Original Article
Analysis of the pathogenesis and clinical features of acute pancreatitis: an observation from 609 cases

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Abstract: Objectives: Acute pancreatitis (AP) is one of the most common and severe diseases in gastroenterology. The main pathological characteristic of AP is still unclear. This study aimed to analyze the pathogenesis and clinical features of AP. Methods: The clinical data of 609 hospitalized AP patients were collected using the EpiData single-disease data software. The general condition of the patients, the etiological factors and causes, the clinical symptoms and signs, laboratory and imaging examination, the severity and complications were analyzed using SPSS 13.0 statistical software. Results: The main causes of AP are biliary disease (35.9%), hyperlipidemia (26.3%), idiopathic pancreatitis (22.7%), and others (15.1%). The patients of biliary pancreatitis are mainly elderly. Patients with hyperlipidemic pancreatitis are mainly young and middle-age. Among the 609 AP patients, heavily drink and overeating were in 44.5% of the patients, and obesity was in 35.5%. The main clinical symptoms are acute persistent upper abdominal pain (95%), mostly accompanied with ventosity, nausea, vomiting and other gastrointestinal symptoms. Serum trypsin level significantly increased in most of the patients. More than three times of imaging examinations were performed in all patients. The common complications of AP include intestinal paralysis, abnormal liver function, pleural effusion and pulmonary infection. Conclusion: The major risk factors of AP for middle- and old-age persons are biliary pancreatitis, while obesity and hyperlipidemia for the young persons. Heavy drinking and overeating are the main causes. The dynamic CT and laboratory examinations are the main measures to determine the severity and complications of AP.

Keywords: Acute pancreatitis, CT examinations, clinical features, hyperlipidemia

Introduction

The pancreas is an organ in the upper abdomen and next to the small intestine that produces digestive fluids and the hormone (insulin) [1]. Acute pancreatitis (AP) is one of the most common and severe diseases in gastroenterology [2]. The main pathological characteristic of AP is the local inflammation in the pancreas result from trypsin activation caused by a variety of etiologies [3, 4]. The inflammation develops quickly and subsides within a few days but can last for a few weeks, accompanied with or without dysfunction of other organs [5].

Approximately 20%-30% of these patients are clinically dangerous and the general mortality rate is around 5%-10%. In recent years, with changes in lifestyle and eating habits, the incidence of AP increases year by year [6, 7]. The causes of AP are multiple and complex. Heavy alcohol intake and Gallstones causes about 30% of cases of acute pancreatitis and usually occurs only after heavy alcohol use [8]. Gallstones cause about 40% of cases of acute pancreatitis [9].

Once a working diagnosis of acute pancreatitis is reached, laboratory tests are obtained to support the clinical impression [10, 11], such as the following: (1) Serum amylase and lipase; (2) Liver-associated enzymes; (3) Blood urea nitrogen (BUN); (4) Creatinine, and electrolytes; (5) Blood glucose; (6) Serum cholesterol and triglyceride; (7) Complete blood count (CBC) and hematocrit; (8) C-reactive protein (CRP); (9) Arterial blood gas values; (10) Serum lactic dehydrogenase (LDH) and bicarbonate; (11) Immunoglobulin G4 (IgG4). Diagnostic imaging

Table 1. The distribution of gender and the underlying diseases in different age groups

	Overall	Youth group	Middle-age group	Old-age group
Cases	609	269	186	154
Sex (male/female)	398/211 (65.4%)	208/61 (77.3%)	125/61 (67.2%)	65/89 (42.2%)
Underlying diseases				
Hyperlipidemia	263/609 (43.2%)	148/269 (55%)	79/186 (42.5%)	36/154 (23.4%)
Fatty liver	258/609 (42.4%)	143/269 (53.1%)	72/186 (38.7%)	43/154 (27.9%)
Biliary diseases	239/609 (39.2%)	69/269 (25.7%)	84/186 (45.2%)	86/154 (55.8%)
Diabetes	65/609 (10.7%)	20/269 (7.4%)	22/186 (11.8%)	23/154 (14.9%)

is unnecessary in most cases but may be obtained when the diagnosis is in doubt, when pancreatitis is severe, or when a given study might provide specific information required.

Therefore, this study aimed to explore the pathogenesis and clinical features of AP, it is significant for the prevention and clinical treatment of AP.

Materials and methods

Medical records

609 AP cases were collected in the Department of Gastroenterology, the Southern Hospital Affiliated to Southern Medical University from January 2012 to June 2015. Among them, all the 609 cases were diagnosed as acute pancreatitis. All the cases were in accordance with the diagnostic criteria established by the Guidance of Diagnosis and Treatment of AP. The cases of acute exacerbation of the chronic pancreatitis were excluded.

Research methods

The information of the patients including age, gender, the place of birth, career, past underlying diseases, onset time, hospitalized date, causes, symptoms and signs, laboratory and imaging examinations and complications were input using the EpiData single-disease data software.

Statistical method

The data was processed and analyzed using Spss 13.0 statistical analysis software. The data was analyzed by Student t test or a one-way analysis of variance (ANOVA), followed by pairwise multiple comparisons to determine any difference between groups. Pearson X^2 tests were carried out for comparing catego-

rized variables. Values of $p < 0.05$ were considered statistically significant.

Results

General condition

Among the 609 patients, 398 were male and 211 were female, with a male-to-female ratio of 1.88:1. The male patients were significantly more than the female patients ($p < 0.01$). The age of the patients ranged from 13 to 89 years, with an average age of 48.91±16.36 years. The average onset age of the males and the females were 45.85±14.79 years and 54.69±17.62 years. The patients were divided into three groups according to age: the youth group (≤ 44 years old) accounted for 44.2% (269/609), the middle-age group (between 44 to 59 years old) accounted for 30.5% (186/609), and the old-age group (≥ 60 years old) accounted for 25.3% (154/609). The youth and middle-age groups are the main groups. In the youth and middle-age groups, the proportion of males was significantly higher than that of the females ($p < 0.01$), whereas the proportion was opposite in the old-age group ($p < 0.01$). Totally, the main underlying diseases appeared in the AP patients were obesity (BMI > 25, 35.5%, 216/609), hyperlipidemia (43.19%, 263/609), fatty liver (42.4%, 258/609), biliary-disease (39.2%, 239/609) and diabetes history (10.7%, 65/609). The main underlying disease of the youth and middle-age groups are fatty liver and hyperlipidemia, whereas biliary and diabetes diseases in the old-age group ($p < 0.05$) (**Table 1**).

Pathogenic factors and causes

96 cases (15.8%) are heavily alcoholic and 208 cases (34.2%) are overeating in the AP patients before onset. The main causes of AP are biliary

Table 2. The distribution of common causes of AP in age, sex and groups

	Biliary	Hyperlipidemic	Alcoholic	Idiopathic	p
Causes	219	160	47	138	-
Sex (male/female)	123/96 (56.2%)	116/44 (71.3%)	46/1 (97.9%)	85/53 (61.6%)	
Ages ($\bar{x} \pm s$, years)	56.27±16.49	42.11±12.33	40.53±10.90	45.67±16.01	< 0.01
Age group					
Youth group	57/219 (26%)	103/160 (64.4%)	31/47 (66%)	67/138 (48.6%)	
Middle-age group	73/219 (33.3%)	42/160 (26.3%)	13/47 (27.7%)	41/138 (29.7%)	< 0.01
Old-age group	89/219 (40.6%)	15/160 (9.3%)	3/47 (6.4%)	30/138 (21.7%)	< 0.01

Table 3. The laboratory test indicators of AP patients

	Range	Cases	Percentage (%)
White blood cells (WBC)	> 9.5 G/L	380	62.4%
Amylase activity	> 220 mmol/L	336	55.2%
Amylase activity	> 660 mmol/L	152	24.9%
Lipase activity	> 60 mmol/L	526	86.4%
Lipase activity	> 180 mmol/L	386	63.4%
Serum trypsin		85	13.6%
C-reactive protein	> 5 mg/L	485	79.6%
Blood glucose	> 6.1 mmol/L	371	60.9%
Serum calcium	< 2.2mmol/L	288	47.3%
Serum triglycerides	> 1.7 mmol/L	222	36.5%
Serum total cholesterol	> 5.2 mmol/L	162	26.6%
ALT	> 40 U/L	240	39.4%
Aspartate aminotransferase	> 35 U/L	266	43.7%
Total bilirubin	> 20.5 µmol/L	229	37.6%
Blood urea nitrogen	> 7.2 mmol/L	83	13.6%

Table 4. Comparison of abdominal B-ultrasound with CT

	Causes	Positive	Negative	Positive rate (%)
B-ultrasound	609	521	88	85.6
CT	609	603	6	99.0

pancreatitis (35.9%, 219/609), hyperlipidemic pancreatitis (26.3%, 160/609), and idiopathic pancreatitis (22.7%, 138/609), and other causes include alcoholic pancreatitis (7.7%, 47/609), pancreatic ampullary pancreatitis (3.6%, 22/609), iatrogenic pancreatitis (3.5%, 21/609), 1 case of traumatic pancreatitis and 1 case of congenital anomalies pancreatitis. As shown in **Table 2**, the patients of all causes are mainly male. The hyperlipidemia and alcoholic pancreatitis prefers the male patients, whereas biliary pancreatitis (40%) likes the female patients (56.2%). Biliary pancreatitis mainly occurs in the middle- and old-age groups, with a ratio of male lower than female. Pancreatitis caused by other common causes predominantly occurs in the youth and middle-age groups, and the male patients are significantly more than the female ($p < 0.01$). In the youth group, the proportion of biliary pancreatitis was significantly lower than that of other causes. In old-age group, the proportions of hyperlipidemia and alcoholic pancreatitis were significantly lower than those of other causes. Moreover, in middle-age group, the causes are equivalent. Totally, according to the age from old to youth, the main pathogenic factors are biliary pancreatitis, idiopathic pancreatitis, hyperlipidemic pancreatitis and alcohol in order.

Clinical manifestations and signs

In the 609 AP patients, there are 606 (99.5%) with abdominal pain as the initial symptom. The pain which usually happened as a sudden persistent attack is mostly in the middle and upper abdomen. Curling body and leaning forward can relieve the pain. Additionally, 564 cases (92.6%) have abdominal distension, 390 cases (64.1%) have nausea and vomiting, 155 cases (25.5%) have fever, 44 cases (7.2%) have jaundice, and 223 cases (36.6%) have stopped anus exhaust and excretion. Another 3 old-age patients with a major clinical manifestation of nausea, vomiting and abdominal discomfort but without abdominal pain sensation were finally diagnosed as AP by laboratory tests and abdominal enhanced CT.

Table 5. AP severity assessment

	Total	MAP	MSAP	SAP	p
Cases	609	239	206	164	-
Gender (male/female)	398/211	150/89	125/81	123/41	< 0.01
Age ($\overline{x} \pm s$)	48.91±16.36	49.02±16.40	51.80±17.32	45.12±14.28	< 0.01
Age groups					
Youth (≤ 44)	269/609	94/269	75/269	100/269	
Middle-age (45-59)	186/609	83/186	68/186	35/186	< 0.01
Old-age (≥ 60)	154/609	62/154	63/154	29/154	
Common causes					
Biliary	219/609	84/219	90/219	45/219	
Hyperlipidemic	160/609	56/160	42/160	62/160	
Alcoholic	47/609	10/47	16/47	1/47	< 0.01
Idiopathic	138/609	58/138	49/138	31/138	

MAP, Mild acute pancreatitis. MSAP, Moderately severe acute pancreatitis. SAP, Severe acute pancreatitis.

In physical examination, the most common clinical sign is middle and upper abdominal local tenderness, with 519 cases (85.6%). 194 cases (32%) have abdominal tension, 160 cases (26.4%) have peritoneal irritation, and 289 cases (47.7%) have weakened or disappeared bowel sounds, 1 case (0.2%) have Gray-Turner sign, 1 case (0.2%) have Cullen sign, and 72 cases (11.9%) don't have any positive signs.

Laboratory test indicators

Among 609 AP patients, laboratory tests often show that the levels of serum trypsin, inflammatory markers and blood glucose markedly elevated while serum calcium decreased. This study shows that there are 380 cases (62.4%) with white blood cells (WBC) > 9.5 G/L, 336 cases (55.2%) with serum amylase activity > 220 mmol/L including 152 cases (24.9%) with amylase activity > 660 mmol/L, 526 cases (86.4%) with serum lipase activity > 60 mmol/L including 386 cases (63.4%) with serum lipase activity > 180 mmol/L, 85 cases with a normal level of serum trypsin, 485 cases (79.6%) with C-reactive protein > 5 mg/L, 371 cases (60.9%) with blood glucose > 6.1 mmol/L, 288 cases (47.3%) with serum calcium < 2.2 mmol/L, 222 cases (36.5%) with serum triglycerides > 1.7 mmol/L, 162 cases (26.6%) with serum total cholesterol > 5.2 mmol/L, 240 cases (39.4%) with ALT > 40 U/L, 266 cases (43.7%) with aspartate aminotransferase > 35 U/L, 229 cases (37.6%) with total bilirubin > 20.5 μmol/L, and 83 cases (13.6%) with blood urea nitrogen > 7.2 mmol/L (**Table 3**).

Imaging examination

Abdomen B-ultrasound and CT examination have been performed on all the 609 patients after hospitalization. The pancreas of 521 patients were abnormal by the abdominal B-ultrasound while the pancreas of the remaining 88 patients were unclear, indicating the positive rate was 85.5%. Abnormal pancreases were shown in 603 cases by abdominal C. The positive rate was 99.0%, which was significantly higher than that of abdominal B-ultrasound (*p* < 0.01, **Table 4**).

Evaluation of AP severity by CT

AP severity was evaluated according to the Guideline on the Diagnosis and Treatment of Acute Pancreatitis in China, 2013 (**Table 5**). For the 609 AP patients, 239 (39.3%) were diagnosed as mild acute pancreatitis, 206 (33.8%) were diagnosed as moderate severe acute pancreatitis (MSAP), and 164 (26.9%) were diagnosed as severe acute pancreatitis (SAP). Based on the age from old to youth, the order is MSAP > MAP > SAP. SAP was more frequent in youth group (*p* < 0.01), and was more frequent in male than MAP and MSAP (*p* < 0.01). As compared with the biliary pancreatitis, the hyperlipidemia is more likely to develop to SAP (*p* < 0.01). Clinically, the Balthazar classification by CT is of great value in judging the severity of the disease. For these patients, 61 (10.0%) were in grade A, 63 (10.3%) were in grade B, 157 (25.8%) in grade C, 148 (24.3%) were in grade D and 180 (29.6%) were in grade E.

The occurrence of complications

AP was often accompanied by a variety of local or systemic complications in the course of the disease. In this study, complications occurred in 507 cases (83.3%), with an average complication number of 2.1±1.6 per case. As many as 8 kinds of complications occurred in one case. More than 5 kinds of complications occurred in 46 cases (9.1%). The common complications include intestinal paralysis (323 cases, 53.0%), abnormal liver function (302 cases, 49.6%), pleural effusion (276 cases, 45.3%) and lung infection (202 cases, 33.2%).

Discussion

Acute pancreatitis (AP) is one of the most common acute abdominal diseases in clinical practice [12]. It is a global consensus that the incidence of AP is rising year by year [13]. There are many reports focused on the epidemiological characteristics of AP at home and abroad [14-16], which showed AP is distinctive according to time, region and population. It is of great significance to explore and study the pathogenesis and clinical features of AP in our country for the prevention and treatment.

The causes of AP are multiple and complex. It is well accepted that the alcohol and biliary are the most important causes of AP. The hyperlipidemia and alcoholic pancreatitis often occur in male patients, while biliary pancreatitis often occurs in female patients [17]. There are few domestic epidemiological reports on AP in China. A survey in 2012 showed that the main cause of AP in China was biliary (57.7%), followed by idiopathic (29.6%) and hyperlipidemia (7.5%). This study showed that biliary AP (40.0%) is still major group, followed by hyperlipidemic AP (26.3%) and idiopathic AP (22.8%). The biliary AP occurred in all age groups. With age increase, the proportion of biliary AP is increased. This result is consistent with the current reports at home and abroad, which show the high incidence of biliary AP may result from the high prevalence of cholelithiasis in the elderly [18, 19]. Hyperlipidemia and alcoholic AP often occurs in young and middle-aged male. This may be caused by the high fat and high protein diet and alcoholism in the young and middle-aged male. In this study, clear diet causes including drinking and overeating exist in 44.5% of AP patients. Notably, following the

biliary AP, the hyperlipidemic AP ranked second. The markedly increased incidence may be related to the improved life standards, and the change of lifestyle and diet, indicating the great importance of healthy life and eating habits in prevention of AP. The declining incidence of biliary AP may be related to the attention and early intervention for biliary disease, while the declining incidence of idiopathic AP may be related to the wide use of endoscopic ultrasound, MRCP applications and the improvement of ERCP diagnosis and treatment level in recent years. For these reasons, some previous rare diseases such as biliary micro-calculus, oddi sphincter of dysfunction and pancreatic anatomical abnormality can be well diagnosed.

In this study, we found obesity is another cause of AP, accounted for 35.5% of the patients. Studies have shown that the incidence of AP is directly related to obesity. This study showed a much higher correlation of obesity and AP than previous reports [20]. In the basic diseases, hyperlipidemia, fatty liver and biliary diseases are common. The main basic diseases of young and middle-age group are fatty liver and hyperlipidemic, while biliary diseases are common in the old-age group. These results demonstrated that the groups with hyperlipidemia, biliary disease or obesity are more prone to AP.

There were no significant differences in the clinical symptoms and signs of AP patients between this study and previous reports. As compared with the non-elderly patients, however, the abdominal pain of elderly patients is not obvious. Therefore, it is easy to escape diagnosis or be misdiagnosed in clinic [21]. In the physical examination, most of the patients showed tenderness in the middle and upper abdomen or the whole abdomen, while a considerable number of patients did not have any positive signs in the examination, which required the combination of relevant laboratory tests and imaging tests as auxiliary diagnose [22]. The increases of serum amylase and lipase are one of the important laboratory indicators for diagnosis of AP. The Guidance of AP Diagnosis and Treatment clearly indicates that the determination of serum lipase has important clinical significance, especially when serum amylase activity reduces to normal level, or serum amylase activity increases caused by other reasons such as acute abdomen, the determination of serum lipase activity has a

complementary effect. However, according to the data in this study, dependence of the serum trypsin level alone cannot reflect the severity of AP. Many studies have shown that combined detection of serum amylase and lipase can improve the sensitivity and specificity of AP diagnosis, and hence avoid misdiagnosis and missed diagnosis [21]. For the AP patients with serum trypsin level three times less than the normal, or recovered to normal [23], abnormity can still be detected by abdominal imaging such as abdominal B-ultrasound or CT, and it is necessary to perform the differential diagnosis [22, 24]. At the first 24-48 h, the morphological changes of the pancreas can be preliminarily determined by abdomen B-ultrasound, and it is also helpful to determine the existence of biliary disease [25]. However, poor display of the pancreas easily appears due to the influence of gastrointestinal tract gas, which caused a lower positive rate of AP diagnosis. Instead, the morphology and periphery of pancreas, bleeding or necrosis, and percolating fluid of pancreas can be clearly observed by abdominal CT, without any influence by gastrointestinal trace gas. The positive rate of AP diagnosis by CT is much higher than that by abdominal B ultrasound. Therefore, abdominal CT is recommended as the standard imaging detection for AP. Studies showed that the extent of pancreatitis exudation and other acute abdomen can be evaluated by CT scan which is performed within 12 hours after emergency treatment [26]. The area of pancreatic fluid accumulation and pancreatic necrosis can be effectively distinguished by enhanced CT examination 72 h after onset [27]. Notably, no positive sign can be detected by abdominal CT in a few of MAP patients in early onset. To avoid missed diagnosis, close observation and reexamination of the abdominal CT were required. For many patients, although serum trypsin significantly reduce or even close to normal level, the symptoms are still obvious, and CT examination still shows severe pancreatic lesions. Therefore, combination with multiple CT examinations and dynamic observation of the change of the pancreatic and peripheral organs is the best measurement to determine the severity of AP and its complications. Although the Balthager classification of CT has been clinically recognized for assessing the severity of pancreatitis, severe pancreatitis cannot be diagnosed at present in iconography.

In conclusion, there are many causes for AP. The proportion of AP caused by biliary disease is declining. Instead, hyperlipidemia, heavy drinking and overeating become the important causes of AP, and the onset age tends to be younger [28]. The clinical diagnosis of AP mainly depends on the combination of the clinical symptoms, serum trypsin level and imaging. Accurate assessment of the disease condition, development, complications at an early stage depends on repeated and dynamic laboratory and imaging examinations. Clinically, attention should be paid to provide specific interventions to the high risk people with different ages. For instance, young people should change the unhealthy lifestyle and eating habits, such as stop drinking, losing weight and control of hyperlipidemia, while the elderly should be treated aggressively for the biliary disease.

Disclosure of conflict of interest

None.

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