic pancreatitis in adults can be attributed to alcohol abuse or gall stone disease. None of our children had gall stones—these are rare in childhood but can cause pancreatitis.⁶⁻⁸ Substantial alcohol intake is unusual in children in Britain, although this is perhaps a growing problem which may tend to affect the incidence of pancreatitis in later age groups.

Pancreatitis may be associated with metabolic

disease. Increased triglyceride concentrations (as in familial hypertriglyceridaemia) may cause pancreatitis, perhaps due to release of toxic free fatty acids within the gland. This may explain the pancreatitis seen in our children with poorly controlled diabetes. It is equally likely, however, that these children have combined exocrine and endocrine disease since most poorly controlled diabetics do not develop pancreatitis. We saw no case of pancreatitis associated with hypercalcaemia—this occurs rarely in children and is usually acute. Pancreatitis can be associated with α_1 antitrypsin deficiency.⁹

Childhood pancreatitis has been described in association with a number of congenital malformations including duodenal and gastric duplications, congenital pancreatic duct stenosis, and intrapapil-

Fig. 4 Idiopathic calcific pancreatitis.

(a) Plain radiograph after insertion of the duodenoscope showing a large calcified stone in the head of the pancreas (arrow).

(b) Endoscopic pancreatogram confirming multiple calculi within a grossly dilated duct system.

lary pancreatic duct diverticula.¹⁰⁻¹⁴ The overall incidence of seven children with congenital defects among 25 with pancreatitis in this series diverges strikingly from adult experience.

Children with congenital bile duct cysts (choledochal cysts) have a long channel common to biliary and pancreatic ducts, which may well explain their increased risk of pancreatitis. The most common congenital anomaly is pancreas divisum, in which most of the pancreas drains through Santorini's duct and the accessory papilla.¹⁵ One of our four patients with pancreas divisum may also have had mumps but this alone rarely leads to relapsing or chronic disease. No alternative aetiological factors were identified in the others. Pancreas divisum occurs in at least five per cent of the population and many authorities believe that it can result in

obstructive pain and pancreatitis,^{15 16} the frequency of 16% in this series adds some support to this hypothesis which we have explored more thoroughly in adults.

Familial pancreatitis is now well recognised and since the first kindred was described by Comfort in 1952¹⁷ more than 40 families with hereditary chronic pancreatitis have been recognised from many parts of the world. The true incidence is unknown. Stafford and Grand have recently reviewed the salient features.⁹ The condition seems to be inherited as an autosomal dominant with variable penetrance and clinical patterns are similar for different members of the same kindred, with some differences between families. There are twin peaks of incidence at about the ages of 10 and 17 years (the latter perhaps precipitated by alcohol) but patients

may present in old age. Pancreatic calcification often occurs in the first decade. An association with abdominal carcinoma remains unconfirmed but may exist in some kindreds.¹⁸⁻²⁰ Despite Kattwinckel's assertion that hereditary chronic pancreatitis is the likely diagnosis in childhood chronic pancreatitis when cystic fibrosis, trauma, and metabolic disease have been excluded,¹⁸ we do not feel that we can assign this diagnosis to our three patients with a positive family history since their pedigrees are not conclusive.

No cause is evident in many adults with pancreatitis; our children with idiopathic pancreatitis may well represent the younger end of the same spectrum. Autoimmune phenomena may be involved²¹ and HLA associations have been suggested.²² Since increasing alcohol consumption seems to have a direct, albeit exponential, relation to the incidence of pancreatitis, it is to be expected that such associations are found in alcoholic and idiopathic chronic pancreatitis.²³⁻²⁴ Calcific pancreatitis is more common in children in equatorial Africa and southern India and may be associated with malnutrition.²⁵ This type is rare in Western children.²⁶

Management and complications. Management has been tailored to the individual case and we have followed the same somewhat arbitrary principles used for adults. A strict low fat diet without alcohol was recommended in every case. Some patients seemed to benefit from enzyme supplements even where exocrine insufficiency was not found.²⁷ Persistent clinical steatorrhoea was a problem in only one patient (case 23) despite a full regimen of pancreatic enzymes and dietary measures. He is the one patient in the series with growth retardation and delayed puberty.

Seven patients with pseudocysts were studied. In children these usually result from trauma¹⁻²⁸⁻²⁹ but our three traumatic cases were excluded. Two of the children had well documented chronic idiopathic pancreatitis before the development of their pseudocysts. The third had definite signs of chronic pancreatitis at presentation to us, with a previous history of acute pancreatitis complicated by pseudocyst which seemed to have resolved spontaneously. The remaining four developed pseudocysts shortly after acute (idiopathic) pancreatitis and three subsequently had features of chronic pancreatitis despite prompt cyst aspiration or drainage. All, however, remain well at follow up of more than one year. Chronic pancreatitis may follow acute pancreatitis complicated by pseudocyst in the absence of other recognised causes.²³ Cooney advocated internal pseudocyst drainage for children;²⁹ this is logical in

traumatic cases with duct damage but we recommend a trial of percutaneous aspiration in most patients when there is no duct obstruction.

Surgery was required in five of our children; overall results have been good (Table 2). Several authors have made recommendations concerning the surgical approach in hereditary chronic pancreatitis. Pancreatojejunostomy is advocated for children with dilated ducts; poor results may follow partial pancreatectomy or sphincterotomy alone, and total pancreatectomy is reserved for patients with end stage disease.³⁰⁻³¹

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