Diagnostic difficulties in patients with a pancreatic mass

M R Zeiderman, A Wyman, H A Euinton, J M Simms, K Rogers

Biopsy specimens of pancreatic masses should be obtained before assuming a diagnosis of cancer.

University Department of Surgery and Department of Radiology, Northern General Hospital, Sheffield
M R Zeiderman, FRCS, lecturer in surgery
A Wyman, FRCS, lecturer in surgery
H A Euinton, FRCR, consultant radiologist
K Rogers, FRCS, professor of surgery

Department of Surgery, Chesterfield and North Derbyshire Royal Hospital, Chesterfield
J M Simms, FRCS, consultant surgeon

Correspondence to: Mr M R Zeiderman, Royal Hallamshire Hospital, Sheffield S10 2JF.

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Although surgery for pancreatic carcinoma offers the only hope of cure, resection is associated with a high morbidity and a perioperative mortality which in some series has been as high as 40%.¹ In those who survive operation the outlook remains poor: more than 80% of patients with adenocarcinoma of the pancreas die within 12 months and only 1-2% survive five years.^{1,2} As resection is inappropriate for most patients internal biliary drainage with an endoprosthesis has become widely accepted as palliative treatment for malignant extrahepatic biliary obstruction,^{3,4} surgery being reserved primarily for those patients in whom the placement of an endoprosthesis is not possible or who develop duodenal obstruction.

As the possibility of prolonged survival in patients with pancreatic carcinoma is remote a nihilistic approach can easily be adopted. After biochemical and radiological investigation many patients with obstructive jaundice and a mass in the head of the pancreas are treated by insertion of an endoprosthesis without a tissue diagnosis. While subsequent pathological findings may concur in up to 96% of patients the following cases show that failure to make a definitive tissue diagnosis before treatment may have serious consequences for the few patients who have a potentially treatable condition or benign disease.

Case 1

A 50 year old woman was admitted with a one week history of progressive jaundice, dark urine, and pale stools. Examination showed hepatomegaly and an epigastric mass 9 cm in diameter. Results of biochemical investigations were as follows: haemoglobin concentration 126 g/l, white cell count $4.83 \times 10^9/l$ with a normal differential, bilirubin concentration 115 $\mu\text{mol/l}$, alkaline phosphatase concentration 1125 IU/l, alanine aminotransferase concentration

186 IU/l. Results of coagulation screening were normal. An ultrasound scan showed a dilated intrahepatic and extrahepatic biliary tree (the common bile duct was 1.3 cm in diameter) and a retroperitoneal mass in the region of the uncinate process of the pancreas, displacing the aorta laterally. There was no evidence of hepatic metastases. A differential diagnosis of pancreatic carcinoma or lymphoma was made. A smooth stricture of the distal common bile duct was identified on percutaneous transhepatic cholangiography and an internal biliary endoprosthesis (Carey-Coons) was inserted. The specimen obtained on ultrasound guided biopsy of the epigastric mass comprised fatty tissue only. When the patient was reviewed in the clinic two weeks later repeat examination showed cervical lymphadenopathy. A subsequent lymph node biopsy specimen provided histological evidence of a follicular non-Hodgkins lymphoma. Chemotherapy resulted in complete remission and within eight weeks there was no clinical evidence of disease. Nine months later she remained in remission with no pancreatic abnormality on ultrasonography or computed tomography. The endoprosthesis was removed at laparotomy. She remained well a year later.

Case 2

A 57 year old West Indian man presented with a short history of malaise and jaundice. He had maturity onset diabetes, and this had recently become difficult to control with oral hypoglycaemic drugs. In addition to a raised blood glucose concentration his liver function test results were also deranged, with a mixed hepatocellular and obstructive pattern (bilirubin concentration 130 $\mu\text{mol/l}$, alanine aminotransferase concentration 799 IU/l, γ -glutamyltransferase concentration 1910 IU/l, alkaline phosphatase concentration 1010 IU/l). Results of coagulation screening were normal. An abdominal ultrasound scan showed dilatation of the common bile duct (by 1 cm in diameter) as far as the head of the pancreas, which measured 3.8 cm and had a homogeneous texture. Computed tomography showed the abnormality in the head of the pancreas to be a well circumscribed mass which did not seem to be infiltrating surrounding structures (figure). Percutaneous transhepatic cholangiography showed a dilated common hepatic duct with a smooth stricture immediately below the origin of the cystic duct extending to the ampulla. The appearances were thought to be due to extrinsic compression from a pancreatic tumour, and an internal biliary endoprosthesis (Carey-Coons) was inserted. No biopsy specimen was taken.

When reviewed one month later the patient was well and without clinical or biochemical evidence of jaundice. Indeed he continued to remain well, raising doubts as to the clinical diagnosis. Repeat computed tomography six months later showed no focal lesion within the pancreas. Ten months after the initial procedure he returned with recurrent jaundice due to blockage of the endoprosthesis. A repeat ultrasound scan showed no evidence of malignant disease. At laparotomy the findings were a thickened pancreas together with patches of fat necrosis, suggesting pancreatitis. There was no evidence of malignancy.

Computed tomogram of upper abdomen showing well circumscribed mass (arrowed) within head of pancreas (case 2)

Because of a fibrous stricture of the common bile duct around the endoprosthesis, most marked at the confluence of left and right hepatic ducts, it was necessary to fashion a hepaticoduodenostomy. The histological appearance of the common bile duct was consistent with a chronic inflammatory process. He made an uneventful recovery, and although his liver enzyme concentrations remained raised (alanine aminotransferase 65 IU/l, alkaline phosphatase 612 IU/l) he remained well 24 months later.

Case 3

An 81 year old white man presented to the outpatient clinic with a two week history of painless obstructive jaundice, having previously been well and without symptoms. Apart from a mild icterus examination was unremarkable. Results of biochemical investigations were as follows: haemoglobin concentration 114 g/l, white cell count $26.9 \times 10^9/l$ ($14.8 \times 10^9/l$ neutrophils, $11.0 \times 10^9/l$ lymphocytes), alkaline phosphatase concentration 1106 IU/l, γ -glutamyltransferase concentration 299 IU/l, bilirubin concentration 38 $\mu\text{mol/l}$. An ultrasound scan showed a dilated intrahepatic and extrahepatic biliary tree and a mass in the head of the pancreas. A presumptive diagnosis of carcinoma of the head of pancreas was made, but when the patient was reviewed in the clinic one month later he was no longer jaundiced (bilirubin 18 $\mu\text{mol/l}$), although his liver enzyme profile was still abnormal (alkaline phosphatase 833 IU/l, γ -glutamyltransferase 331 IU/l). A repeat ultrasound scan showed no evidence of dilated bile ducts, although the pancreatic mass persisted.

He was lost to follow up but returned 12 months later in extremis. He was profoundly cachexic but not jaundiced. Abdominal examination showed gross ascites. Results of biochemical investigations were as follows: haemoglobin concentration 97 g/l, white cell count $30.1 \times 10^9/l$. He died 24 hours later. At necropsy there was a dense fibrous mass around the head of the pancreas which had resulted in incomplete obstruction of the extrahepatic biliary tree. The body of the pancreas was also replaced by dense white fibrous tissue. While the right adrenal gland was not obviously enlarged the medulla had a similar macroscopic appearance to the pancreas. Histological appearances in sections taken from both the pancreas and the adrenal glands were consistent with tuberculosis. There was no evidence of pulmonary tuberculosis.

Discussion

These three cases show that an accurate diagnosis is essential in order to identify those patients with potentially curable disease. While differentiation of patients into those with benign disease and those with malignant disease on clinical and laboratory data alone may be difficult, diagnostic rates in excess of 90% have been reported from a combination of ultrasonography, percutaneous transhepatic cholangiography, and computed tomography.⁵⁻⁷

Diagnostic difficulties are most commonly encountered in differentiating between pancreatic carcinoma and chronic pancreatitis, particularly as the two may coexist.⁵ Misdiagnosis occurred in case 2 and probably accounted for the prolonged survival of patients with

"malignant extrahepatic biliary obstruction" reported by others.⁸ Clearly what is needed to help clarify the situation is a tissue diagnosis, yet for many years clinicians have been reluctant to perform biopsy on the pancreas because they have believed that this carries an appreciable risk of bleeding, fistula formation, infection, and even death. However, much of the present day concern that surrounds pancreatic biopsy was generated over 15 years ago because of surgeons' experience of peroperative wedge or core needle biopsy.⁹ With the introduction of finer needles and aspiration cytology the complication rate of peroperative biopsy has been greatly reduced.¹⁰ As various diagnostic techniques for localising pancreatic lesions have become available fine needle aspiration has assumed a new dimension in the diagnosis of pancreatic malignancy. Ultrasonically guided percutaneous fine needle aspiration can yield sufficient tissue for analysis in about 80% of patients, allowing a cytological diagnosis of carcinoma in about 90% of these—an overall clinical success rate of 76%.¹¹ By using an 18 gauge needle (Tru-Cut) to obtain samples for histological examination an accurate diagnosis can be achieved in up to 94% of patients.^{12,13} No false positive results have been reported, and complications are rare despite the passage of the needle through abdominal viscera.

On reviewing the notes of patients with obstructive jaundice who had presented to our hospital over the past five years a histological diagnosis was available in only 25%. With modern techniques for imaging and biopsy this is no longer acceptable. Most patients thought to have inoperable pancreatic carcinoma are given an endoprosthesis; it is important to ensure that the absence of a definitive histological diagnosis does not deny some patients the chance of cure.

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