Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Pancreatitis

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Brit. med. J., 1968, 1, 813-815

There are three major forms of pancreatitis: acute, relapsing, and chronic. Though in some cases either relapsing or chronic pancreatitis can be shown to have followed one or more episodes of acute pancreatitis, the three forms of the disease are not mutually interdependent and therefore they merit individual consideration.

Acute Pancreatitis

Aetiology

The aetiology of acute pancreatitis remains obscure. With the development of each new "fashion"—bacterial, viral, ischaemic, autoimmune, etc.—so a new theory is advanced for the aetiology of pancreatitis. It is generally accepted, however, that there is a causal connexion between disease of the biliary tract and acute pancreatitis, and it is commonly thought that an important factor is reflux of bile along the main pancreatic duct. Attempts to clarify this point by experiments on animals are not entirely successful, since the dog, the animal most used, lacks the junction of the common bile duct with the pancreatic duct behind the sphincter of Oddi, which is the normal pattern in the human. It is significant that in experiments on the dog acute pancreatitis of a type most similar to that seen in man is produced by the retrograde injection of infected bile into the pancreatic duct. The mechanistic hypothesis is strengthened by the known incidence of acute pancreatitis as a complication of surgical operations on the sphincter of Oddi (transduodenal sphincterotomy or sphincteroplasty).

Clinical Features

Clinically acute pancreatitis is characterized by sudden severe illness necessitating urgent admission to hospital. In its mildest form it is associated with diseases of the biliary tract such as cholecystitis (with or without gallstones) and cholangitis, but in this form it rarely constitutes a threat to life and the pancreatitis can be expected to regress spontaneously during the successful treatment of the primary biliary tract disease. The most virulent form is acute haemorrhagic pancreatitis, a disease which carries a high mortality. All gradations of severity between these two extremes will be encountered, and the mortality rate (approximately 20% overall) is directly proportional to the severity of the attack.

The patient usually complains of a continuous intense upper abdominal pain which radiates centrally to the back, and this is accompanied by clinical shock as shown by pallor, coldness of the extremities, a thin thready radial pulse, and hypotension. A cyanotic discoloration of the extremities occurs in the worst cases.

The severity of the abdominal signs depends on the degree of peritoneal irritation caused by escape of the pancreatic enzymes from the confines of the gland into the peritoneal cavity. If the gland remains intact the absence of abdominal signs in association with upper abdominal pain and in the presence of shock may well cause diagnostic confusion with coronary thrombosis. If pancreatic enzymes escape into the lesser sac of the peritoneum a tender rounded mass may be detected in the epigastrium—but this would be unusual. If the general peritoneal cavity is contaminated by escaping pancreatic enzymes the widespread abdominal guarding and rigidity which result may lead to diagnostic confusion with perforation of a peptic ulcer. The classical signs of Grey Turner (local discoloration of the skin in the loin) and Cullen (periumbilical discoloration) are not commonly seen because they occur late in the disease, time being required for the tracking of haemoglobin breakdown products along the tissue planes.

Though coronary thrombosis and perforation of a peptic ulcer are the main conditions to be considered in differential diagnosis, acute pancreatitis may mimic almost any of the acute abdominal emergencies commonly met with in surgical practice. Confirmation of the diagnosis is usually obtained by a finding of elevation of the serum amylase level above the normal range of up to 150 Somogyi units/100 ml. Elevation of the serum amylase level may occur in certain other disease processes, but in these the clinical findings will usually preclude misdiagnosis.

Further confirmatory evidence may be provided by the development of glycosuria, said to occur in 30% of the patients and produced by disruption of the islet cells of Langerhans. This is of minor practical value unless it is known that the patient was previously free of glycosuria.

Treatment

The treatment of acute pancreatitis is determined by the speed, accuracy, and circumstances of the diagnosis.

When physical and serological examination leads to confident diagnosis without laparotomy treatment is conservative and is designed to combat the state of shock. With the patient at rest in bed intravenous therapy in the form of blood, plasma, or plasma expanders is given to combat hypotension. Fluid and electrolyte requirements are maintained by intravenous saline and dextrose solutions. In very severe cases it may be necessary to administer vasoconstrictive agents such as noradrenaline to maintain the blood pressure. Central venous pressure recordings may be helpful in monitoring the correction of the circulating blood volume. Frequent clinical examination, accurate fluid balance recordings, and repeated electrolyte estimations are necessary to determine the order, volume, and speed of administration of the several intravenous fluids. Because of the severe

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stress adrenal failure may occur, and the administration of systemic corticosteroids may be necessary.

Gastric aspiration and restriction of oral fluids to 30 ml. of water hourly rest the bowel. Spasm of the sphincter of Oddi, which could encourage retrograde entry of bile into the pancreatic duct, is best combated by antispasmodics. Propantheline bromide is of considerable value here as it has the additional action of reducing both the rate and volume of pancreatic secretion. Pain should be controlled by pethidine, as unlike morphine it will not stimulate contraction of the sphincter of Oddi.

Rarely it is necessary to give insulin to replace the products of the islet cells of Langerhans in those patients who develop glycosuria. Widespread fat necrosis by pancreatic lipase will lead to diminution of the circulating level of calcium and this in turn may produce clinical tetany. The tetany should be treated by the intravenous administration of calcium gluconate. The level of serum calcium may be of prognostic value in that it has been reported that if the level falls below 7 mg./100 ml. the patient's chances of recovering from the pancreatitis are slim. The progress of the patient can be judged by clinical examination and by serial estimations of the serum amylase level.

Because of the high mortality of acute pancreatitis attention is now being directed to the problem of the direct inhibition of pancreatic enzymes and also to the removal of these enzymes from abnormal situations. When contamination of the peritoneal cavity by pancreatic enzymes has been diagnosed peritoneal dialysis may prove beneficial firstly in limiting the further development of intraperitoneal fat necrosis by the removal of pancreatic lipase and secondly by reducing the potential resorption of all pancreatic enzymes—lipase, amylase, trypsin, and chymotrypsin—into the circulating bloodstream.

Direct inhibition of trypsin and chymotrypsin may be achieved by the use of the drug Trasylol.¹ This is a biological preparation consisting of 58 amino acids in a chain distribution linked by three disulphide bonds and it is extracted from bovine parotid tissue. When injected intravenously it is rapidly distributed throughout the tissues but does not cross the blood-brain barrier. It has a biological half-life of 150 minutes, so administration should be by continuous intravenous infusion. Trasylol has no action against pancreatic lipase or amylase and therefore cannot reverse or neutralize all the effects of pancreatic enzyme maldistribution. Because it is active against trypsin and chymotrypsin, the enzymes largely responsible for the production of the shock-like state in acute pancreatitis, the administration of Trasylol might be expected to prove beneficial; in practice reports of its clinical value have been conflicting, and until a controlled trial of adequate dosage has been completed final judgement on the value of this preparation in pancreatitis cannot be made. However, reports on the safety of Trasylol in high dosage have been encouraging, the few reactions reported having been idiosyncratic or "allergic," and there have been no fatalities. Because of the known high mortality in the more severe cases of pancreatitis it seems reasonable to treat gravely ill patients by the intravenous administration of Trasylol in adequate dosage (such as 200,000 units immediately, followed by 800,000 units daily for five days) in addition to the conventional resuscitation measures already outlined.

After the patient has recovered, the biliary tract should be investigated and remediable abnormalities corrected surgically to lessen the chance of recurrence. This will usually entail cholecystectomy and exploration of the common bile duct if the duct is found to contain gallstones. If after recovery the patient remains diabetic appropriate antidiabetic treatment should be given.

If the diagnosis of pancreatitis is not made until laparotomy the biliary tract should be assessed, and operation at that time confined to ensuring both free drainage of bile and relief of any possible back pressure on the pancreatic duct. This is best

achieved by cholecystostomy or by T-tube drainage of the common bile duct after the removal of all gallstones. After recovery from the pancreatitis definitive operative correction of any abnormality of the biliary tract should be carried out.

Occasionally the pancreas is found to be replaced by a necrotic abscess. This should be drained to the exterior through the flank. The resulting pancreatic fistula may later require implantation into the upper intestine. In the presence of gross peritoneal contamination peritoneal dialysis can be continued after laparotomy.

Late sequelae include relapsing pancreatitis and chronic pancreatitis, which will be considered below, and pancreatic cyst and pseudo-cyst formation. Pancreatic pseudo-cyst is treated by marsupialization into the posterior wall of the stomach. Pancreatic cysts may be similarly marsupialized or else treated by external drainage, the resulting chronic pancreatic fistula being treated later by implantation into the upper intestine or by excision combined with partial pancreatectomy.

Relapsing Pancreatitis

The essential feature of this form of pancreatitis is the recurrence of acute episodes of the disease at irregular intervals superimposed on a background varying from near normality to increasing pancreatic insufficiency. If the course of the disease cannot be checked the pancreas eventually becomes so disorganized by the exacerbations that true chronic pancreatitis supervenes.

The patient will present in an acute exacerbation with the signs and symptoms of acute pancreatitis but may be distinguished from pancreatitis *de novo* by the past history of similar episodes of disease. As the disease progresses it is likely that there will be a depreciation in the patient's general health between attacks, making the diagnosis more certain.

The management of the acute problem is identical with that of acute pancreatitis, the vigour of resuscitation depending upon the severity of the signs and symptoms. When the patient has recovered from the particular acute episode of relapsing pancreatitis a thorough investigation should be carried out to determine whether any treatment can be offered to prevent further acute exacerbations.

Plain x-rays of the abdomen, barium meal, and duodenography may show calcification or other abnormal signs in the pancreas. Rarely it is possible to detect calculi lying in the line of the pancreatic duct; these are a source of recurrent exacerbations as they can cause intermittent obstruction to the outflow of pancreatic secretions. The biliary tract should be investigated. If gallstones are found in the gall bladder or in the common bile duct they should be removed. If there is stenosis of the sphincter of Oddi sphincteroplasty should be considered as a means of reducing the risk of retrograde entry of bile into the pancreatic duct. This operation may itself be complicated by acute pancreatitis; prophylactic treatment with Trasylol may possibly protect against this complication.

The degree of permanent damage to the pancreas should be assessed by specific function tests. Fat balance studies give an assessment of the reduction in lipase. In normal subjects the injection of secretin causes an elevation of the serum amylase level. In chronic pancreatitis the response is abnormal, and there is no elevation of serum amylase following secretin injection. The fluid, electrolyte, and enzyme secretion of the pancreas in response to the simultaneous injection of both secretin and pancreozymin can be measured; but as this test involves duodenal intubation and aspiration painstaking technique must be applied to ensure that the total secretion of the pancreas is aspirated free from gastric or jejunal contributions. The difficulties of collection of the duodenal fluid make interpretation of this test more uncertain than interpretation of the simpler secretin test.

Management

Conservative management may be chosen, and indeed is the most widely used treatment. Close surveillance of the patient allows the application of prompt and vigorous treatment in the early states of threatening exacerbation. Laparotomy may occasionally be considered because of the frequency and severity of the exacerbations and because of increasing pancreatic insufficiency. The advantages of the several alternative operations in relapsing pancreatitis must be weighed against the risks of the operations themselves. The choice includes sphincterotomy, sphincteroplasty, retrograde pancreatic drainage (possibly with removal of stones from the pancreatic duct), and partial or even total pancreatectomy.

Retrograde drainage of the pancreas produced by excision of the tail of the gland and implantation of the body into the upper jejunum carries a high risk of pancreatic fistula.

Total pancreatectomy has a high operative mortality and morbidity, but occasionally the procedure may be justified by the severity of the patient's symptoms. Replacement therapy is an essential part of the long-term postoperative management.

Chronic Pancreatitis

Chronic pancreatitis presents in several ways, and since the symptoms are often unspecific in character it is probable that many cases are undetected. When there are repeated attacks of relapsing pancreatitis the gradual deterioration in pancreatic function enables the diagnosis to be more readily suspected and therefore more confidently made.

In some patients chronic pancreatitis concentrated in the head of the pancreas causes progressive obstructive jaundice by compression of the common bile duct and will mimic carcinoma of the head of the pancreas. Such cases seldom present with a history of previous pancreatitis and may be indistinguishable from carcinoma even at laparotomy. The diagnosis may be established by pancreatic biopsy, but a biopsy may yield an inconclusive result, particularly if the specimen is examined by the frozen section technique. The correct procedure in such a case is to perform a bypass operation—either choledochoduodenostomy or cholecystojejunostomy with relieving enteroanastomosis across the base of the jejunal loop—which will relieve the jaundice. In the event of misdiagnosis of a carcinoma of the head of the pancreas such a bypass operation provides acceptable palliation and it is unlikely that diagnostic confusion will be met with in those cases of carcinoma in the region of the ampulla of Vater which would be suitable for treatment by duodenopancreatectomy.

In another large group of patients the onset of the symptoms of chronic pancreatitis is insidious with no premonitory episodes of either acute or relapsing pancreatitis. In this group compression of the common bile duct does not occur and the patients do not develop jaundice.

Pain is usually upper abdominal and may spread to the back. It is intermittent, varying in intensity from a nagging ache to a severe gripping pain and does not bear a strict relationship to meals. The patients usually complain of anorexia and loss of weight. They suffer from alteration in bowel habit often amounting to steatorrhoea and all complain of general malaise.

X-ray of the abdomen may reveal pancreatic calcification, but this is not always present. Because of the unspecific nature of

the patient's symptomatology, barium-meal examination and cholecystography are usually performed, but they rarely prove helpful in establishing a positive diagnosis of chronic pancreatitis. Radiology of the duodenum may yield more useful information about the condition of the head of the pancreas. An assessment of pancreatic function should be made, as described for relapsing pancreatitis.

Chronic pancreatitis without obstructive jaundice is best treated by conservative measures. These include the oral administration of pancreozymin or other pancreatic substitutes to replace the natural pancreatic secretions. A high protein low fat diet should be given, and coexisting anaemia should be corrected by iron. The symptomatic relief of abdominal pain should be provided by mild analgesics.

Cases which prove resistant to conservative treatment may require surgical intervention with all its attendant risks.

Conclusion

The inaccessibility of the pancreas to clinical examination and the difficulties met with in attempting to delineate it by radiography contribute to diagnostic challenge presented by pancreatitis. New methods of investigation are under consideration in the search for more certain means of diagnosing pancreatic abnormalities. The ability of the pancreas to take up certain amino acids from the bloodstream can be utilized by carrying out radioisotopic scanning after the injection of amino-acid tagged selenium-methionine, and this technique combined with radiography of the duodenum may prove a useful diagnostic tool of the future. Ultrasonic techniques are also being studied in the hope that they too will be of diagnostic value. Until these tests become established, the best possible use must be made of existing methods of investigation combined with sound clinical judgement.

Pancreatitis also presents a challenge in the field of therapeutics. The high morbidity and mortality associated with the surgical treatment of pancreatic disorders is well known, and conservative management of both acute and chronic pancreatitis is likely to produce the best overall results at present.

REFERENCE

Brit. med. J., 1966, 2, 1580.

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