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Pancreatic ischaemic lesions without fat necrosis associated with disseminated intravascular coagulation

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Abstract We examined the primary ischaemic changes in the pancreas in 35 patients with disseminated intravascular coagulation. In 7 (20%), multiple patchy lesions composed of degenerative acinar cells indicating coagulation necrosis were noted. None of these lesions was accompanied by fat necrosis. The patchy lesions involved the islets of Langerhans in only 1 case. The interlobular arteries of the pancreas near these lesions contained fibrin thrombi in all 7 cases. We suggest that these lesions, without fat necrosis, are the distinctive ischaemic change associated with disseminated intravascular coagulation.

Key words Pancreas · Ischaemia · Necrosis · Disseminated intravascular coagulation

Introduction

Disseminated intravascular coagulation (DIC) is a life-threatening disorder characterized by activation of the coagulation sequence leading to the formation of microthrombi throughout the microcirculation [2]. Focal ischaemic necrosis associated with DIC has been reported in many organs [4, 10, 12]. In the human pancreas, however, primary ischaemic necrosis is extremely rare [1], and pancreatic necrotic lesions associated with DIC have not been elucidated. This article describes the incidence and distinctive features of some primary ischaemic changes of the pancreas in patients with DIC.

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Materials and methods

Thirty-five postmortem pancreases, without autolysis, taken from patients clinically diagnosed as having DIC were examined histopathologically. In all cases, the presence of fibrin thrombi was confirmed in the renal glomeruli. No cases of primary pancreatic cancer were included. In only 1 of these 35 cases had a clinical diagnosis of acute pancreatitis been made. The postmortem interval before autopsy ranged from 1 to 8 h.

All pancreases were fixed in 10–20% buffered formalin. Representative pancreatic sections (3–4 blocks for each case) were paraffin-embedded, cut, and stained with haematoxylin and eosin. Additional phosphotungstic acid haematoxylin (PTAH) staining was performed in selected sections.

Results

The clinicopathological profiles of all cases are sumarized in Table 1. Well-demarcated patchy lesions of the pancreas were detected in 7 of the 35 pancreases (Fig. 1). These patchy lesions were composed of degenerative acinar cells showing deeply eosinophilic cytoplasm and pyknotic or disappearing nuclei, which suggested coagulation necrosis due to ischaemia. None of the lesions was accompanied by fat necrosis. Only 1 case (case 5) had been clinically diagnosed as acute pancreatitis, but fat necrosis was not found in this case although patchy ischaemic lesions were extensive. Inflammatory infiltration was scant both in the pancreatic tissues surrounding these lesions and in most of these lesions themselves. In some cases, small areas of acinar necrosis were also found in the vicinity of the patchy lesions (Fig. 2). In case 3, the necrotic acinar cells had mostly disappeared, and loose oedematous tissues surrounded the necrotic focus, with mild neutrophilic infiltration (Fig. 3). In case 4, the patchy lesions were accompanied by haemorrhages (Fig. 4) and contained minute fibrin thrombi, as was confirmed by PTAH stain. In 6 of the 7 cases the patchy lesions did not involve the islets of Langerhans, which were involved only in case 5 (Fig. 5). Fibrin thrombi were detected focally near the patchy lesions within the interlobular arteries of the pancreas in all 7 cases (Fig. 6).

Table 1 Characteristics of 7 patients with DIC showing pancreatic ischaemic lesions (*SqCC* squamous cell carcinoma, *PIL* pancreatic ischemic lesions, *FT* fibrin thrombus, *ILA* interlobular artery of the pancreas, *ASO* atherosclerosis obliterans)

Case no.	Age (years)/sex	Main diagnosis	Main cause of DIC	PIL involving the islets	FT in PIL	FT in ILA
1	70/M	Non-Hodgkin's lymphoma (diffuse, large-cell type)	Neoplasm	(–)	(–)	(+)
2	77/M	ASO	Thrombosis	(–)	(–)	(+)
3	71/F	Lung cancer (SqCC)	Neoplasm	(–)	(–)	(+)
4	86/M	Lung cancer (SqCC)	Neoplasm	(–)	(+)	(+)
5	19/M	Bronchopneumonia	Sepsis	(+)	(–)	(+)
6	59/M	Non-Hodgkin's lymphoma (diffuse, large-cell type)	Neoplasm	(–)	(–)	(+)
7	69/F	Rheumatoid arthritis	Vasculitis	(–)	(–)	(+)

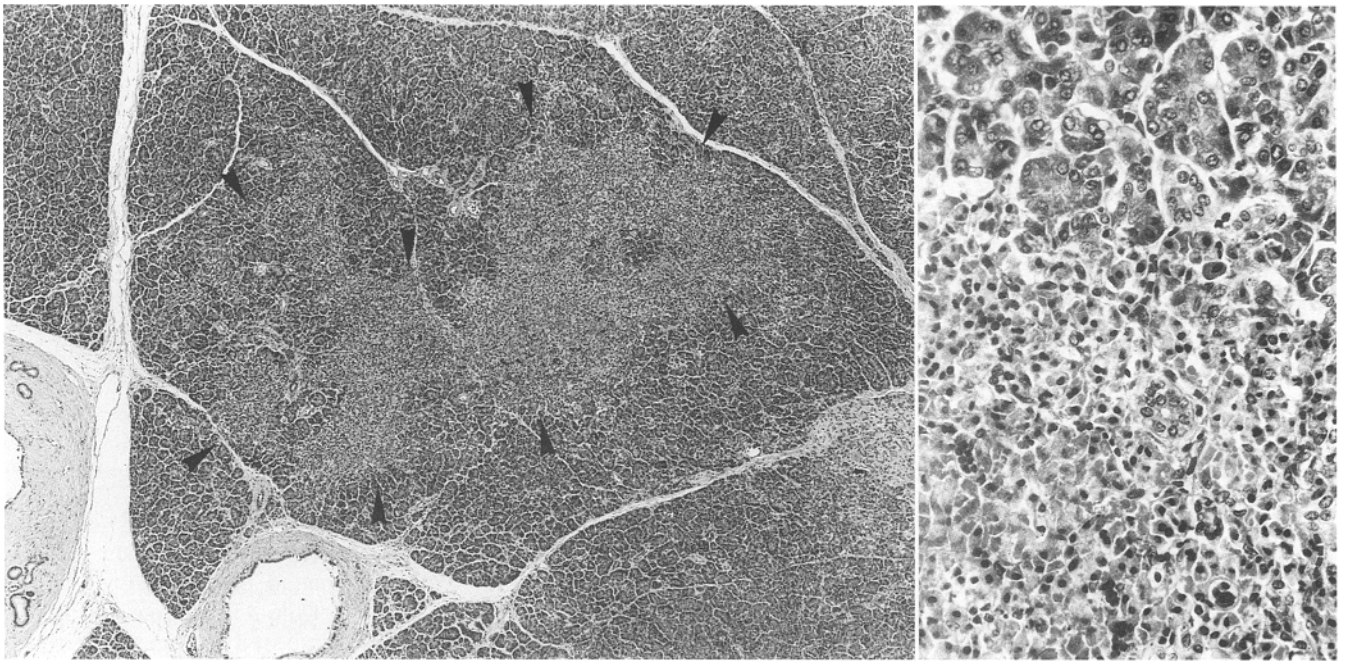


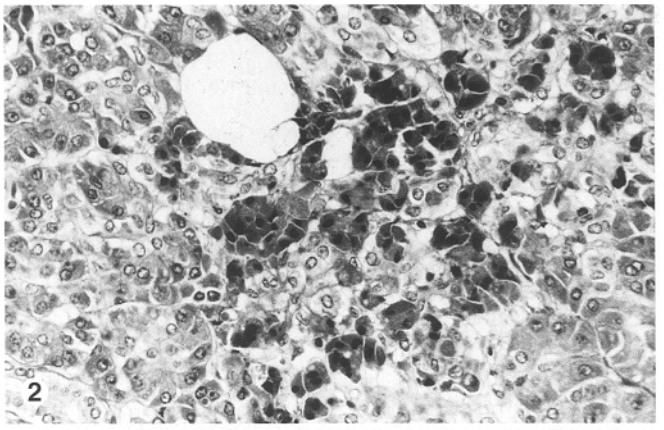
Fig. 1 *Left* Case 1: patchy ischaemic lesions (*arrowheads*) in the pancreatic lobules. (×40). *Right* High magnification of patchy lesions composed of degenerating acinar cells, showing deeply eosinophilic cytoplasm and pyknotic or disappearing nuclei. Compare these cells with the intact acinar cells in the upper zone. (×300)

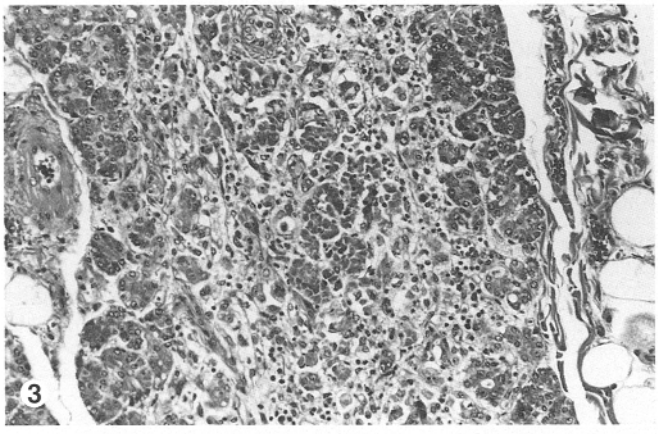
In 6 of all 35 cases (17.1%), fat necrosis was found focally in the pancreas. However, none of these 6 cases showed the patchy ischaemic lesions.

Discussion

Ischaemic changes in the human pancreas are extremely rare [1]. McKay et al. [7] found pancreatic infarctions in only 0.19% of 21,481 necropsies at the Mayo Clinic. This rarity may be attributable to the rich arterial blood supply with numerous vessel anastomoses [1, 3]. However, focal pancreatic necrosis with fat necrosis (tryptic necrosis) is not uncommon in patients with lightning stroke or shock [3]. Becker et al. [1] found tryptic necrosis in 11% of the cases of shock they examined. From the morphological and pathogenetic points of view, there are fundamental differences between tryptic necrosis and primary ischaemia [1]. Tryptic necrosis results from autodigestion of the pancreatic tissues caused by extravasated pancreatic juice containing activated enzymes; pancreatic circulatory disturbances including ischaemia may be the trigger for this condition [2]. Recent studies [5, 8] have suggested that fat necrosis is the definitive hallmark of the onset of acute pancreatitis. However, the pancreatic ischaemic lesions detected in the present study were not accompanied by fat necrosis. We emphasize that the patchy pancreatic lesions detected in the present study are primary ischaemic changes caused by hypoxaemia and differ from tryptic necrosis.

DIC is a disorder of the coagulation sequence and is caused by sepsis, burns, malignant neoplasm, liver disease and many other diseases [2]. It is characterized by the formation of microthrombi throughout the microcir-





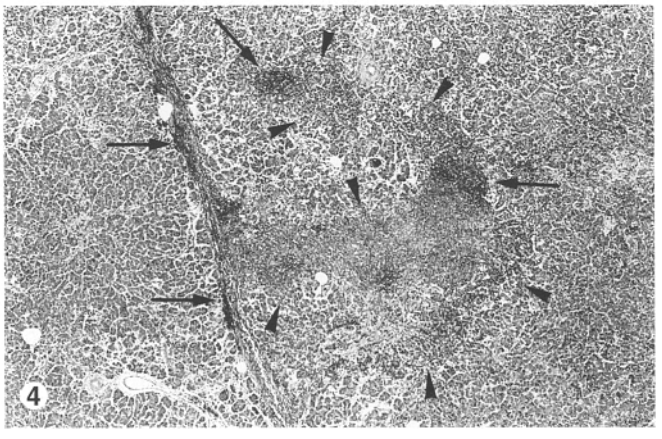
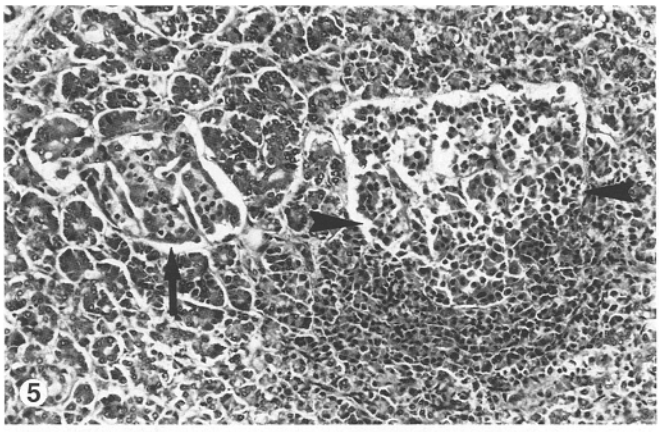


Fig. 2 Case 4: scattered nests of primary acinar necrosis, showing deeply eosinophilic cytoplasm and pyknotic nuclei. Note the closely located fat without necrosis. (×400)

Fig. 3 Case 3: loose tissues with a mild inflammatory infiltrate surrounded small foci of acinar cells necrosis. (×200)

Fig. 4 Case 4: patchy ischaemic lesions without fat necrosis (*arrowheads*) and accompanying haemorrhages (*arrows*). (×40)



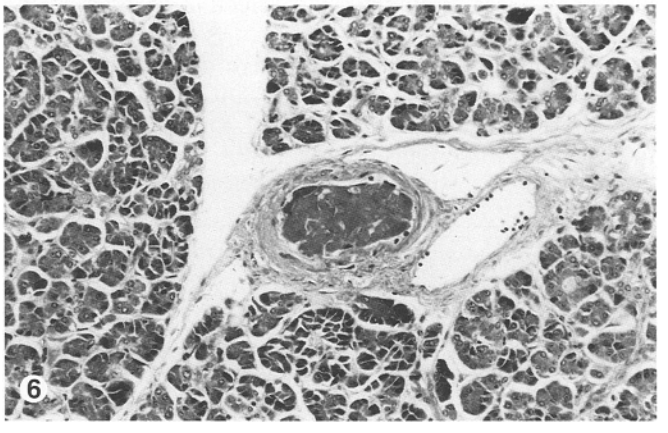


Fig. 5 Case 7: ischaemic lesions involving the islet of Langerhans (*arrowheads*). The neighbouring islet (*arrow*) is intact. (×200)

Fig. 6 Case 3: fibrin thrombus in the interlobular artery. (×200)

culation [2], and histologically, fibrin thrombi are frequently found in the glomerulus of the kidney or in the lung [4]. In the present study, all the subjects were patients with DIC in whom histological examination confirmed the presence of fibrin thrombi in the renal glomeruli. The study detected primary ischaemic changes of the pancreas in 20% of the DIC cases examined. These lesions had multiple patchy forms. To our knowledge, the incidence and distinctive histological features of primary ischaemic lesions of the pancreas associated with DIC have not been elucidated, although such lesions have been reported in the kidney, heart, central nervous system, intestine, liver, adrenal glands, pituitary gland, spleen, and vertebrae [4, 10, 12].

Using a correlation with the from of the pancreatic microvasculature [13], Takahashi et al. [11] classified pancreatic ischaemic injuries into three categories: (1) "peripheral necrosis", chiefly occurring in the peripheral areas of the pancreastic lobules and not involving the islets, (2) "central necrosis", representing a microinfarction of acinar cells and the islets, and (3) "peripheral atrophy", characterized by the thinner and more degranulated pattern of acinar cells in the peripheral areas of the pancreatic lobules. These authors suggested that central necrosis is caused by obstruction of the terminal arterioles centrally placed in the pancreatic lobules. According to the form of the microvasculature proposed by Yaginuma et al. [13], most of the terminal arterioles supply the islets directly. Takahashi et al. [11] also concluded that peripheral necrosis is caused by stenosis of arteries that are more proximal than the terminal arterioles, such as the interlobular arteries or even larger vessels. In the

present study, peripheral necrosis was found in 6 cases and central necrosis was noted in only 1 case, suggesting that the ischaemic lesions associated with DIC result from the involvement of arteries that are more proximal than the terminal arterioles. The high incidence of fibrin thrombi in the interlobular arteries of our cases supports this theory. Infrequently, however, circulatory disturbance of the terminal arterioles may occur and cause ischaemic necrosis of both acinar cells and the islets of Langerhans. Some authors [6, 9] have noted selective ischaemic changes of the islet of Langerhans in patients with various forms of shock and have emphasized the vulnerability of the islets to shock-related injury in the newborn and the young infant. Our patients did not include newborns or infants, and selective changes in the islets were not found.

Our study has detected distinctive primary ischaemic lesions in the pancreas in 20% of DIC cases examined. These lesions had multiple patchy forms and involved the islets of Langerhans in only a case.

References

1. Becker V, Stollhoff K (1985) Shock and terminal pancreatitis. Pathol Res Pract 179:512–516
2. Cotran RS, Kumar V, Robbins SL (1994) Robbins pathologic basis of disease, 5th edn. Saunders, Philadelphia, pp 623–627, 899–902
3. Cruickshank AH (1986) Pathology of the pancreas. Springer, Berlin Heidelberg New York, pp 60, 69–75, 195–232
4. Fukusato T, Mori W (1979) Pathology of disseminated intravascular coagulation. Igaku No Ayumi 109:745–753
5. Klöppel G, Gerkan R von, Dreyer T (1984) Pathomorphology of acute pancreatitis – analysis of 367 autopsy cases and 3 surgical specimens. In: Gyr KE, Singer MV, Sarles H (eds) Pancreatitis – concepts and classification. Excerpta Medica, Amsterdam, pp 29–35
6. Klöppel G, In't Veld PA, Stamm Bernhard, Heitz PU (1991) The endocrine pancreas. In: Kovacs K, Asa SL (eds) Functional endocrine pathology. Blackwell, Cambridge, Mass, pp 426–427
7. McKay JW, Baggenstoss AH, Wollaeger EE (1958) Infarcts of the pancreas. Gastroenterology 35:256–264
8. Schmitz-Moormann P (1981) Comparative radiological and morphological study of the human pancreas. IV. Acute necrotizing pancreatitis in Man. Pathol Res Pract 171:325–335
9. Seemyer TA, Osborne C, De Chadarévian JP (1985) Shock-related injury of pancreatic islets of Langerhans in newborn and young infants. Hum Pathol 16:1231–1234
10. Sugiura M, Ueda K (1979) Clinical features and diagnosis of the cardiac lesions in disseminated intravascular coagulation. Igaku No Ayumi 109:803–808
11. Takahashi T, Yaginuma N (1985) Ischemic injury of the human pancreas – its basic patterns correlated with the pancreatic microvasculature. Pathol Res Pract 179:645–651
12. Watanabe T (1995) Pathology of disseminated intravascular coagulation (DIC). Byori To Rinsho 13:152–158
13. Yaginuma N, Takahashi T, Saito K, Kyogoku M (1986) The microvasculature of the human pancreas and its relation to Langerhans islets and lobules. Pathol Res Pract 181:77–84