Retroperitoneal fibrosis associated with pancreatic disease

A. JOHN WEBB*  
M.B., Ch.B., F.R.C.S.  
Senior Surgical Registrar  
Queen Elizabeth Hospital, Birmingham

P. DAWSON-EDWARDS  
M.B., Ch.B., F.R.C.S.  
Consultant Surgeon and Urologist  
Queen Elizabeth Hospital, Birmingham

EMPHASIS in the literature of retroperitoneal fibrosis is rightly directed towards the urinary tract as this is where its most serious effects are produced (Raper, 1956; Talbot & Mahoney, 1957).

Gastro-intestinal symptoms may characterize the early stage of the illness and a gastro-intestinal tract origin cannot be excluded (Ormond, 1965). In addition, the duodenum, pancreas, mesenteric root, small and large bowel may be involved by the fibrosis (Paull, Causey & Hodges, 1955).

Our studies on a total of fifteen patients with retroperitoneal fibrosis have indicated that the benign and malignant forms are difficult to distinguish.

In two patients, the fibrosis was clearly associated with pancreatic lesions one benign and the other malignant—and each demonstrates the usual problems in diagnosis and management (Hume, Erb & Stevens, 1963).

Case No. 1: Miss R.A., age 20

A mild abdominal injury sustained in October 1961 while playing hockey, was followed by some lumbo-dorsal discomfort. In October 1962 this girl presented with polydipsia, frequency of micturition, left loin and groin pain dating back some months. A tender mass was felt in the left loin and an IVP showed poor renal function on the left side with a left ureteric block on retrograde pyelography at lumbar 2 level. Surgical exploration was advised.

Operation (P.D.E., 6 October 1962)

Through a left renal incision, a hard mass was found involving the aorta, duodeno-jejunal flexure and left renal hilum. Malignancy was diagnosed but the histological report was that of fibrous inflammatory tissue. Abdominal exploration disclosed a thick-walled cyst originating from the pancreatic body; 50 ml of clear fluid was aspirated and tube drainage was instituted. Histological examination demonstrated epithelium consistent with a pancreatic origin. The diagnosis of a traumatic pancreatic cyst was made. Thereafter a persistent urinary infection with *E. coli* and *Staph. albus* developed. Intermittent mild loin pain persisted and in December 1962 nausea, vomiting, lassitude, backache and right-sided abdominal pain returned with a palpable left hypochondrial mass.

An intravenous pyelogram in March 1964 showed good right-sided secretion but on the left side, non-function and a minimum of renal tissue. At this stage, Dr W. Trevor Cooke undertook a full gastro-intestinal investigation.

Investigations

- Haemoglobin, 70%.
- Serum urea, 18 mg/100 ml. Serum albumin, 4.4 g/100 ml. Serum globulin, 3.1 g/100 ml.
- Barium enema: Extrinsic compression of the hepatic flexure was noted.
- Barium meal and small bowel studies: The stomach was displaced anteriorly with partial extrinsic obstruction of the duodenal third part.

On 22 June 1964 laparotomy confirmed a left abdominal cystic mass (4 in. diameter) arising from the pancreatic body, with evidence of early portal hypertension. Internal drainage of the cyst into the stomach was performed. In spite of adequate hydration, the patient became anuric with right loin pain and tenderness. Retrograde pyelography showed ureteric obstruction.

Exploration on 12 July 1965 revealed a right ureteric block from fibrous tissue at L3 level extending across the mid-line from the left side. The ureter was completely freed, with intra-peritoneal transposition.

Her progress was poor with recurrent right loin pain and urinary infection; intravenous and retrograde pyelography in November 1964 confirmed further right ureteric block, on this occasion at the pelvic brim. The serum urea level was 88 mg/100 ml, haemoglobin 58%.

Operation, 23 November 1964

This confirmed the new site of obstruction some 5 cm below the previous narrowing. Ureterolysis and a further intraperitoneal transposition was performed but the ureter was noted to be involved in the fibrotic process (Fig. 1).

An intravenous pyelogram in March 1965 showed

*Present address: Bristol Royal Infirmary.
improvement on the right side but because of her precarious renal function, a left-sided ureterolysis was carried out. This extended over 10 cm, requiring a considerable intraperitoneal transposition. The left kidney was encased in fibrous tissue and to date no function has reappeared. Her pyuria with *E. coli* infection persists.

**Investigations**

Serum albumin, 3.9 g/100 ml. Serum globulin, 3.9 g/100 ml.

Electrophoresis: raised alpha 3 and gamma fractions.

Intravenous pyelography (November 1965) demonstrated dilated and blunted calyces on the right side (Fig. 2).

**Comment**

The extensive and crippling fibrosis in this girl is considered to be the sequel of a traumatic pancreatitis with cyst formation. In common with other reports, malignancy was suspected at the first operation (Dineen, Asch & Pearce, 1960; Samellas, 1961). A connection between fibrosis and trauma has been suggested but not clearly substantiated in the reports of MacLean (1954) and Hackett (1958).

The operative appearance of portal hypertension together with the radiological evidence of duodenal and colonic obstruction is of interest. Portal hypertension has been reported by Inkley & Abbot (1961), Eiseman & Yeoh (1962) and Schneider (1964); bleeding from oesophageal varices may develop. The first report of biliary tract involvement was that of Raper (1956) but others have followed (McMillan, Swarts & Knudtson, 1964; Hardy, 1962) and retroperitoneal fibrosis appears to be one form of sclerosing cholangitis (Bartholomew *et al.*, 1963). In another case from our series hepato-spleno-megaly with irregular fatty change and portal round-cell infiltration was present in the liver biopsy (Webb & Dawson-Edwards, 1966).

Intra-abdominal fibrosis may be very extensive and either diffuse or nodular in form. Patoir & Spy (1962) described a case with recurrent icterus, hepatomegaly and radiological evidence of duodenal and transverse colon deviation and compression. At laparotomy the fibrotic plaque extended to the diaphragm and involved the mesenteric root and colon.

It appears that by the time this girl developed anuria her left kidney was irretrievably damaged. Her present state of chronic pyelonephritis gives cause for concern and urinary diversion by a uretero-ileo-cystoplasty (Hache, Utz & Woolner, 1962) may be required or alternatively, ureterotomy and T-tube drainage (Marion, 1935; MacKelvie & McKelvie, 1963). The functional recovery of fibrotic ureters is uncertain and deserves further study.

**Case No. 2: Mr L.S., age 54**

For 10 years this man had suffered intermittent epigastric pain appearing an hour after meals; antacids had been prescribed on suspicion of a duodenal ulcer. In February 1965 severe pain had persisted for 10 weeks with associated vomiting and one episode of melaena. He had experienced
aching in the hips, thighs and buttocks for 3 years. A left orchidectomy had been performed in 1942 for seminoma. Examination elicited epigastric tenderness. Many investigations were carried out under the care of Dr Trevor Cooke, and some relevant ones are as follows:

Haemoglobin, 90%. WBC, 10,000/mm³, normal differential count.

Serum proteins, 6.59 g/100 ml. Albumin, 4.95 g/100 ml. Globulins, 2.69 g/100 ml.

Faecal fat estimations, 4.3 g/fat/24 hr excretion.

Serum amylase, 204 units. Serum bilirubin, 0.2 mg/100 ml.

Serum calcium, 9.5 mg/100 ml. Serum phosphorus, 4.1 mg/100 ml.

Several mid-stream urine examinations: E. coli cultured on occasions.

A barium meal examination showed no duodenal ulcer but outlined a calcified lesion with small scattered satellite opacities. A pancreatic or renal lesion was suspected and intravenous pyelogram produced normal right-sided function with none on the left (Fig. 3). In view of these findings, he was transferred to the care of one of us (P.D.E.). Further questioning established that for a year
bilateral loin, groin and hip pain had been increasing with vomiting and frequency of micturition.

On examination the blood pressure was 140/110 mmHg, with left loin tenderness; the serum urea level was 65 mg/100 ml.

Cystoscopy (25 August 1965) indicated some increase in vascularity at the bladder base and easy passage of a ureteric catheter to the left renal pelvis. Retrograde pyelography showed a ureteral stenosis 1.5 cm below the left pelvi-ureteric junction (Fig. 4). The calcification was regarded as perinephric; possibly a chronic tuberculous abscess. Operation was performed (1 September 1965) through a left loin incision without a firm pre-operative diagnosis. The left kidney was hydro-nephrotic with a large rock-hard mass arising from the pancreatic body lying to the medial side of the renal pelvis. The appearances were those of a pancreatic tumour. The peritoneum was opened and the lesion deemed to be irremovable. Further assessment showed retroperitoneal fibrosis to be present extending across the mid-line and appearing to deviate the aorta to the right side. The left ureter was involved in fibrosis over some 4 cm length and ureterolysis was performed (Fig. 5). The ureteric wall was thickened. In addition to the fibrosis some myxomatous tissue was curedt from between the ureter and the calcified mass. This was submitted to both histological and cytological examination. The histological report described masses of mucin, containing haematoxophil granules and cellular fibrous tissue with clumps of a regular low columnar epithelium. The origin of these cells was obscure but neoplasia was not apparent.

His post-operative recovery was good. The serum proteins and electrophoretic strip were examined and found to be normal. His serum urea level remained slightly elevated to 60 mg/100 ml.

**Progress report**

In November 1965 the patient complained of lumbo-sacral pain; radiologically Paget's disease of the sacrum was probable but the pain could equally have been due to the retroperitoneal plaque. Intravenous pyelography failed to show a return of function.

**Comment**

A biopsy of the actual pancreatic tumour was not taken, as specimens from around the ureter and the plaque were considered to be adequate for diagnostic purposes. Both fibrous tissue and calcified myxomatous tumour were obtained. Whereas the histological opinion on this latter material did not exclude malignancy, a cytological assessment on smears made from it was definite (Class V diagnosis). Amidst a PAS positive stroma were groups of malignant cells consistent with a pancreatic origin (Figs. 6 and 7).

The clinical presentation of epigastric pain simulating a duodenal ulcer is characteristic of cystic pancreatic tumours (Cornes & Azzopardi, 1959); likewise the episode of melaena occurring earlier in the year. The mechanism of intestinal bleeding is discussed by Campbell & Cruickshank (1962) who invoke either on erosive gastritis from local pressure or local invasion.

The radiological appearances are particularly clear and post-operative re-assessment suggests they are typical of a pancreatic cyst-adenocarcinoma. Cystadenoma of the pancreas is a rare tumour and carcinomatous change even more unusual (Speese, 1915; Lichenstein, 1934; Smith, 1958). The satellite calcification in our case is notable and is a firm indication of local malignant spread with focal deposits of calcium. The calcification was confirmed by a Von Kossa stain for phosphate on the histological material. Haukol & Melamed (1950) reported two malignant pancreatic cysts both of which demonstrated irregular fragmentary and spicule calcification. They regarded calcification as an important radiological diagnostic feature and in one of the cases reported by Cornes & Azzopardi
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FIG. 6. Case 2: Cytological smear of the peri-ureteric tissue. The PAS positive stroma (St) and calcified granules are seen on the left with a group of malignant cells showing an acino-papillary pattern. Jenner-Giemsa, × 320.

FIG. 7. Case 2: Cytological view of the epithelial cells. Apart from their obvious malignancy these appearances are consistent with a carcinoma of pancreatic origin. A malignant karyorrhexis is seen (K). Jenner-Giemsa, × 800.

(1959) the rim of the cyst was thinly outlined. Campbell & Cruickshank (1962) reported the largest series in the literature of fourteen cystadenomata and three cystadenocarcinomata—in only two were foci of calcification seen and these were microscopic. Cullen, Remine & Dahlin (1963) reporting sixteen cases of cystadenocarcinoma from the Mayo Clinic, do not mention calcification but note the thick colloid jelly-like material found in these tumours. Warren, McDonald & Veidenheimer (1964) collected 148 cystic pancreatic lesions from
the Lahey Clinic of which twelve were cystadenocarcinomata; three had appeared in the last 8 years; the 5-year survival rate following all forms of surgery was 43%.

Local spread in the form of mucoid deposits, as in our case, is most exceptional. Willis (1960) records an example of mucoid secondaries in the cisterna chyli, lungs and hilar lymph nodes. The primary was a mucus-secreting pancreatic carcinoma; retroperitoneal fibrosis was not present.

Pancreatic lesions have been reported as confusing a urological diagnosis; Ormond, Wadsworth & Morley (1943) quoted a patient where the right urinary tract was symptomatic from and grossly distorted by a cystic tumour in the pancreatic head. Thompson & Culp (1963) describing nine perplexing cystic masses near the kidney, include one pancreatic cystadenocarcinoma and one calcified cystic hypernephroma. This present case appears to be the first report of retroperitoneal fibrosis resulting from myxomatous deposits of pancreatic cystadenocarcinoma although pancreatic carcinoma was found at autopsy in the patient reported by Kaude (1966).

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References


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A. John Webb and P. Dawson-Edwards

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