Progress report

Cholestasis and lesions of the biliary tract in chronic pancreatitis

The occurrence of jaundice in the course of chronic pancreatitis has been recognised since the 19th century. But in the early papers it is uncertain whether the cases were due to acute, acute relapsing, or to chronic pancreatitis, or even to pancreatic cancer associated with pancreatitis or benign ampullary stenosis.

With the introduction of endoscopic retrograde cholangiopancreatography (ERCP), there has been a renewed interest in the biliary complications of chronic pancreatitis (CP). However, papers published recently by endoscopists have generally neglected the cholangiographic aspect of the lesions and are less precise and less well documented than papers published just after the second world war, following the introduction of manometric cholangiography. Furthermore, the description of obstructive jaundice due to chronic pancreatitis, classical 20 years ago, seems to have been forgotten until the recent papers.

Radiological aspects of bile ducts in chronic pancreatitis

If one limits the subject to primary diseases of the pancreas, particularly chronic calcifying pancreatitis (CCP), excluding chronic pancreatitis secondary to benign ampullary stenosis, cancer obstructing the main pancreatic duct and acute relapsing pancreatitis secondary to gallstones, the most common radiological aspect of the main bile duct is type I choledocus (Figure). This description has been repeatedly confirmed. It is a long stenosis of the intra- or retropancreatic part of the main bile duct. The length of this segment is variable. It is long when the papilla is in the third part of the duodenal loop, short when it is in the upper part of the second duodenum or in the duodenal cap. The effect on bile flow is variable. In mild cases, when the contrast medium is injected into the gallbladder or the hepatic duct, the pressure necessary for it to pass into the duodenum may be in the physiological range. When the stricture is severe, abnormally high pressures are necessary (30 to 35 cm of water, always less than 23 cm of water). But in contrast with cancer, it is always possible to visualise the entire bile duct and the duodenum. Above the stricture, while the common bile duct may be normal, it is generally moderately dilated. Exceptionally, this dilatation may be as great as in cancer and, in two cases reported, resulted in cystic dilatation of the bile ducts.

The gallbladder and cystic duct may be distended but usually to a lesser extent than in cancer.

The sphincter of Oddi was immobile and patulous, offering no resistance to the passage of the contrast medium. This probably explains the fact that
Figure   Type I (long retropancreatic stenosis) and 3 (hourglass stricture) are characteristic of chronic pancreatitis. Type 2 (dilatation of the main bile duct, stricture of the sphincter of Oddi) is typical of ampullary lesions. Type 4 is symptomatic of either cyst (a) or cancer (b and c). Type 5: cancer of the pancreas; when the stricture is impassable, the diagnosis of chronic pancreatitis may be eliminated.

high volumes of fluid are sometimes recovered by duodenal suction. The sphincter may be normal and is never stenosed as in benign ampullary stenosis (type II choledocus, Figure).

Reflux of contrast medium from the biliary tract into the pancreatic duct was never observed by Caroli and Nora. Sarles and his colleagues found bile reflux into the pancreatic duct in only three of 59 cases examined by operative cholangiography. In one case, the reflux was seen only after removing a pancreatic stone. The frequency of bile pancreatic reflux is therefore lower than in patients without pancreatic diseases, where, with the same method, it has been found in 46% of cases. After pancreatic surgery (pancreaticojejunal anastomosis), the bile duct stenosis persists.

Type I stenosis may be diagnosed by oral cholecystography after a fatty meal or an intravenous injection of cholecystokinin, intravenous cholangiography, peroperative or endoscopic cholangiography. It is easy to distinguish strictures due to cancer, which are usually complete so that contrast medium does not pass into the duodenum. However, in rare cases of cancer, the hepatic duct is dilated above an incomplete and lateral stenosis (type IV) (Figure). Below this neoplastic stenosis the common bile duct is normal and the sphincter of Oddi is normal and contractile. Another difficulty encountered during oral or intravenous cholangiography is that the narrow segment may not be visible but only the dilated duct above the stricture. In this case, type I may be interpreted as a benign ampullary stenosis (type II) with a papilla located high in the duodenum. Type I stenosis has been observed in 61 out of our first 100 chronic pancreatitis patients. Type I has been found rarely in acute pancreatitis, where it disappears when the lesions heal, and, exceptionally, in pancreatic cancer.

Type I stenosis is due to peripancreatic sclerosis. During the acute
episodes characteristic of this disease, a labile peripancreatic oedema verified during the course of surgical operations still decreases the calibre of the duct, which may explain transient and recurrent jaundice. One less frequent type equally characteristic of CCP has been described under the name of type III. (Figure). This is an hourglass-shaped stricture localised at the upper border of the pancreas. It is not responsible for cholestasis and can disappear completely after pancreaticojejunostomy. It was found in 2% of our 100 cases of CP. During the course of chronic pancreatitis, the choledocus may also be obstructed by a cyst of the head of the pancreas. In these cases, the lateral compression (type IV) (Figure) of the duct is regularly rounded with a large radius. This deformation disappears after puncture or anastomosis of the cyst. Finally in chronic calcifying pancreatitis, the common bile duct was normal in 23% of our 100 cases.

The types I and III are so characteristic of CP that their finding on intravenous cholangiography is an important diagnostic sign. It can be useful when endoscopic cannulation of the pancreatic duct has failed but cannulation of the bile duct has succeeded.

In France, the relative frequency of radiological modifications of the biliary tract decreased from 1971 to 1976 because minor forms are most frequently diagnosed and advanced cases less frequently. In a multicentre study that included 210 cases of CP, type I was found in 63% of advanced forms and 9% of minor forms; type III respectively in 24% and 2% and type IV (lateral compression by a cyst) in only 7% of advanced cases. Cases were classified into advanced or minor forms according to clinical and endoscopic (endoscopic retrograde catheterisation) criteria.

Cholestasis in chronic pancreatitis

In the most frequent form of chronic pancreatitis, chronic calcifying pancreatitis, jaundice is observed in approximately one-third of patients. These recurrent attacks of mild jaundice generally last less than eight days. As is the case with common bile duct stones, this transient jaundice usually follows an attack of pain. Rarely, jaundice can precede the pain. But, in contrast with gallstones, the attack of pain is usually not accompanied by chills and fever (at the most temperature reaches 38°C, and only in exceptional cases may it be higher than 39.5°C for one or two days). In some cases, there is no pain during the entire course of the disease, which is marked only by recurrent episodes of jaundice. A transient and recurrent obstructive jaundice without associated symptoms in an alcoholic man aged 35 to 45 years is frequently due to CCP.

Scott et al. (1977) reported 11 patients with an association of jaundice and chronic pancreatitis. Ten of the 11 developed transient cholestasis during exacerbations of the chronic pancreatitis. In six, cholestasis persisted a longer time. The radiological modifications of the common bile duct were similar to those described by Caroli and Nora.

Jaundice prolonged more than one month was observed in 3% of our cases. It is generally due to a cyst of the head of the pancreas, compressing the bile duct, or to an abscess. In a small percentage of cases, persistent jaundice is due to an uncomplicated but severe intrapancreatic (type I) stricture of the common bile duct. This was seen in seven out of 253 cases.
studied by Gullo and his colleagues (1977)\textsuperscript{23}. In some patients, transient or prolonged rises of hepatic alkaline phosphatase may occur without jaundice. Snape and others\textsuperscript{24} reported six such cases. Bilirubin was normal. The maximum retention of BSP was 7\%. Two patients complained of pruritus. In every case a type I stenosis was observed. Above the stricture, the diameter of the bile duct was 16 to 25 mm, which was wider than the usual dilatation of the hepatic duct in our cases ($\bar{m} = 10.5$ mm, SD: 0.86). This suggests that such silent cases may be due to a more chronic disease.

In non-operated cases, cholangitis is exceptional. It is characterised by high and irregular fever, chills, jaundice and pain\textsuperscript{11}. It may be complicated by liver abscesses\textsuperscript{25}. Warshaw and colleagues\textsuperscript{26} reported six cases of jaundice secondary to chronic pancreatitis with an unusually high frequency of cholangitis. Enteric bacteria, most commonly gram-negative rods, were found in four out of the six specimens studied. Three of these patients suffered from recurrent attacks of acute cholangitis and one a hepatic abscess. As judged by the cholangiograms published in this paper, they were extremely advanced cases. After surgery—and especially biliary anastomosis—cholangitis is more frequent.

As cholestasis is often mild and transient, hepatic lesions are rarely described. Bile stasis but not bile infarcts have been observed by Snape \textit{et al.}\textsuperscript{24} in four cases, of which two were associated with prominent bile duct proliferation. Secondary biliary cirrhosis is rare\textsuperscript{11}. In one case of Warshaw \textit{et al.}, serial liver biopsies performed one year apart documented the progression from cholestasis with mild fibrosis to marked pericholangitis and biliary cirrhosis. Biliary cirrhosis has never been found in 300 cases of chronic calcifying pancreatitis from Marseille. But in 60 hepatic biopsies Leger and colleagues\textsuperscript{27}, found hepatic lesions in 39 cases: in 31 cases, inflammatory infiltration and fibrosis in the portal tracts and, in six cases, biliary cirrhosis. Thirteen patients had alcoholic liver disease (steatosis, eight cases; alcoholic cirrhosis, five cases). Scott \textit{et al.}\textsuperscript{28} published one case of biliary cirrhosis in 11 patients with transient jaundice. However, these studies concerned patients with severe disease and, as a rule, biliary cirrhosis is probably exceptional in the course of chronic pancreatitis.

**Treatment of cholestasis**

The wide range of severity and frequency of biliary obstruction may explain the different therapeutic attitudes. We reserve anastomosis of the common bile duct for narrow strictures. In the case of a relatively mild stricture, only the pancreatic lesion is treated, if possible by side-to-side anastomosis between a dilated pancreatic duct and a Roux-en-Y loop. If the duct of Wirsung is not sufficiently dilated, a cephalic duodenopancreatectomy may be performed. When a cholecystojejunostomy or an end-to-side hepatico-jejunostomy without section of the common bile duct are performed, or when the jejunal loop anastomosed to the biliary tract is not long enough to forbid reflux, angiocholitis and secondary gallstones may be observed. Cholecysto- or choledochojejunostomy or duodenostomy have been recently carried out\textsuperscript{28}. But, in our experience, these operations are a frequent cause of postoperative cholangitis.

In cases of mild obstruction, after pancreaticojejunostomy and avoidance of alcohol, the bile stricture generally stops progressing. Nevertheless, in
two of our cases, it was necessary to operate a second time because jaundice recurred some years after pancreatic surgery. For this reason, some surgeons perform either systematically\textsuperscript{28} or in certain cases\textsuperscript{29} a treble derivation of the common bile duct and the main pancreatic duct on the same Roux-en-Y loop and of the stomach by gastroduodenostomy. Nevertheless, long-term postoperative results are significantly better when biliary anastomoses are not performed than when this procedure is systematically carried out.

**Frequency of gallstones associated with chronic pancreatitis**

Excluding acute recurrent pancreatitis secondary to gallstones, the frequency of gallstones in chronic pancreatitis has been variously reported. Howard and Jordan\textsuperscript{30} found three cases of gallstones in 94 patients with alcoholic pancreatitis, but found no case of gallstones in a series of 32 patients whose biliary tract was explored surgically or at necropsy. In our first series\textsuperscript{16}, two cases of gallstones were found in 100 patients. Marks and colleagues\textsuperscript{31} found in 6\% out of 172 cases of chronic calcifying pancreatitis gallstones or common duct stones but the majority of these were pigment stones. Ammann and others\textsuperscript{32} found four cases with gallstones in 63 patients with chronic pancreatitis.

In recent studies, the number of gallstones seems to have increased in certain places and not in others. In Paris, Bernades and colleagues\textsuperscript{33} found 15\% of cases with associated gallstones. In our last 73 cases of CCP (unpublished data), the frequency of gallstones was 8-2\%. In contrast, in Brazil\textsuperscript{34}, Dani et al. (1974) found no cases of gallstones in 54 patients with CCP and Gullo et al.\textsuperscript{23} in Italy five in 253 cases. These differences between countries and times are probably not due to the accuracy of the diagnosis of gallstones increasing with time and being better in some places than in others. Howard and Jordan's cases\textsuperscript{30}, for instance, were surgical and necropsy cases. It is known that the mean age at onset of clinical symptoms of chronic pancreatitis is relatively young (38 years\textsuperscript{35}). On the contrary, the frequency of gallstones increases all through life. It is possible that better medical and surgical care permit CCP patients to reach the age of gallstone formation, the frequency of which could be increased by cholestasis, which is a late complication of chronic pancreatitis. The low frequency of gallstones in some countries, especially Brazil and Italy, could be explained by the fact that low calorie, low protein, fibre-rich diets are not favourable conditions for the development of gallstones\textsuperscript{36,37}. The assumption that biliary lithiasis, which is a cause of acute relapsing pancreatitis, could be a frequent cause of chronic pancreatitis, especially of CCP, has been frequently rejected\textsuperscript{38}. In our opinion, if one admits the classification of Marseille, with the exception of very rare cases of stricture of the Wirsung duct secondary to gallstone-induced acute pancreatitis and necrotic pseudocysts, there is no proof that biliary lithiasis could induce a chronic pancreatitis—that is to say, pancreatic lesions persisting when the biliary disease has been correctly treated\textsuperscript{38}. On the contrary, different arguments favour the assumption that CP could increase the frequency of gallstones. According to Bernades et al.\textsuperscript{33}, when these two diseases are associated, gallstones develop later than CP. Bile stones found by Marks et al.\textsuperscript{31} are pigment stones and therefore could be secondary to bile stasis. The frequency of cholecystitis secondary to acute attacks of pancreatitis, as shown by Weiner et al.\textsuperscript{39}, could also play a part.
References

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