PANCREATITIS IN YOUNG CHILDREN

BY

J. COLLINS

From the Roan Antelope Copper Mines, Luanshya, N. Rhodesia

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Pancreatitis is rare in very young children and the medical literature contains comparatively few accounts of the associated pathology. The purpose of this paper is to describe the findings in the pancreas in four cases in which disease of this gland was discovered at autopsy and to discuss the pathogenesis of the condition. Three of the children concerned were Bantu of N. Rhodesia and were the only ones found to have pancreatitis in the routine examination of material from 100 consecutive autopsies on African children. The fourth child, included for comparison, was an Edinburgh girl and the only case of pancreatitis in the records of 1,812 consecutive post-mortem examinations conducted during the five years 1952-56 by the staff of the Pathology Department of the Royal Hospital for Sick Children, Edinburgh.

Case Histories

Case 1. A female Bantu child, aged 18 months and weighing 13 lb. 4 oz., was admitted to the African Hospital, Luanshya, where she was found to have bronchopneumonia, diarrhoea and vomiting (of several days' duration) with marked dehydration and kwashiorkor of moderate severity. She responded well to treatment but relapsed on the eighth day with further vomiting and diarrhoea for which she again required parenteral fluids. Soon after resuming oral feeding she suddenly collapsed and died in less than three hours. At necropsy the typical appearance of an acute haemorrhagic pancreatitis was found with haemorrhage extending for a considerable distance in the retro-peritoneal tissues both proximally and distally to the pancreas. Fat necrosis was not obvious and no abnormality was present in gall bladder, bile ducts or the terminal portion of the main pancreatic duct. On microscopical examination of the pancreas, the most striking changes were in the interlobular ducts most of which were dilated, some to a remarkable extent, while many contained eosinophilic material which had completely occluded the lumen. This material had often a distinctly laminated appearance and was sufficiently soft to be readily cut by the microtome knife, although tearing of the tissues in the immediate vicinity had occurred in some instances (Fig. 1). The epithelium lining some of these occluded ducts was unusually tall and

columnar, and was occasionally more than one cell layer in thickness, but squamous metaplasia was not present in any of numerous sections examined.

In a few ducts rupture of the wall had occurred with herniation of the contents and in these situations there was a varying degree of round cell infiltration, many of the cells being polymorphs, but elsewhere the dilated and occluded ducts did not appear to have excited any significant reaction, only a very few lymphocytes being found in their walls and immediate surroundings. The main pancreatic duct was normal.

Haemorrhage, although widespread, was confined

FIG. 1.—Case 1. Dilated and ruptured intralobular duct filled with inspissated secretions. (H. and E. $\times 70$.)

mainly to the interlobular septa and the external pancreatic surface, where too the early changes of fat necrosis were present. The walls of a few vessels close to ruptured ducts showed the partial necrosis described by Rich and Duff (1936).

Apart from a few small foci of necrosis near ruptured ducts, the gland parenchyma and islets of Langerhans showed no abnormality except in one area where there had been former destruction and healing by fibrosis was occurring (Fig. 2) and in which the remains of ducts and

tion revealed an acute haemorrhagic pancreatitis, very similar in appearance to that of Case 1, but with less haemorrhage. The interlobular ducts were dilated and occluded by eosinophilic, laminated material (Fig. 3) and some had ruptured, but the duct epithelium showed neither hyperplasia nor metaplasia.

Case 3. A Bantu girl, aged 2 years and weighing 14 lb. 4 oz., was admitted to hospital at Luanshya with a history of convulsions for 24 hours and diarrhoea and vomiting

FIG. 2.—Case 1. Healing by fibrosis of an area of former destruction (H. and E. $\times 70$.)

FIG. 3.—Case 2. Dilated and ruptured intralobular duct filled with inspissated secretions. (H. and E. $\times 70$.)

eosinophilic material could, with difficulty, be distinguished.

Case 2. (71/53. Edinburgh). She was aged 2 years 9 months, and was under treatment for scalds involving 30% of the body surface. After some initial difficulty she had responded satisfactorily for 10 days; she then suddenly developed abdominal distension and vomiting, became shocked and collapsed, and, in spite of all attempts to improve her condition, died in 48 hours. Her previous history included hospitalization at 6, 9 and 14 months of age for persistent vomiting for which no cause was discovered. At autopsy an extensive pneumonia was present and some excess of free fluid in the abdomen. The pancreas appeared normal, but microscopic examina-

tion revealed an acute haemorrhagic pancreatitis, very similar in appearance to that of Case 1, but with less haemorrhage. The interlobular ducts were dilated and occluded by eosinophilic, laminated material (Fig. 3) and some had ruptured, but the duct epithelium showed neither hyperplasia nor metaplasia.

for six or seven days. She was unconscious, very dehydrated, had a severe pneumonia with marked respiratory distress and died shortly after admission. At autopsy a confluent bronchopneumonia was found with numerous pin-head-size abscesses, subsequently shown to be staphylococcal in origin. There was no meningitis. The pancreas appeared unduly pink, but no actual haemorrhage was noted and no abnormality of the gall bladder, bile ducts or the terminal portion of the main pancreatic duct. Microscopically sections from the body of the pancreas showed many dilated interlobular ducts occluded by eosinophilic material similar in all respects to that already described. Some of these ducts had ruptured with partial herniation of contents, and in these areas round cell infiltration was evident (Fig. 4). The duct

epithelium was of normal appearance as was the main pancreatic duct. In a few areas some dilatation of pancreatic acini and ducts was present without duct occlusion being found.

Case 4. A Bantu girl, aged 2 years and weighing 18 lb., was admitted to the African Hospital, Luanshya, with bronchopneumonia, moderately advanced kwashiorkor with oedema of the feet and legs and some areas of skin exfoliation, and also severe gastro-enteritis. After initial improvement she developed thrombocytopenic

FIG. 4.—Case 3. Dilated and ruptured intralobular duct filled with inspissated secretions. (H. and E. $\times 70$.)

purpura and rapidly succumbed to intestinal haemorrhage.

At autopsy the presence of bronchopneumonia, purpura and intestinal haemorrhage was confirmed, but the pancreas appeared to be normal. Microscopically sections of the lungs showed a giant-cell pneumonia. Sections of the body of the pancreas showed a small, completely disorganized area, with foci of necrosis surrounded by dilated and partly necrotic acini. Early fibroblastic proliferation was present and a patchy round cell infiltration. A few severely damaged ducts were recognizable and seemed to be occluded by eosinophilic material. Staining with P.A.S. simplified recognition of these ducts and one is shown in Fig. 5.

Comment

The pathology in Cases 1 and 2 was that of a typical acute haemorrhagic pancreatitis, while that in Case 3 was of lesser severity. In the pancreas of Case 1, however, there was also a small scarred area from a previous incident, not yet completely healed, and Case 4 showed the picture of a similar area at a much earlier stage.

In the first two cases, death was due to the

FIG. 5.—Case 4. Severely damaged duct, filled with inspissated secretion, in area of destruction. (P.A.S. $\times 120$.)

pancreatic condition and this too may have contributed to the fatal outcome in the third, although the pneumonia alone was sufficient to have caused the death of the child. The very small focus of healing pancreatic damage found in Case 4 cannot be regarded as other than an incidental finding.

Discussion

Our knowledge of the pathogenesis of acute haemorrhagic pancreatitis was considerably extended by the work of Rich and Duff (1936) and since that date many others have stressed the

importance of the mechanical factor in the initiation of this condition. In Rich and Duff's series of cases this factor was duct occlusion caused by epithelial hyperplasia and metaplasia, but they also mention three cases in which inspissated secretions, staining irregularly with eosin, were present and which were sometimes associated with inflammatory signs in the walls of the affected ducts.

More recently, Wainwright (1951) found, in the routine examination of material from 2,500 autopsies on persons over 25 years of age, four instances in which inspissated material alone was present in pancreatic interlobular ducts and 81 others in which it was associated with duct epithelial hyperplasia; he suggested that the presence of this material could contribute to duct obstruction. As there can be little doubt that the intraductal material in the four cases presented here did in fact cause duct obstruction it seems worthwhile to discuss the nature and probable cause of these eosinophilic plugs.

In these four cases, the absence of any significant tissue reaction in the vicinity of affected ducts, except where rupture has occurred, and the general similarity of the appearance of the intraductal material to that found in cases of fibrocystic disease of the pancreas, seems to confirm that these eosinophilic plugs are in fact inspissated secretions; moreover their somewhat laminated appearance points to formation over a period of time with enlargement occurring at intervals.

Andersen (1938), referring to similar material, believed that its formation was due to a disturbance of the autonomous nervous stimulation of glandular pancreatic secretion and Baggenstoss (1948) thought that such inspissation could be caused by vagal stimulation, dehydration and possibly malnutrition, especially protein deficiency.

That vagal stimulation does result in the formation of an unnaturally thick and viscid pancreatic juice, rich in enzymes, is a known physiological fact but that protein deficiency can exert a similar effect must be regarded as doubtful, for in kwashiorkor, a disease of protein deficiency the pathology of which has been extensively studied, inspissated pancreatic secretions are very infrequently found (Trowell, Davies and Dean, 1954) and the main pancreatic lesion is a loss of zymogen granules and collapse of the acinar cells (Davies, 1948), a condition hardly compatible with the production of viscid secretion.

The formation of these plugs may be connected with dehydration as the presence of slightly dilated ducts filled with eosinophilic secretions is a common finding in children and others dying in a dehydrated state (Bodian, 1952). Fig. 6 shows a portion of pancreas from such a case and it is possible that in

certain circumstances such pools of secretion may become inspissated and form pancreatic ductal obstructions.

In Central Africa, dehydration in children is most often the result of diarrhoea and vomiting which, at certain seasons of the year, is so widespread that most young African children are affected and many at such frequent intervals that the weights recorded for Cases 1, 3 and 4 are by no means unusual. Since vomiting and diarrhoea may be expected to give rise to vagal stimulation as well as dehydration, the combination of these factors should result in the formation of an abnormally viscid pancreatic secretion. Furthermore, children suffering severely from diarrhoea and vomiting usually refuse all food, and few African mothers in such circumstances would make any effort to coax them to take anything other than perhaps a little water, thereby removing any stimulus for the pancreas to commence the production of more normal secretions to wash out the unnaturally thick and viscid material present in the ducts.

It seems reasonable to assume that if such a state of affairs continued over a period of days, as it

FIG. 6.—Pooled secretions in intralobular duct of a child dying from gastro-enteritis and dehydration. (H. and E. $\times 120$.)

frequently does, inspissation would occur and the seed be sown for future pancreatic damage.

Once inspissation is present it is probable that further deposition would follow, as occurs for example in the case of renal calculi, particularly on any fresh occurrence of similar circumstances, so giving rise to the laminated appearance of the deposit as well as the dilatation and finally obstruction of the affected ducts.

Such a mechanism could account for the occluded ducts found in all three Bantu cases and probably too for those in the Edinburgh child, whose early history contains episodes of persistent vomiting requiring admission to hospital on three occasions. It is also probable that in the latter case her scalds gave rise to some degree of dehydration, as well as vagal stimulation, which may have added to inspissations already present.

Once duct obstruction has occurred rupture is probably inevitable sooner or later, but that the resulting pancreatitis can be confined to a very small area is illustrated in Cases 1 and 4 and the detection of such minute lesions on naked eye examination may be impossible.

If this theory of the cause of these intraductal obstructions is correct then, apart from the normal procedures to remedy dehydration, other measures to overcome vagal stimulation (where this is present) and to encourage normal pancreatic secretions are indicated in all very young sick children.

Summary

The pathology in four cases of pancreatitis in children is described and illustrated.

In each instance inspissated secretions had caused the dilatation, obstruction and subsequent rupture of intralobular ducts and in two cases the resulting pancreatitis had been confined to a very small area and was undergoing healing by fibrosis.

It is suggested that this inspissation is brought about by a combination of vagal stimulation, dehydration and the absence of normal pancreatic secretions over a period of time probably measured in days.

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