Distal Pancreatic Duct Inflammation

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WHILE pancreatitis continues to be a frequent clinical syndrome, its cause remains the subject of conflicting theories. Whatever the initiating mechanisms, the final common pathway is the escape of activated pancreatic enzymes into the interstitial tissues and body spaces. Numerous etiologic factors have been suggested to explain the development of this process. It is known to occur in association with parotitis, alcoholism, and certain endocrine disorders such as hyperparathyroidism.[9, 13, 22] In these cases, a direct metabolic insult to the gland parenchyma would seem to be the important initiating agent. However, in the majority of cases, local factors appear to be responsible as clinical and experimental evidence has shown. Opie[20] first popularized the common channel theory with bile reflux occurring secondary to obstruction of the ampulla by a stone. Subsequently, several authors[4, 5, 16, 19, 24, 25] have drawn attention to the importance of outflow obstruction in the etiology of pancreatitis irrespective of biliary reflux. It is probable that in the majority of cases several factors come into play, such as the presence of pathogenic organisms, an actively secreting gland, and a degree of obstruction to the outflow of pancreatic juice through the duct system. In the absence of a stone, obstruction may be caused by spasm,[8, 23] or by fibrotic narrowing of the ampulla as a result of chronic inflammation.[1, 2, 7, 10, 15, 21]

In up to 90% of cases, the pancreatic duct and bile duct may terminate in a common channel.[6] Obstruction of the pancreatic outflow may, therefore, be produced by narrowing of the ampulla.[11, 12] However, the pathological changes which involve the ampulla may spread to involve the termination of the pancreatic duct and fibrosis here results in narrowing of this duct lumen. Moreover, it is possible for stenosis of the orifice of Wirsung's duct to occur independently of ampullary stenosis. In either of these circumstances, in order to relieve obstruction it is necessary not only to carry out ampullary sphincterotomy but to apply this procedure to the pancreatic duct orifice as well.

The purpose of this paper is to document the frequent occurrence of chronic inflammatory changes leading to stenosis involving the pancreatic duct opening in association with biliary tract disease and pancreatitis.

Material and Method

Twenty-five patients were operated upon with presumptive diagnoses of recurrent pancreatitis. These patients had been selected for operation on the basis of history, cholangiography, evocative enzyme tests, pancreatic scans and other criteria as previously described.[19] None had calculous disease. Ampullary sphincteroplasty was per-

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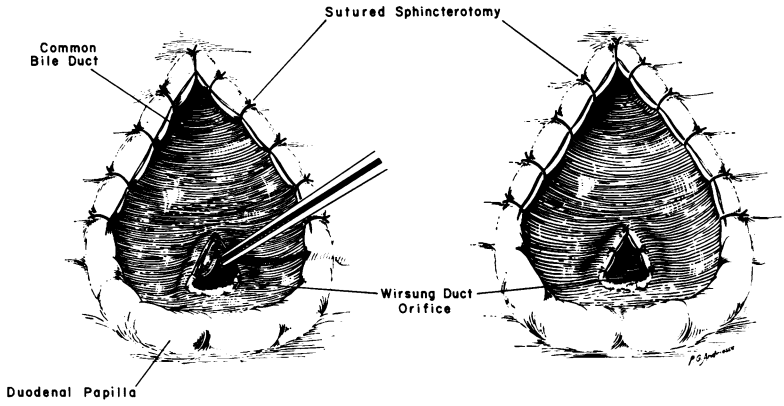

FIG. 1. Postsphincterotomy appearances of the ampulla of Vater showing on the left a wedge of tissue being removed from the Wirsung duct orifice and on the right the final appearance after completion of the procedure.

formed and the orifice of the Wirsung's duct identified.[18] A wedge of tissue was then removed by scissors or sphincterotome from the upper lip of the pancreatic duct orifice in an upward direction for 5–10 mm. with a 2 mm. base (Fig. 1). This wedge of tissue was, in fact, part of the septum which separates the lower ends of the common bile and Wirsung's duct. Its removal enlarged the orifice and provided tissue for biopsy purposes. The mucosa of the pancreatic duct was approximated to that of the common bile duct by fine interrupted sutures.

The biopsy material was stained by Hematoxylin-Eosin, Masson's Trichrome, and Van Gieson stains. Polarized light microscopy was also used to assess the amount and distribution of fibrosis. In order to accurately evaluate our findings, a study by a similar technic was performed of 25 "normal" fresh autopsy specimens from subjects who died from non-biliary and non-pancreatic disease. On the basis of clinical and operative findings, the 25 patients comprising the surgical material have been divided into three groups as shown in Table 1.

Group I. In this group, the preoperative diagnosis was doubtful as there was no unequivocal evidence of pancreatitis. Four patients had histories of psychiatric disorders, drug addiction, or alcoholism, and the fifth had previously undergone three negative laparotomies. Because of persistent pain, suggestive of pancreatic disease, exploratory laparotomy was undertaken. At operation, the pancreases and common bile ducts were normal in all cases. Because the ampulla appeared stenosed and did not admit a #3 Bakes dilator, the duodenum was opened and ampullary sphincteroplasties and Wirsungotomies were performed. Operative pancreatography in this group was uniformly normal.

Group II. In this group, there was a definite history of pancreatitis confirmed by elevation of the serum amylase and lipase levels. One patient had a history of alcoholism. Grossly abnormal pancreases with evidence of chronic pancreatitis and normal biliary systems were found at operation in these patients. Pancreatography was normal or showed only minimal changes of dilatation and filling of secondary branches.

Group III. As in Group II, these patients had classical histories and laboratory evidence of pancreatitis. None had a history

TABLE 1. *Diagnosis Based on Clinical and Operative Findings*

Group I	Without pancreatitis	5
Group II	Pancreatitis alone	4
Group III	Pancreatitis with associated biliary tract disease	16
Total		25

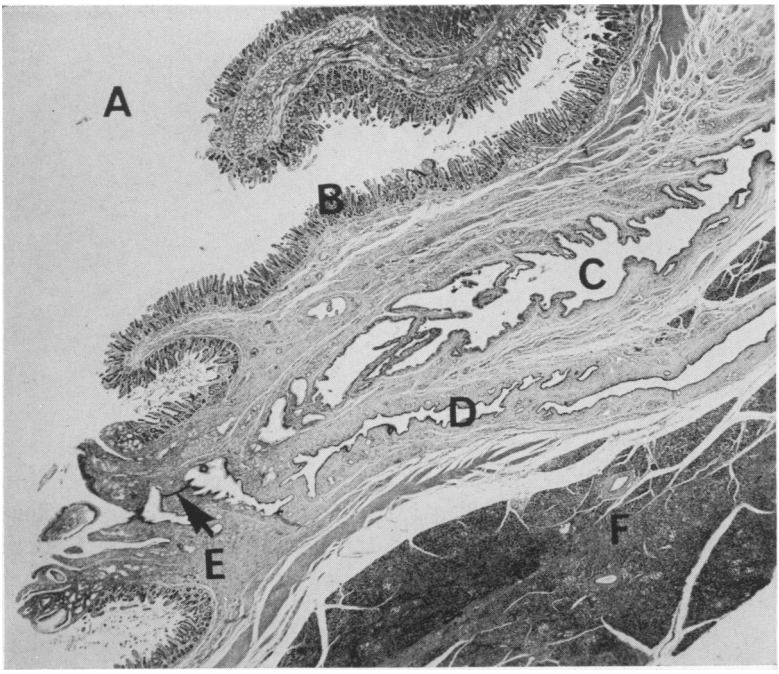

FIG. 2. Photomicrograph, H. E. ×11. Longitudinal section of the ampulla of Vater showing the termination of both the bile and pancreatic ducts. A) Duodenal lumen. B) Duodenal mucosa. C) Lumen of the common bile duct. D) Lumen of the Wirsung duct. E) Ampulla of Vater. F) Pancreas.

of alcoholism. At operation, the pancreatitis was confirmed grossly. Dilated and thickened bile ducts were present in all cases. Eight patients had histories of obstructive jaundice. Biliary calculi were not present. Pancreatography showed uniform dilatation of the main pancreatic duct from the point of obstruction at the stenosed Wirsung's duct orifice with filling of secondary and tertiary ductules.

Results

Control Material. Normal Histology. The mucosa at the lower end of the common bile duct is continuous with that of the pancreatic duct and in both it is thrown into prominent villous folds (Fig. 2). The lining epithelium is simple columnar type. Deep to the epithelial layer in the submucosa there are numerous mucous secreting glands. The muscularis mucosae is poorly formed. Surrounding the lower end of both ducts is the smooth muscle of the sphincter of Oddi. A portion of the sphincter is seen in the septum between the termination of the two ducts. Interposed between the muscle bundles of the sphincter is a small amount of loose connective tissue (in Fig. 3, this is shown under polarized light microscopy). The submucosa of the ampulla and of the termination of the common bile and pancreatic ducts is also of loose texture, but it becomes more dense in the pancreatic duct proximal to the sphincter. There is a marginal difference also in the density of the fibrous tissue of the submucosa at the termination of the Wirsung duct compared with that of the ampulla. In the former, it is slightly more dense.

Surgical Material. Pathologic Findings. In eight cases, the histological appearance of the biopsies was normal. One patient had undergone sphincterotomy previously and the histological features were considered due to postoperative cicatrization. The remaining 16 cases showed varying degrees of inflammatory changes at the Wirsung duct orifices. These were similar to those previously described involving the

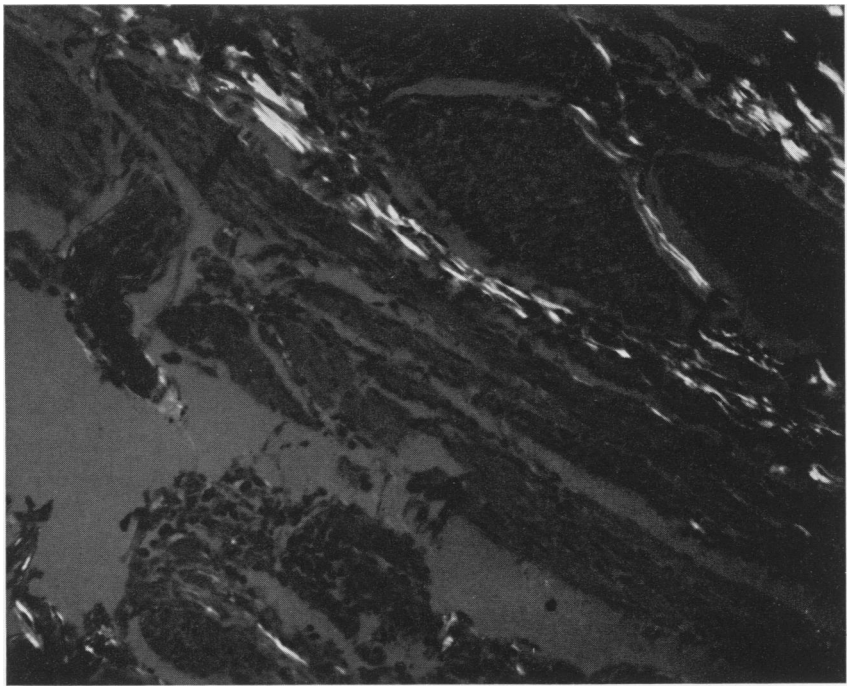

FIG. 3. Photomicrograph. H. E. × 170. (Polarized light.) Section of a portion of the normal sphincter of Oddi showing in the right upper aspect of the photograph fine strands of connective tissue interposed between the muscle bundles.

ampulla.[3, 4] Both acute and chronic inflammation may be seen. One of several pathological features may be present; namely, ulceration (Fig. 4), excess granulation tissue formation (Fig. 5), glandular hyperplasia and fibrosis (Figs. 6 and 7). Depending on the predominant changes, the biopsy specimens were categorized as in Table 2. In some cases, several of these pathological changes coexisted. A chronic

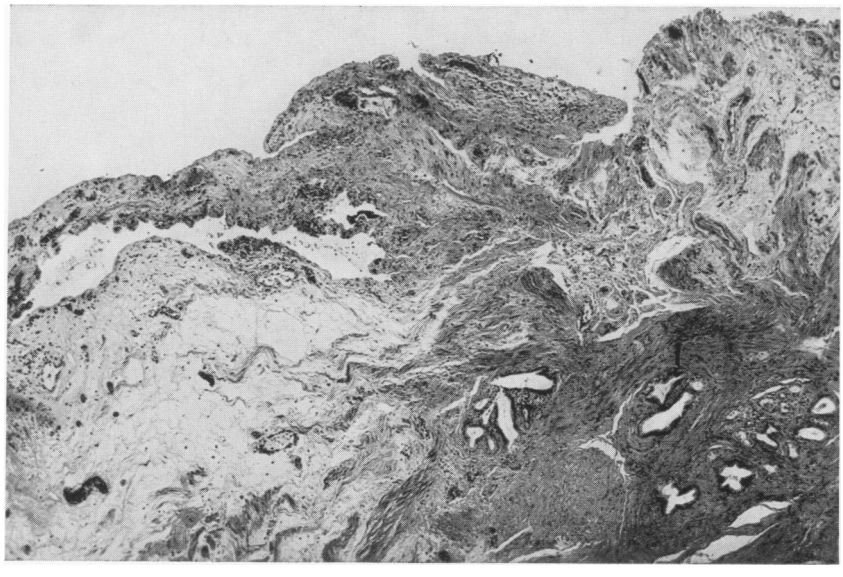

FIG. 4. Photomicrograph, H. E. × 54. Ulcerative lesion, showing well marked cellular infiltrate.

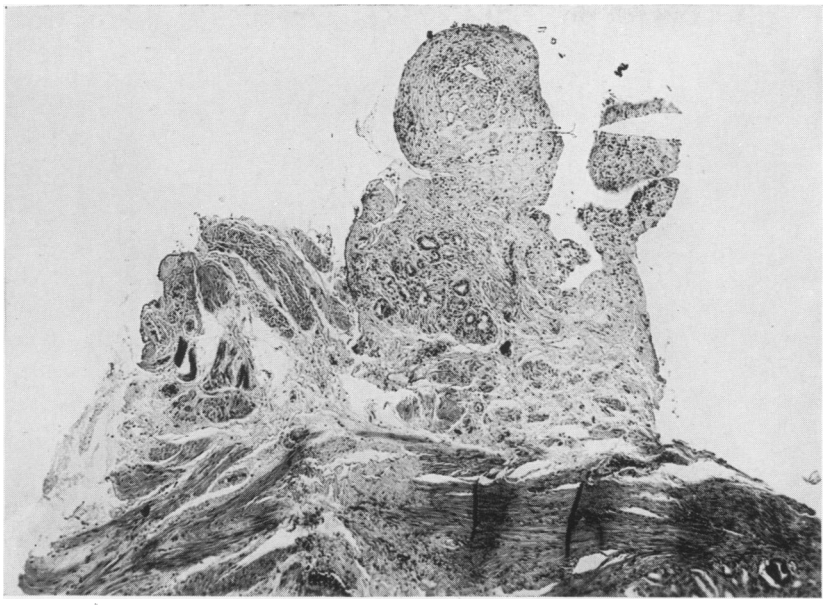

FIG. 5. Photomicrograph, H. E. ×57. Excess granulation tissue with the production of a pseudopolyp.

inflammatory infiltrate was present in all cases. Acute inflammatory changes alone as evidenced by polymorphonuclear infiltration, edema, and capillary dilatation was present in six cases.

Clinico-pathological Correlation

In Group I, despite the stenotic appearance of the duct orifices to the surgeon, the biopsies were normal. The biopsy result correlates, therefore with the findings of a

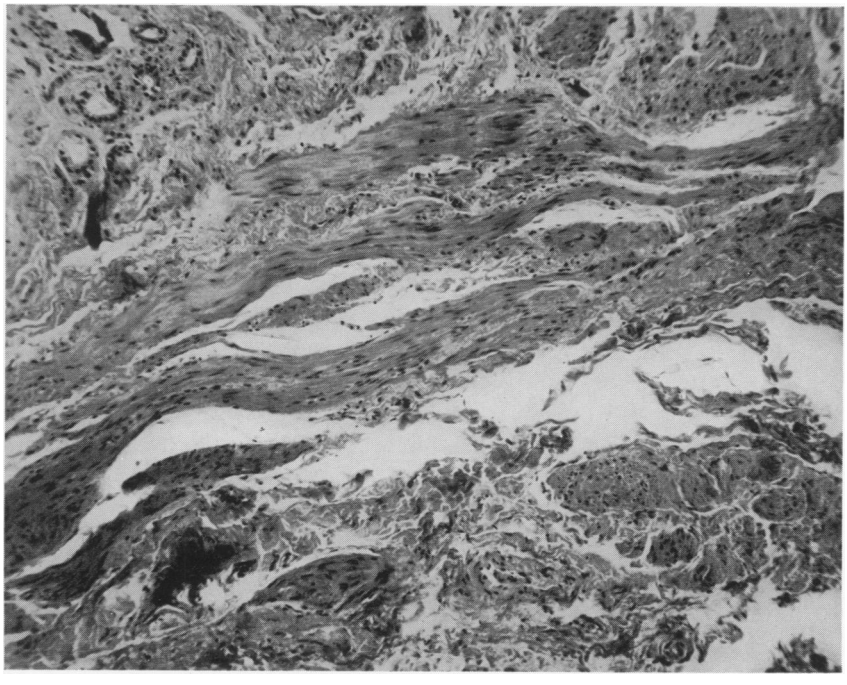

FIG. 6. Photomicrograph, H. E. × 130. Postinflammatory fibrosis with partial replacement and disruption of the muscle bundles of the sphincter of Oddi.

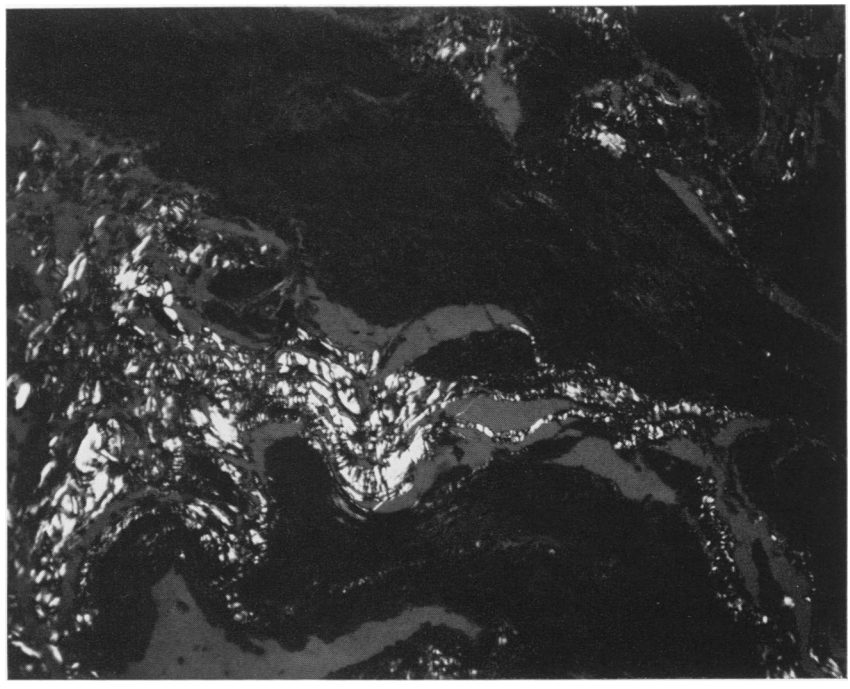

FIG. 7. Photomicrograph, H. E. × 130. (Polarized light.) Postinflammatory fibrosis revealed by polarized light microscopy with thickened collagen fibers between the muscle bundles of the sphincter.

normal pancreas and biliary tract in these cases. On follow up, four patients were symptomatically unchanged; one claimed relief but the period of observation was too short to be significant.

Of the four patients in Group II, three had normal biopsies and the fourth showed minimal inflammatory changes only. Only one patient failed to gain relief and 10 weeks after sphincteroplasty, a caudal pancreatectomy was performed. The other three were cured of symptoms.

The 16 patients of Group III all had biopsies that were abnormal; six showing fibrosis, and the other ten varying degree of inflammatory changes (Table 2). All had gross abnormalities of the common bile duct. One patient died in the postoperative period and two others required reoperations for immediate postoperative complications but both are now well. Twelve patients are symptom free with a total follow-up period of 1–7 years; two are similarly well after a short period of follow-up.

TABLE 2. *Histopathological Classification*

Ulcerative	5
Granulomatous	3
Adenomatous	2
Fibrosing	6
Total	16

Discussion

In Group I, the preoperative diagnoses were incorrect. All were believed to have stenosis at the ampullary or pancreatic duct orifice, but this was not confirmed by histological examination. It is probably unnecessary to comment further on this group except to stress the fallibility of surgical assessment of stenosis at the time of operation by the blind passage of a probe or bougie from above down to the ampulla or by the naked eye appearances on opening the duodenum. The most reliable method is by operative cholangiography or retrograde pancreatography employing Leger's tech-

nic.[17] This group should also draw attention to the difficulty in some instances of diagnosing pancreatitis clinically and differentiating it from abdominal pain of functional origin.

In the majority of patients with pancreatitis, pathological changes affecting the ampullary area were clearly demonstrated histologically. These organic changes may cause stenosis and obstruction produced by this means may be more important in the development of pancreatitis than spasm and on our service is more common than obstruction by an impacted ampullary gallstone. However, such changes were not present in four patients of Group II despite well marked pancreatitis. In these patients, therefore, pancreatitis may have been secondary to a functional or spastic obstruction at the orifice or the result of primary parenchymal damage. Although not a feature of any case in this series, it is known that the pancreatic duct may be the seat of multiple areas of stenosis scattered throughout its length. These stenotic lesions occur with pancreatitis but whether they initiate the process or are secondary to parenchymal damage is unknown. It may be that the cases of Group II represent an early stage of this entity and would in time progress to ductal abnormalities. There is no relationship, however, between this picture and demonstrable disease limited to the Wirsung duct orifice.

All patients of Group III showed pathological changes at the orifice of the Wirsung duct and, in addition, similar changes involved the ampulla in all except one. The severity of the inflammatory changes is not uniform and fibrosis and stenosis may affect one orifice more than the other. In a previous report,[3,4] it has been shown that ampullary disease can occur independently of disease of the Wirsung duct opening. The converse may occur but rarely.[14] In such situations ampullary sphincteroplasty *per se* might be inadequate. Thus, it seems that Wirsungitis is almost always secondary to and associated with ampullary disease. Because of the close anatomical proximity of these ducts, it is likely that disease of the Wirsung orifice arises as a result of direct spread of the inflammatory process from the ampulla.

Obstruction to pancreatic outflow may thus arise from either stenosis at the ampulla or stenosis at the Wirsung orifice or both. Whereas it is not difficult to recognize ampullary stenosis, it may be difficult to diagnose stenosis of the Wirsung orifice with certainty. Naked eye appearance may be misleading. Confirmatory evidence may be obtained by pancreatographic demonstration of uniform dilatation of the pancreatic duct distal to the point of obstruction at its orifice. This ductal dilatation does not seem to be a feature of pure ampullary stenosis presumably because the patent Wirsung orifice allows pressure increases to be shared by the biliary system.

Summary

A series of 25 patients with preoperative diagnoses of pancreatitis underwent sphincteroplasty with extension of this to widen the Wirsung duct orifice. A similar number of normal autopsy specimens were examined and the normal histology is described.

The pathologic features of surgical specimens obtained from the pancreatic duct orifice are described. The changed noted included acute inflammation and varying degree of chronic inflammation culminating in fibrosis.

The clinical data, operative findings, and the results of operation are reported and correlated with the pathological material.

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