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Angiographic Features in Acute Pancreatitis: The Severity of Abdominal Vessel Ischemic Change Reflects the Severity of Acute Pancreatitis

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ABSTRACT

Context Assessment of tissue microcirculation is one of the important aspects of pathological evaluation in acute pancreatitis. Severe ischemic change sometimes leads to the development of organ dysfunction and/or infectious complications.

Objective To evaluate the angiographic features of acute pancreatitis and correlate them with the severity of the disease.

Design Retrospective study.

Patients Twenty-seven consecutive patients with acute pancreatitis who had undergone angiography were retrospectively investigated.

Main outcome measures Vascular findings and Ranson score.

Results Ischemic changes were found in 18 patients (66.7%); 11 (40.7%) were severe changes. Pseudoaneurysm, bleeding, and staining were seen in 4 (14.8%), 2 (7.4%) and 5 (18.5%) patients, respectively. The rate of severe ischemic changes was significantly correlated with the Ranson score (P=0.012).

Conclusions Angiographic findings are useful for the evaluation of severe acute pancreatitis.

INTRODUCTION

Acute pancreatitis is a potentially fatal disease with an overall mortality of 7-11% [1, 2, 3]. Severe acute pancreatitis is frequently associated with pancreatic necrosis [4, 5], whose mortality exceeds 20%. One of the possible mechanisms of pancreatic necrosis is thought to be microvascular obstruction caused by local vascular spastic change and increased intravascular coagulability. Such vascular complications can also occur in other organs if the inflammatory insults are of sufficient intensity. Indeed, vascular complications, such as renal cortical necrosis, splenic infarction, colonic necrosis, ischemic heart disease, brain ischemia and retinal infarction have been reported with severe acute pancreatitis [6, 7, 8, 9, 10, 11, 12, 13, 14, 15].

As already mentioned, the assessment of tissue microcirculation is an important aspect of the pathological evaluation of acute pancreatitis. Microcirculatory deterioration is often observed in severe acute pancreatitis. Severe ischemic change sometimes leads to the development of organ dysfunction and/or infectious complications. Since angiography is one of the most useful examinations with which to assess tissue circulation, we evaluated the angiographic features of acute pancreatitis and correlated them with the severity of the acute pancreatitis.

Table 1. Characteristics of the118 patients with acute pancreatitis.

	Patients not examined with angiography (n=91)	Patients examined with angiography (n=27)	P value
Sex			1.000 [a]
Males	63 (69.2%)	19 (70.4%)	
Females	28 (30.8%)	8 (29.6%)	
Age (m±SD)	51.8±15.6	50.6±14.3	0.721 [b]
Ranson score			<0.001 [c]
0-2	71 (78.0%)	3 (11.1%)	
3-4	9 (9.9%)	12 (44.4%)	
5-11	11 (12.1%)	12 (44.4%)	
Deaths	5 (5.5%)	5 (18.5%)	0.048 [a]

[a] Fisher's exact test
[b] ANOVA
[c] Mantel-Haenszel linear-by-linear association

METHODS

Patients

A total of 118 patients with acute pancreatitis were managed in our department from April 1992 through August 2002. Among them, the 27 patients who had undergone angiography were retrospectively investigated with respect to the state of their acute pancreatitis and their vascular findings. The characteristics both of the patients who had undergone and those who had not undergone angiography are reported in Table 1. Among the patients who had undergone angiography, there were 19 men and 8 women. Their ages varied from 13 to 79 years (average 50.6 years). The frequency of patients who underwent angiography was positively related to the severity of the pancreatitis and more deaths occurred in these patients (18.5% vs. 5.5%). The diagnosis was based on a history of acute upper abdominal pain associated with an increase in serum pancreatic amylase and was confirmed by abdominal US and/or contrast-enhanced CT. The causes of acute pancreatitis were: alcohol abuse in 14 patients; pancreatitis after endoscopic pancreatographic examination and/or treatment in 4 patients; gallstone pancreatitis in 3 patients; steroid-induced pancreatitis in 1 patient; L-asparginase-induced pancreatitis in 1 patient; pancreatitis complicated with metabolic disease in 1 patient. No cause could be found in 3 patients, thus they were labeled as having idiopathic pancreatitis. The patients were divided into 3 groups according to their Ranson score (Table 2) [16, 17]. Two of the 5 patients with a fatal outcome died of non-occlusive mesenteric ischemia (NOMI)-associated diffuse intestinal necrosis [18, 19] while the causes of death in the other three patients were multiple organ failure for two patients and shock for one patient.

Angiographic Examinations

Conventional and/or digital subtraction angiography was performed with selective catheterization into the celiac and superior mesenteric arteries. This procedure was followed by automatic injection of 15-25 mL of a low-osmolarity non-ionic contrast agent (Optiray 350, Yamanouchi, Tokyo, Japan)

Table 2. Patient characteristics according to the severity of acute pancreatitis

Ranson score	Gender (M:F)	Age (years old; mean±SD)	Mortality
0-2 (n=3)	2 (66.7%):1 (33.3%)	53.0±10.5	0 (0%)
3-4 (n=12)	8 (66.7%):4 (33.3%)	48.2±16.8	0 (0%)
5-11 (n=12)	9 (75.0%):3 (25.0%)	52.3±13.0	5 (41.7%)
P value	0.679 [a]	0.942 [b]	0.015 [a]
Total (n=27)	19 (70.4%):8 (29.6%)	50.6±14.3	5 (18.5%)

[a] Mantel-Haenszel linear-by-linear association
[b] Linear trend ANOVA (polynomial contrast)

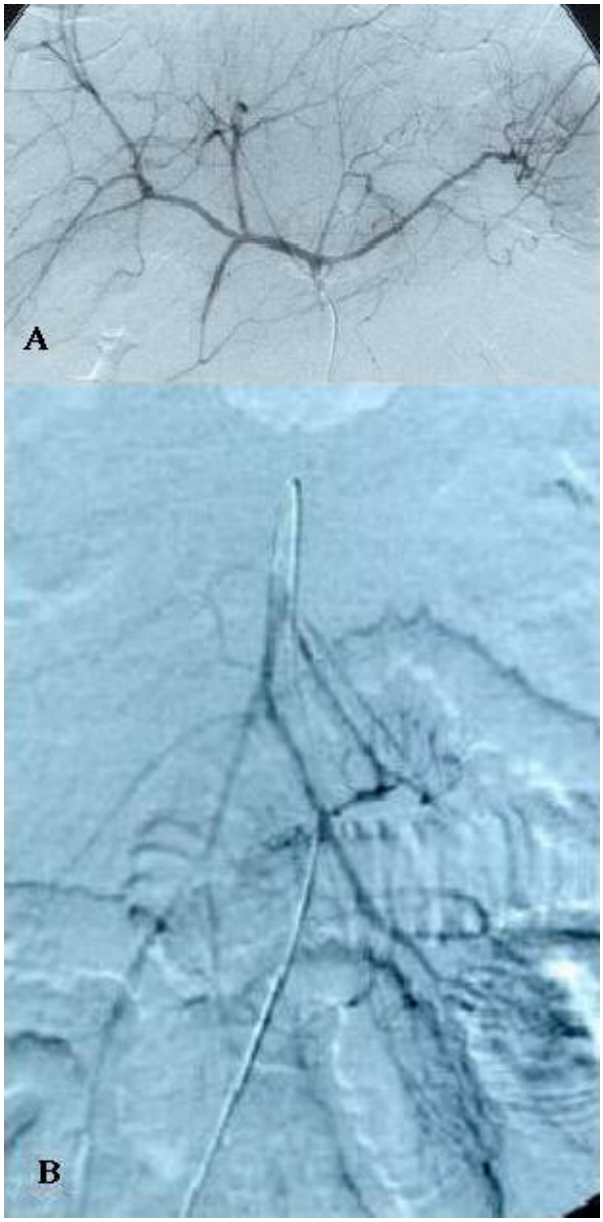

Figure 1. Severe diffuse ischemic change. Celiac (A) and superior mesenteric (B) angiograms of a patient with alcoholic pancreatitis. (Male, 40 years old).

diluted with saline and having a flow rate of 3-5 mL/sec. In one patient with a pseudoaneurysm at the celiac trunk, an aortography was performed. A therapeutic team with expert knowledge of severe acute pancreatitis carried out the evaluation of the angiographic findings. The presence of ischemic changes (spasm and obstruction), aneurysm, bleeding, and accumulation of contrast medium (staining) were evaluated. We defined diffuse spasm and/or obstruction of the abdominal vessels as severe ischemic change.

ETHICS

Written informed consent was obtained from each patient. The protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as revised in 1983; it was not submitted to Ethical Committee, because angiography for severe acute pancreatitis is not a rare procedure in Japan and it was performed during normal clinical practice.

STATISTICAL ANALYSIS

Frequencies, means, standard deviations, and ranges were used as descriptive statistics. The statistical significance of the data was determined using the Fisher's exact test, the Mantel-Haenszel linear-by-linear association, and the analysis of variance (ANOVA). Two-tailed P values less than 0.05 were considered significant. Statistical analysis was performed by running the SPSS 8.0 (SPSS Inc., Chicago, IL, USA) package on a personal computer.

RESULTS

Arterial Changes

Ischemic changes at arteriography were observed in 18 patients (66.7%). Such ischemic changes can occur either diffusely, as in Figure 1, or focally, as in Figure 2. Severe ischemic changes such as diffuse spasm and obstruction of the large splanchnic vessels were seen in 11 patients (40.7%).

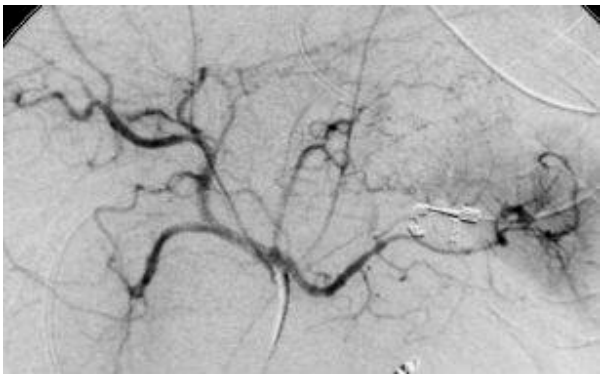

Figure 2. Focal ischemic change. Celiac angiogram of a patient with alcoholic pancreatitis. Note the focal spasm in the splenic artery. (Male, 41 years old)

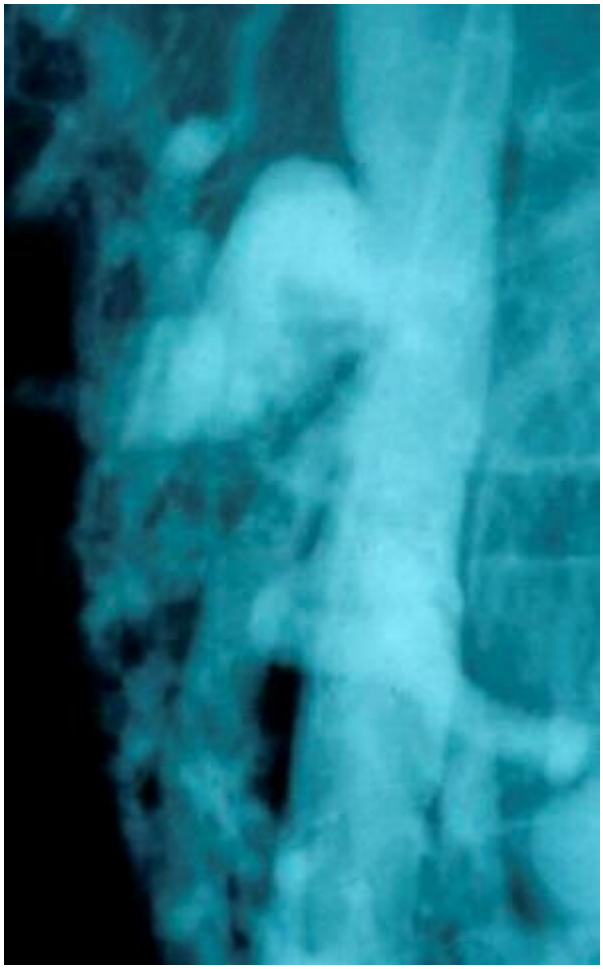

Figure 3. Pseudoaneurysm at the celiac trunk. Arteriogram of a patient with steroid-induced pancreatitis, which was performed upon admission during the second attack of pancreatitis. (Female, 35 years old)

Destructive changes, such as pseudoaneurysm (Figure 3), were observed in 4 patients (14.8%) and bleeding was observed in 2 patients (7.4%).

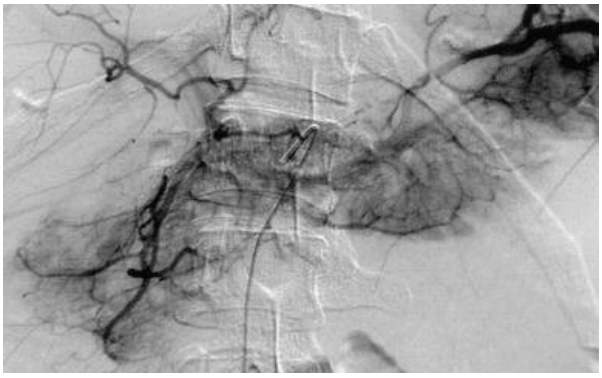

Figure 4. Accumulation of contrast medium. Celiac angiogram of a patient with steroid-induced pancreatitis which was performed upon admission during the first attack of pancreatitis. (The same patient as in Figure 3).

Parenchymal and Venous Changes

Inflammatory changes, such as an increased (Figure 4) or an irregular accumulation of contrast medium (staining), were seen in 5 patients (18.5%). Obstruction of the intrahepatic portal vein (posterior branch) and stasis of the splenic and the portal veins were seen in 1 patient (3.7%).

Association of Vascular Change and Severity of Acute Pancreatitis

Angiographic findings according to the Ranson score are summarized in Table 3. The frequency of severe ischemic change was significantly correlated with the Ranson score (P=0.012) and was seen more often (66.7%) in the severest group (Ranson score of 5 or

Table 3. Relationship between angiographic findings and the severity of acute pancreatitis

Ranson score	Ischemic change	Severe ischemic change*	Staining	Pseudoaneurysm	Bleeding
0-2 (n=3)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3-4 (n=12)	8 (66.7%)	3 (25.0%)	5 (41.7%)	4 (33.3%)	2 (16.7%)
5-11 (n=12)	9 (75.0%)	8 (66.7%)	0 (0%)	0 (0%)	0 (0%)
P value	0.220 [a]	0.012 [a]	0.224 [a]	0.288 [a]	0.471 [a]
Total (n=27)	18 (66.7%)	11 (40.7%)	5 (18.5%)	4 (14.8%)	2 (7.4%)

* Diffuse spasm and/or obstruction of abdominal vessels
[a] Mantel-Haenszel linear-by-linear association

more). Pseudoaneurysm and bleeding were seen only in the group with a Ranson score of 3 or 4.

DISCUSSION

A review of detailed angiographic findings in acute pancreatitis has not been reported previously because angiography is not always necessary for diagnosing acute pancreatitis. However, since 1992, we performed angiography in 27 patients with acute pancreatitis to perform continuous regional arterial infusion (CRAI) of protease inhibitor and antibiotics. We have found that cases with severe acute pancreatitis tend to show severe ischemic changes in the splanchnic arteries. Hence, we analyzed the relationship between the angiographic findings and the severity of acute pancreatitis. We found that the degree of the ischemic change on angiography was associated with the severity of the acute pancreatitis, although the frequency of patients who underwent angiography was significantly related to the severity of the pancreatitis. In addition, these angiographic findings were useful in determining the therapeutic strategy.

Clinical signs, laboratory data, US, CT, and magnetic resonance imaging (MRI) are useful when making the clinical diagnosis of acute pancreatitis. In particular, contrast enhanced CT is considered necessary to make the diagnosis of pancreatic necrosis. MRI is also useful in assessing the severity of acute pancreatitis [20]. On the other hand, angiography was not thought to be useful in diagnosing or evaluating the severity of acute pancreatitis. Therefore, the angiographic findings associated with acute pancreatitis have not often been reported. When reported, the angiographic findings of acute pancreatitis have included irregularity, displacement, accumulation of contrast medium (staining), change in vessel diameter, and occlusion [21, 22, 23, 24]. Previously, the relationship between these angiographic findings and the severity of acute pancreatitis had not been elucidated. In this report, we correlated the angiographic findings in 24 acute pancreatitis patients with the severity of their acute pancreatitis.

The pancreas is sometimes swollen due to the formation of edema caused by increased vascular permeability of the intra- and peri-pancreatic vessels. Parenchymal accumulation of the contrast medium (staining) may correspond to this accelerated permeability in and around the pancreas. This staining found on angiography would appear to correspond to mild or moderate states of acute pancreatitis. Indeed, these findings were seen only in the group with a Ranson score of 3 or 4.

Some of our patients showed spastic changes of the abdominal vessels. We defined such a diffuse spasm and/or obstruction as a severe ischemic change. We analyzed the relationship between these severe ischemic changes and the severity of the acute pancreatitis. Most of the severe ischemic changes in the abdominal arteries were seen in patients belonging to the severest group (a Ranson score of 5 or more). These severe changes were found not only in the intra- and peri-pancreatic arteries, but also in the extra-pancreatic arteries. Since intravascular coagulability is markedly increased in severe acute pancreatitis [25], the progressive ischemia caused by such vascular changes can develop into necrosis. In patients with severe acute pancreatitis, angiographic assessment of the vascular changes and the identification of severe ischemic change can help in determining the therapeutic strategy.

The pathogenesis of acute pancreatitis involves acinar cell injury caused by pancreatic protease (e.g. trypsin) activation and a systemic inflammatory response mediated by proinflammatory cytokines and secondary mediators. However, when considering the therapeutic options in cases of acute pancreatitis, it is important to keep in mind that local inflammation can sometimes lead to pancreatic as well as peri-pancreatic necrosis, such as intestinal necrosis and fat necrosis. Intravascular hypercoagulability and progressive ischemia can lead to vascular alterations that can produce pancreatic and peri-pancreatic necrosis. The pathogenesis of

intravascular hypercoagulability and progressive ischemia may involve the activity of proteases, such as trypsin and thrombin, and may even sometimes involve vasoactive substances activated by these proteases.
Recently, CRAI has mainly been performed in Japan [19, 26, 27, 28]. CRAI therapy involves the infusion of a protease inhibitor and antibiotics into the pancreas-perfusing artery. Synthetic protease inhibitors suppress the actions of many kinds of proteases, such as trypsin, thrombin, and complement, which are associated with the progression and exacerbation of acute pancreatitis. Intravenous administration of a conventional dose of nafamostat mesilate (20 mg/day) or gabexate mesilate (200 mg/day) does not reach a high enough blood concentration to suppress protease activities. On the other hand, local intra-arterial administration of synthetic protease inhibitor may result in high enough concentrations of the inhibitor where it is needed. Indeed, it has been reported that the concentration of protease inhibitor and antibiotics reaches high levels in pancreatic tissue with CRAI [28, 29]. Thus, CRAI is expected to decrease protease activity and to prevent the development of pancreatic necrosis in acute pancreatitis. If severe ischemic changes are found at angiography, CRAI may be the preferred therapeutic option.
In conclusion, angiographic findings are useful for evaluating the severity of acute pancreatitis. Angiography deserves to be considered when the patient's Ranson score is 5 or more.

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Keywords Angiography; Mesenteric Vascular Occlusion; Pancreatitis; Pancreatitis, Acute Necrotizing
Abbreviations CRAI: continuous regional arterial infusion; NOMI: non-occlusive mesenteric ischemia
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