Mass in the Head of the Pancreas in Cholestatic Jaundice

Carcinoma or Pancreatitis?

SIMON WAPNICK, M.D., F.R.C.S., NAFTALI HADAS, M.D., M.S., ELIAS PUROW, M.D., SAUL J. GROSBERG, M.D., F.A.C.P.

The clinical, biochemical and radiological findings in 16 patients with carcinoma of the head of the pancreas were compared with that of 13 with cholestatic jaundice due to chronic pancreatitis. Patients presenting with malignancy had more severe hyperbilirubinemia (18.5 \pm 2.1 vs 5.6 \pm 1.6 p < 0.001). The course of the bilirubin during the first seven to ten days of hospital admission was the single most accurate test distinguishing carcinoma from pancreatitis. The mean bilirubin rose in carcinoma but fell in pancreatitis (mean net change 15.1 \pm 2.9 vs 3.9 \pm 0.6, p < 0.001). Calcification in the pancreatic region was identified on a flat plate of the abdomen in 8/13 with pancreatitis but 0/16 with malignancy. Preoperative percutaneous transhepatic cholangiography was helpful in defining the site of biliary obstruction but the radiologist was unable to clearly predict the definitive diagnosis in five of the 29 patients. A point score based upon the major significant differences noted, predicted the presence or absence of malignancy in all patients (16/16 vs 0/13, p < 0.01).

IFFICULTY IN DETERMINING whether obstructive jaundice is caused by carcinoma of the head of the pancreas or chronic pancreatitis remains a diagnostic challenge.¹⁰ DiMagno et al.,¹ evaluated prospectively different tests used in the diagnosis of pancreatic carcinoma. They suggested that a positive finding on ultrasound or pancreatic function test should be followed by endoscopic retrograde cholangiography and pancreatography. This series of tests, however, could confirm pancreatic carcinoma in only 80% of cases. Indeed the surgeon is often hard put to make a definitive diagnosis even at laparotomy.^{8,10} The biopsy specimen showing pancreatitis may represent sites remote from a tumor lesion. The surgeons decision is fairly critical as performance of a Whipple operation carries a mortality around 5-10% in specialized centers but much

From the Department of Surgery and Medicine, Veterans Administration Medical Center, Downstate Medical Center, SUNY, Brooklyn, New York

higher elsewhere.^{3,5} The present paper reports the results of a study comparing the clinical biochemical and radiologic features of cholestatic jaundice due to chronic pancreatitis or carcinoma of the head of the pancreas. A point score system was evolved in an attempt to find a more accurate method of distinguishing pancreatitis from carcinoma.

Materials and Methods

Twenty-nine consecutive patients with extrahepatic biliary duct obstruction attributed to pancreatic disease were evaluated between January 1976 and June 1978 at the Brooklyn V A Medical Center. The diagnosis of biliary duct stenosis was confirmed either by percutaneous transhepatic cholangiography (PTC) or intraoperative cholangiography. Clinical manifestations were noted and calcific pancreatitis sought on plain film of the abdomen. The amylase/creatinine clearance ratio (C_{am}/C_{cr}) was determined shortly after admission in some patients from the following formula:

$$\frac{\text{Uam}}{\text{Sam}} \times \frac{\text{Scr}}{\text{Ucr}} \times 100^*$$

Liver function studies including bilirubin, alkaline phosphatase, SGOT, and LDH were determined. The hematocrit and WBC was noted. In all 16 patients with malignancy histological confirmation was

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Reprint requests: Simon Wapnick, M.D., Department of Surgery, VA Medical Center, 800 Poly Place, Brooklyn, New York 11209.

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^{*} Uam—Urine amylase; Scr—Serum creatinine; Sam—Serum amylase; Ucr—Urine creatinine.

| TABLE 1. Point Score to Differentiate Carcinoma | of | the |
|---|----|-----|
| Pancreas from Pancreatitis | | |

| | Carcinoma (+) | Pancreatitis (-) |
|---|---------------------------------------|---------------------|
| Bilirubin | · · · · · · · · · · · · · · · · · · · | |
| admission bilirubin >10 mg/dl | 2 | |
| bilirubin rise* >4 mg/dl | 3 | |
| bilirubin rise* >4 mg/dl after PTC | | |
| of ERCP | 3 | |
| bilirubin fall* $^{+}$ >2 mg/dl after PTC | | |
| of ERCP | | 2 |
| Clinical features | | |
| age <40 years | | 2 |
| palpable gallbladder | 2 | |
| weight loss >20 lb/4 weeks | 1 | |
| Radiologic features | | |
| diffuse calcific pancreatitis | | 2 |
| CBD suggestive of carcinoma‡ | 1 | |
| CBD suggestive of pancreatitis‡ | | 1 |

* Within 7-14 days of admission. \dagger Or return to normal. \ddagger On PTC or ERCP.

obtained. Nine of the 13 patients with pancreatitis had an operative procedure performed to overcome cholestasis. Four patients diagnosed as chronic pancreatitis were not subjected to surgery. In two a pseudocyst in the head of the pancreas resolved spontaneously. Two patients refused surgery. All patients with pancreatitis have been followed up more than 12 months and ten for more than two years after entry into the study. In none of these patients has malignancy subsequently been detected.



FIG. 1. Chronic pancreatitis occurs more frequently in younger patients whereas carcinoma occurs in the older age group.

A point score system was evolved to differentiate chronic pancreatitis from carcinoma of the head of the pancreas. The features and point allocation for scoring are shown in Table 1.

Results

All patients in the V. A. series were male. The age distribution is shown in Figure 1. The mean age of patient admitted with carcinoma was significantly higher than that in pancreatitis ($61.7 \pm 2.6 \text{ vs } 47 \pm 3.9$, p < 0.01). Of the 13 patients with pancreatitis nine were less then 55 years at the time of hospital admission; only two of 16 patients with pancreatic carcinoma were less than 55 years. All four patients less than 40 years had pancreatitis.

The nature, severity, position and duration of pain and amount of weight loss was not helpful in distinguishing between carcinoma and inflammatory disease of the pancreas. Pruritis was common in patients with malignancy (9/16) but rare in those with pancreatitis (2/13) (Table 3). The gallbladder was palpable in 5 of 16 with carcinoma but in none with pancreatitis.



 F_{IG} . 2. Bilirubin recorded on admission. Shaded area indicates overlap of bilirubin values between patients with pancreatitis and carcinoma of the pancreas.

 TABLE 2. Mean ± SEM Values on Admission to Hospital

| | No. | Carcinoma | No. | Pancreatitis | Statistical Analysis |
|-------------|------|----------------|------|----------------|----------------------|
| Age | (16) | 61.7 ± 2.6 | (13) | 47 ± 3.9 | p < 0.01 |
| Weight loss | (13) | 24.6 ± 5.9 | (8) | 12.8 ± 3.9 | NS |
| Bilirubin | (15) | 18.5 ± 2.1 | (13) | 5.6 ± 1.6 | p < 0.001 |
| Alk. phos. | (16) | 788 ± 135 | (13) | 680 ± 157 | NS |
| Amylase | (13) | 178 ± 53 | (9) | 393 ± 149 | NS |
| ACCR | (7) | 9.7 ± 3.7 | (6) | 6.3 ± 0.6 | NS |

NS-not significant.

Jaundice was seen in 8/13 with pancreatitis; it was present in all patients with carcinoma.

The mean (\pm SEM) bilirubin in patients admitted with malignancy was significantly higher than that encountered in pancreatitis (18.5 \pm 2.1 vs 5.6 \pm 1.6, mg/dl, p < 0.001) (Fig. 2). The mean bilirubin level declined significantly (p < 0.02) during the second week after hospital admission in pancreatitis (Table 2) and rose significantly in carcinoma (Fig. 3). The highest bilirubin recorded between the seventh and fourteenth days after hospital admission was above 9 mg/dl in 16/16 patients with carcinoma and 0/13 in patients with pancreatitis (p < 0.05) (Fig. 3). In those with equivocal changes on P.T.C. a subsequent fall in bilirubin invariably indicated pancreatitis; in malignancy the bilirubin level continued to rise following this procedure.

Mean alkaline phosphatase serum amylase and amylase/creatinine clearance ratio (ACCR) in patients with pancreatitis was not significantly different from that in pancreatic carcinoma (Table 2).

Diffuse calcific pancreatitis was noted in eight of 13 patients with chronic pancreatitis but in none with malignancy. The cholangiographic findings were fairly characteristic in chronic pancreatitis: smooth, gradual tapering of the intrapancreatic portion of the common bile duct. In malignancy the stricture was more irregular, had an abrupt cut off or showed a shelf or nipple configuration at its termination. In two of the 16 patients who underwent percutaneous cholangiography, the findings were initially thought to be that of pancreatitis but the histological specimens showed the

 TABLE 3. Clinical Features Differentiating

 Carcinoma from Pancreatitis

| | Carcinoma (16) | Pancreatitis (13) | Statistical Analysis |
|----------------------------------|-------------------|----------------------|-------------------------|
| Age <55 yrs. | 9 | 2 | NS |
| Pruritis | 9 | 2 | NS |
| Palpable gallbladder | 5 | 0 | NS |
| Jaundice | 16 | 8 | NS |
| Diffuse calcific pancreatitis | 0 | 8 | NS |

NS-not significant.

presence of carcinoma of the head of the pancreas invading the common bile duct. One patient showed radiological features of malignancy but the excised pancreaticoduodenectomy specimen showed only pancreatitis. In two further patients the radiologist was unable to determine whether malignancy or pancreatitis was present. The point score system shown in Table 1 clearly delineated patients with pancreatitis from carcinoma (Fig. 4).

Discussion

Courvoisieur's astute observation concerning palpation of a gallbladder in the jaundiced patient was a milestone in the diagnosis of obstructive jaundice. The advent of endoscopic retrograde pancreaticocholangiography (ERCP), percutaneous transhepatic cholangiography (PTC) and B mode ultrasonography (S) has facilitated identification of the site and at times the cause of extrahepatic obstructive jaundice. Following these comprehensive tests the surgeon may still not be able to decide at laparotomy whether the cause of



FIG. 3. Mean net fall in bilirubin 7-14 days after admission was significantly (p < 0.001) lower in chronic pancreatitis than carcinoma.



FIG. 4. All patients with carcinoma had a positive score (Table 1) whereas those with pancreatitis had a negative score.

jaundice is attributed to carcinoma or inflammation of the pancreas. This differentiation is of the utmost importance as confirmation of malignancy will require a radical operation whereas a biliary enteric procedure would suffice if benign disease alone is present.

The single most useful test in this study that differentiated malignancy from inflammatory disease was the change in bilirubin value during the first two weeks of hospital admission. All patients with pancreatitis had an admission bilirubin which fell within two weeks below 5 mg/dl; in all patients with malignancy this measurement continued to rise. Following percutaneous transhepatic cholangiography the bilirubin increased at a more rapid rate in patients with carcinoma but showed a consistent decline in pancreatitis (unpublished data). The alkaline phosphatase dose not discriminate the two entities.

In patients less than 40 years of age pancreatitis is likely to be present. The nature, severity and duration of pain and extent of weight loss in carcinoma was not significantly different from that in pancreatitis. Both pruritis and the presence of a palpable gallbladder are pointers towards a diagnosis of carcinoma. The presence of calcification of the pancreas occurs almost exclusively in chronic pancreatitis. Cholangiography obtained with a skinny needle of endoscopically is of aid insofar as it defines the extent and location of common bile duct obstruction. Initial enthusiasm to rely entirely on radiological findings to distinguish between carcinoma and pancreatitis has been dampened by incorrect prediction in approximately 10-20% of the cases studied.⁶

Pancreatic cytology obtained via an endoscope may confirm malignancy in the region of the head of the pancreas.⁷ The test requires interpretation by an experienced cytophatologist and in one series this test provided a positive yield in only 23% of patients with pancreatic carcinoma. Biopsy of the pancreatic mass can also be obtained by percutaneous fine needle aspiration which has proven to be a relatively safe procedure.¹¹

Although the surgeon may feel that a localized mass in the head of the pancreas is malignant, uncertainty always exists if a positive biopsy specimen is not available. The point score system evolved in the present report is an attempt to differentiate between these two pancreatic conditions. The findings of this study require confirmation from a larger series of patients with obstructive jaundice. The point score system should not be used unless cholangiography (by PTC or ERCP) has identified a stricture at the lower end of the common bile duct. A possible pitfall to this rule may exist if necrosis of an ampullary carcinoma occurs. Unexplained anemia may be present and direct endoscopy of the ampullary region may be helpful in identifying this type of lesion. The point score assessment may be invalidated if choledocholithiasis, hepatitis or a different cause of jaundice is known to be present. Passage of a common bile duct stone in four patients resulted in temporary narrowing of the lower end of the common bile duct with the bilirubin value falling towards normal (personal observation). The point score appears more sensitive than that recorded by pancreatic function

tests,² ultrasonography,⁹ arteriography,⁴ CAT scan or a combination of these tests.¹

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