Pancreatogram in cholestasis

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SUMMARY Endoscopic retrograde pancreatograms have been examined in patients presenting with cholestasis caused by either primary sclerosing cholangitis (13 subjects), or high cholangiocarcinoma (15 subjects), and in normal individuals (13 subjects). Pancreatograms were reported by two independent observers who had no knowledge of the diagnosis in any case and abnormalities were graded using a conventional scoring system. Pancreatograms were abnormal in 77% of cases of primary sclerosing cholangitis and in 60% of cholangiocarcinoma patients. These abnormalities usually consisted of side branch irregularities, although in five patients with primary sclerosing cholangitis and in two with cholangiocarcinoma, the main pancreatic duct was also markedly irregular.

Epstein *et al*¹ have reported that endoscopic pancreatography is frequently abnormal in subjects with primary biliary cirrhosis. This led to the suggestion that primary biliary sclerosis may be a multisystem 'dry gland' disease involving the liver and pancreas. Abnormal pancreatic morphology, however, was also found by this group in three out of 20 subjects with primary sclerosing cholangitis. This suggests that cholestasis alone may result in pancreatic abnormalities. We have therefore reviewed a consecutive series of endoscopic pancreatograms from patients with primary sclerosing cholangitis and cholestasis because of high common bile duct or common hepatic duct tumours.

Methods

PATIENTS

Endoscopic retrograde cholangiopancreatograms obtained from a consecutive series of 13 subjects with primary sclerosing cholangitis, 15 patients with bile duct tumours and an age and sex matched control group of 13 patients were studied. None abused alcohol or had a clinical history of pancreatitis.

The diagnosis of primary sclerosing cholangitis was established by the findings of typical biliary stricturing and beading in subjects with cholestasis and negative mitochondrial antibody test. Eight of these also had ulcerative colitis. The age ranged

from 25-72 years with a mean of 43 years, which was significantly less than that of the biliary tumour group. Six individuals had undergone cholecystectomy but in no case was there evidence of secondary sclerosing cholangitis because of recurrent sepsis.

Bile duct tumour was diagnosed by the finding of a high bile duct or common hepatic stricture with intrahepatic duct dilatation. Fine needle biopsy confirmation was available in seven cases, and three had been diagnosed at laparotomy. The age range of this group was 47-92 years, with a mean of 76 years. Four subjects had undergone cholecystectomy.

The control group comprised subjects in whom all investigations for abdominal pain eventually proved negative. None had undergone cholecystectomy. The age range was 24-97 years, with a mean of 53 years.

Pancreatograms were reported independently at two sittings, by two experts (PBC and MC). These observers were unaware of the diagnosis and the cholangiograms were made unavailable. Pancreatograms were scored as: 0, normal; 1, possibly abnormal; 2, abnormal; and 3, grossly abnormal. The total score for each pancreatogram was determined by adding the score of each observer. Reproducibility, as judged by reporting a proportion of the same pancreatograms at an interval of two months, was excellent for both observers.

Results

Examples of abnormal pancreatograms are presented in Figures 1-3. Radiological assessment is

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Fig. 1 *Grade I (possibly abnormal) pancreatogram from 32 year old woman presenting with primary sclerosing cholangitis. Main duct is probably normal while the secondary radicals are clumped.*

summarised in the Table. Only three subjects with primary sclerosing cholangitis were considered by both observers to have a normal pancreatogram. Abnormalities in the remainder comprised side branch clumping and irregularity in five, additional irregularity of the main duct was present in five subjects. The total score of this group was 32, maximum possible score (if all pancreatograms had

grade 3 changes) being 78.

Both observers agreed that six subjects with bile duct tumours had normal pancreatograms. The remainder were abnormal, two grossly. The total score of this group was 28, maximum possible score 90.

Possible abnormalities in the pancreatograms of the control group were noted in seven instances by

Fig. 2 *Grade II (abnormal) pancreatogram from 42 year old man with inoperable hilar cholangiocarcinoma. Major duct is slightly irregular; the side branches are markedly abnormal throughout the gland.*

Fig. 3 Grade III (grossly abnormal) pancreatogram of 76 year old woman with cholestasis due to cholangiocarcinoma. Major and minor ducts are all severely irregular and tortuous.

the two observers, though in no case did a pancreatogram score more than one unit. The maximum possible score of this group was 78.

Discussion

We have shown abnormalities of the pancreatogram in patients with primary sclerosing cholangitis and bile duct tumour, the frequency and severity of changes being similar in both groups (32/78 and 22/90 respectively). The scoring system used in this study was designed to minimise the variation in reporting which is inevitable between two independent observers. Although there were indeed

minor differences, usually of the order of one unit in reporting any one pancreatogram, one reporter did not consistently score more heavily than the other. The total scores for each observer were thus similar (35 and 32).

We have confirmed the observation of Epstein *et al* that there is an association between primary sclerosing cholangitis and an abnormal pancreatogram. Our additional findings of pancreatic abnormalities in patients with high bile duct tumours suggests that such abnormalities are secondary to cholestasis and argues against the suggestion that primary sclerosing cholangitis is primarily a multi-system 'dry gland' disease.

The mechanism by which cholestasis leads to abnormal pancreatography is not clear. It is widely believed that the pancreatic duct becomes more dilated and irregular with advancing years,² but this has not been documented in endoscopic studies,³ and it is unlikely that this accounts for our observation in the bile duct tumour patients. Activation of pancreatic enzymes by raised circulating bile acids is unprecedented. It is possible that altered metabolism of gastrointestinal hormones may be responsible; it is known, for example, that cholecystokinin has a trophic effect upon the hamster pancreas,⁴ but we have no evidence to support such a mechanism.

Table Summary of endoscopic pancreatography in control, primary sclerosing cholangitis, and bile duct tumour patients

Radiological assessment	Pancreatograms (no)		
	Control (n=13)	Primary sclerosing cholangitis (13)	Bile duct tumour (15)*
Grossly abnormal (score 3)	0	4	4
Abnormal (score 2)	0	6	5
Possibly abnormal (score 1)	7	8	6
Normal (score 0)	19	8	7
Total score	7†	32	28

* Eight pancreatograms from this group were inadequate.

† Differs from the other two groups at $p < 0.01$ ($\chi^2 = 35.1$).

References

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