

Case reports

Necrotizing arteritis causing fatal massive intraperitoneal hemorrhage from a pancreatic pseudocyst

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Summary. We report the histopathological findings from a medicolegal autopsy case caused by sudden massive hemorrhage from a necrotic pancreatic cyst into the abdominal cavity. The histological examination revealed that the wall of the cyst was filled with hematoma and consisted of granuloma at a relative early stage, involving marginating lymphocytes, foamy lipophages, cholesterol crystals, foreign body giant cells with neutrophils, mast cells and fibrous tissues. Since there was no epithelial lining, the lesion was diagnosed as a pseudocyst. In the wall of this pseudocyst, small arteries showed acute intense necrotizing inflammatory reactions in association with fresh thrombi. Trace of elastic fibers remained in the wall of the arteries. Since the small veins in the wall showed varix-like changes without necrosis or inflammation, it is proposed that the lethal bleeding was caused by rupture of the small arteries that exhibited severe arteritis.

Key words: Sudden death – Pancreatitis – Pseudocyst – Hemorrhage

Zusammenfassung. Berichtet wird über histologische Befunde bei einem rechtsmedizinischen Obduktionsfall, bei welchem der Tod durch eine massive Blutung aus einer nekrotischen Pankreas-Zyste in die Bauchhöhle verursacht wurde. Die histologische Untersuchung deckte auf, daß die Wand der Zyste mit einer Blutung angefüllt war und aus granulomatösem Gewebe in einer relativ frühen Phase bestand, unter Einbeziehung randständiger Lymphozyten, schaumiger Lipophagen, Cholesterin-Kristallen, Fremdkörper-Riesenzellen mit Neutrophilen, Mastzellen und fibrösen Geweben. Da kein epithelialer Überzug vorhanden war, wurde die Läsion als "Pseudozyste" klassifiziert. In der Wand dieser Pseudozyste zeigten kleine Arterien akute intensive nekrotisierende entzündliche Reaktionen in Verbindung mit frischen Thromben. Spuren elastischer Fasern verblieben in der Wand der Arterien. Da die kleinen Venen in der Wand der Pseudo-

zysten varixähnliche Veränderungen ohne Nekrose oder Entzündung aufwiesen, wird vorgeschlagen, daß die letale Blutung durch die Ruptur kleiner Arterien verursacht wurde, welche eine schwere Arteriitis aufwiesen.

Schlüsselwörter: Plötzlicher Tod – Pankreatitis – Pseudozyste – Hämorrhagie

Introduction

In cases of sudden death investigated by a medical examiner, pancreatic diseases have been rarely given as the cause of death [1]. Only in 2 out of 1000 consecutive autopsies of natural death investigated by one medical examiner's office, has pancreatitis been determined to be the cause of death [2]. There are relatively few reports on histological examinations of fatal necrotizing pancreatitis because autopsy specimens have frequently been damaged, although considerable attention has been focused on the intervention management of pancreatic pseudocysts with successful results among surgeons [3–6]. Here, we describe the histological examination of a medicolegal autopsy case in which the direct cause of death was discovered to be sudden massive bleeding from the small arteries in the wall of a pseudocyst in the course of necrotizing pancreatitis, superimposed on the underlying chronic pancreatitis.

Case report

The patient was a Japanese male aged 47. He had been in hospital about 7 years previously suffering from a fatty liver and chronic pancreatitis due to alcoholic toxicosis. He had no history of abdominal trauma. One day, he suddenly complained of a severe abdominal pain radiating to the back, and was admitted to hospital. After treatment by an intravenous drip injection of analgesic, he recovered to a fair condition and attempted to return home by taxi. After a short while, in the taxi, he lost consciousness and died about one hour later in the emergency intensive care unit.

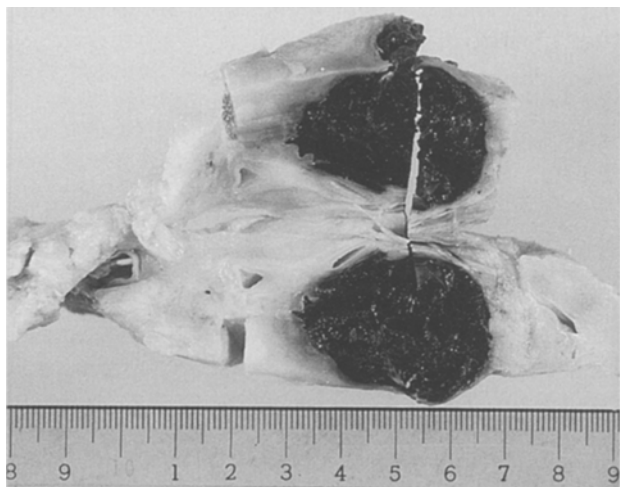


Fig. 1. A clearly demarcated hematoma in the body of the pancreas

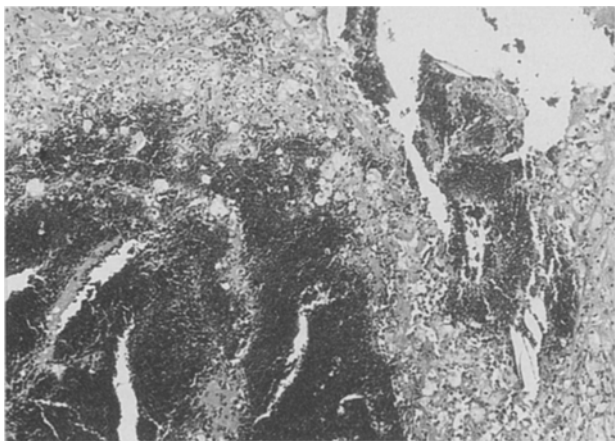


Fig. 2. Histological features of the cystic wall with no epithelial lining. Intense hemorrhaging and cell infiltration were present. (HE, ×200)

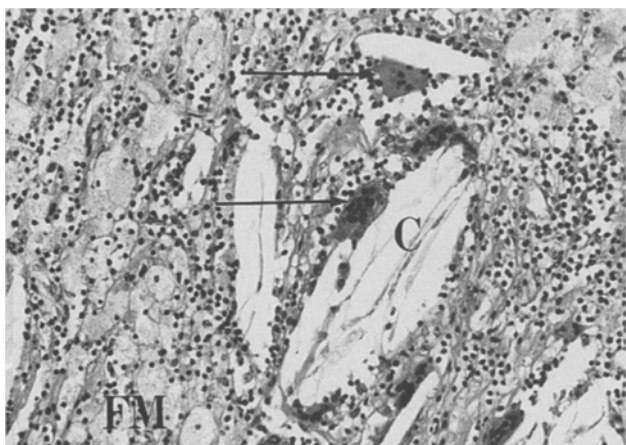


Fig. 3. Cholesterol crystals (C), foreign body giant cells (arrows) and foamy macrophages (FM) were found in the relatively early granulomatous cystic wall. (A; HE, ×400)

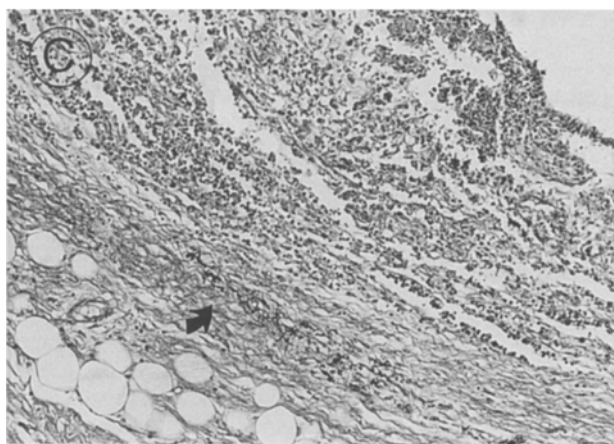
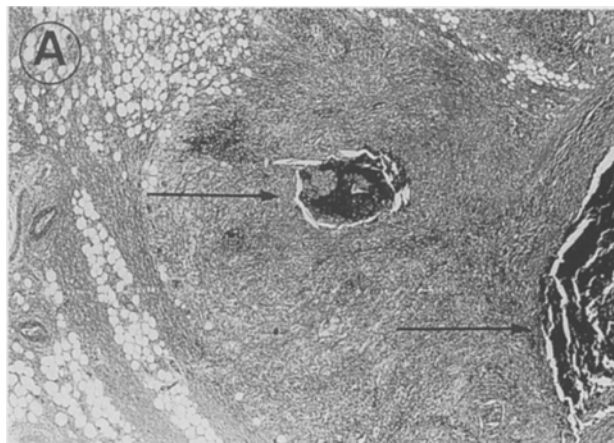


Fig. 4A–C. Acute necrotic arteritis (arrows) with fresh thrombus including neutrophils (A and B), surrounding edematous lesions (B) and traces of elastic fibers (curved arrow) (C). (A; HE, ×40, B; HE, ×200 and C; EvG, ×200)

Autopsy findings and microscopic examination. Macroscopical findings: an autopsy was performed about 10 h after death. The patient was 61 kg in weight and 180 cm length. No external injury was found on the body. There was about 2000 ml of fresh blood in the abdominal cavity and a large cystic hematoma in the body of the pancreas behind the transverse colon. The hematoma measured ca. $2.5 \times 3.5 \times 4$ cm (Fig. 1) and the cystic wall was red in color with congestion. The liver weighted 2300 g and was remarkably fatty in agreement with previous reports [7–10]. No stones were

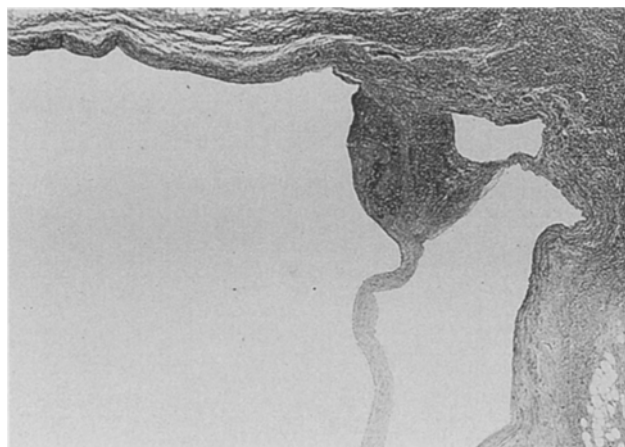


Fig. 5. Varix-like dilated small veins in the cyst wall (HE, $\times 40$)

found in the bile duct or in the gall bladder. In the esophagus, no sign of any varices was found. The heart (360 g) and the lungs (left 240 g, right 250 g) showed intact structures. No pathological changes were found in any other organs except for the left kidney which had a small cyst.

Microscopical findings: specimens from various parts of the pancreas, including the wall of the cyst, were fixed in 10% neutral buffered formalin and embedded in paraffin, cut into 5 μ sections, and stained with hematoxylin and eosin (HE) for histological studies. Some sections were stained with special stains, including Mallory's phosphotungstic acid-hematoxylin stain (PTAH), Azan-Mallory stain, and Elastica van Gieson's stain. Inside the cyst, the structures of the pancreas, including both exocrine parenchyma and Langerhans' islets, were completely destroyed and were replaced by intense lesions which had hemorrhaged with extensive cell infiltration (Fig. 2). The cyst wall consisted of granuloma of a relative early stage, involving marginating lymphocytes (some of which had formed follicles), foamy macrophages which had lipid material, cholesterol crystals, foreign body giant cells with neutrophils, mast cells and slight formation of fibrous tissue (Fig. 3). Since there were no true epithelial linings, the lesion was diagnosed as a pseudocyst. Additionally, in a few small arteries in the wall of the pseudocyst, showed acute intense necrotizing inflammatory arteritis (mainly consisting of neutrophils) accompanied by fresh thrombi (Fig. 4A). The intima, inner elastic plate and muscle layers of the arteries were destroyed and traces of elastic fibers remained in the wall of necrotic arteries (Fig. 4B and C). No fibroid necrosis or dense fibrosis was found in the arteries. Some veins showed varix-like changes, with no hemorrhagic, necrotic or inflammatory reactions (Fig. 5).

In other portions of the pancreas, chronic pancreatic changes were histologically observed, including intense diffuse interstitial fibrosis, dilatation of the pancreatic ductules, protein plugs and pancreatic stones. However, no inflammatory, necrotic, hemorrhagic or malignant lesions were found. In the liver, pan-lobular fatty degeneration was demonstrated by fat staining. The pathological examinations of the other main organs revealed no specific lesions, with the heart having only a slight shearing of muscle cells. From these observations, it is suggested that the pseudocyst developed from acute necrotizing pancreatitis several weeks prior to death, and sudden bleeding into the pseudocyst resulted in abdominal pain and subsequent rupture into the peritoneal cavity.

Discussion

Formation of a pseudocyst in the pancreas from a disruption in the pancreatic duct or one of the smaller ductules is

a relatively common phenomenon (10–50%) in the early phases of moderately-severe pancreatitis [3–5, 11, 12]. While some pseudocysts of the pancreas undergo slow spontaneous regression, massive hemorrhage from a pseudocyst is an unpredictable serious complication and is the prime cause of death in patients with a pseudocyst in the pancreas [3, 13]. Sankaran and Walt [13] reported that 16 out of 112 patients with a pseudocyst in the pancreas incurred an associated massive hemorrhage with a subsequent mortality rate of 61%, while the mortality rate after surgical treatment of 97 uncomplicated pseudocysts was only 6%. Intracystic bleeding caused by erosion of the major arteries has been reported to have been successfully treated by surgery [6, 14].

In the present study, we found that some of the arteries in the wall of the pseudocyst showed acute intense necrotizing inflammatory reactions, resulting in the presence of traces of elastic fibers in the wall of the arteries (Fig. 4). We also discovered varix-like changes in the small veins of the pseudocyst wall, but without inflammatory reactions (Fig. 5). While gastric variceal bleeding secondary to obstruction of the portal or splenic vein by a pseudocyst has been reported [15], the presence of varices in the wall of a pseudocyst is uncommon. From these observations, we propose that severe erosion by the pancreatic digestive enzymes during a recent attack of acute pancreatitis led to necrotic arteritis in the wall of a pre-existing pseudocyst, resulting in sudden rupture into the peritoneal cavity. In this study, we have histologically identified the arteries of the wall of the pseudocyst from which the hemorrhage occurred.

Since acute pancreatitis is generally uncommon as the principle cause of sudden death, it is important to make a differential diagnosis between blunt abdominal trauma and intrinsic pancreatic lesions in the forensic autopsy.

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References

1. Williams G (1954) Acute pancreatic necrosis as a cause of sudden death. *BMJ* 1: 1184–1185
2. Di Maio VJ, Di Maio DJM (1991) Natural death as viewed by the medical examiner: a review of 1000 consecutive autopsies of individuals dying of natural disease. *J Forensic Sci* 36: 17–24
3. Warshaw AL, Rattner DW (1985) Timing of surgical drainage for pancreatic pseudocyst. *Ann Surg* 202: 720–724
4. Frey CF (1978) Pancreatic pseudocyst – operative strategy. *Ann Surg* 188: 652–662
5. Crass RA, Way LW (1981) Acute and chronic pancreatic pseudocysts are different. *Am J Surg* 142: 660–663
6. Wu TK, Zaman SN, Gullick HD, Powers SR (1977) Spontaneous hemorrhage due to pseudocysts of the pancreas. *Am J Surg* 134: 408–410
7. Enquist IF, Gliedman ML (1958) Gross autopsy findings in cases of fatal acute pancreatitis. *Arch Surg* 77: 985–991
8. Renner IG, Savage WT, Pantoja JL, Renner VJ (1985) Death due to acute pancreatitis. A retrospective analysis of 405 autopsy cases. *Dig Dis Sci* 30: 1005–1018
9. Moberg A, Svenham K, Wagermark J (1968) Acute "idiopathic" pancreatitis. A post-mortem etiological study. *Acta Chir Scand* 134: 369–372

10. Klöppel G, Maillet B (1991) Pseudocysts in chronic pancreatitis. A morphological analysis of 57 resection specimens and 9 autopsy pancreata. *Pancreas* 6:266–274
11. Gonzalez AC, Bradley EL, Clements JL (1976) Pseudocyst formation in acute pancreatitis: ultrasonographic evaluation of 99 cases. *Am J Roentgenol* 127:315–317
12. Bradley EL, Gonzalez AC, Clements JL (1976) Acute pancreatic pseudocysts. Incidence and implications. *Ann Surg* 184:734–737
13. Sankaran S, Walt AJ (1975) The natural and unnatural history of pancreatic pseudocysts. *Br J Surg* 62:37–44
14. Stanley JC, Fey CF, Miller TA, Lindenauer SM, Child CG (1976) Major arterial hemorrhage. A complication of pancreatic pseudocysts and chronic pancreatitis. *Arch Surg* 111:435–440
15. Salam AA, Warren WD, Tyras DH (1973) Splenic vein thrombosis: a diagnosable and curable form of portal hypertension. *Surgery* 74:961–972