

Recurrent acute pancreatitis and its relative factors

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Abstract

AIM: To evaluate the causes and the relative factors of recurrent acute pancreatitis.

METHODS: From 1997 to 2000, acute pancreatitis relapsed in 77 of 245 acute pancreatitis patients. By reviewing the clinical treatment results and the follow-up data, we analyzed the recurrent factors of acute pancreatitis using univariate analysis and multivariate analysis.

RESULTS: Of the 245 acute pancreatitis patients, 77 were patients with recurrent acute pancreatitis. Of them, 56 patients relapsed two times, 19 relapsed three times, each patient relapsed three and four times. Forty-seven patients relapsed in hospital and the other 30 patients relapsed after discharge. Eighteen patients relapsed in 1 year, eight relapsed in 1-3 years, and four relapsed after 3 years. There were 48 cases of biliary pancreatitis, 3 of alcohol pancreatitis, 5 of hyperlipidemia pancreatitis, 21 of idiopathic pancreatitis. Univariate analysis showed that the patients with local complications of pancreas, obstructive jaundice and hepatic function injury were easy to recur during the treatment period of acute pancreatitis ($P = 0.022 < 0.05$, $P = 0.012 < 0.05$ and $P = 0.002 < 0.05$, respectively). Multivariate analysis showed that there was no single factor related to recurrence. Of the 47 patients who had recurrence in hospital, 16 had recurrence in a fast period, 31 after refeeding.

CONCLUSION: Acute pancreatitis is easy to recur even during treatment. The factors such as changes of pancreas structure and uncontrolled systemic inflammatory reaction are responsible for the recurrence of acute pancreatitis. Early refeeding increases the recurrence of acute pancreatitis. Defining the etiology is essential for reducing the recurrence of acute pancreatitis.

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INTRODUCTION

With the knowledge of progress and prognosis for acute pancreatitis, the diagnosis and treatment of acute pancreatitis are more and rational. But some acute pancreatitis patients have frequent occurrence in hospital or after discharge. These patients obviously had increased hospital-stay and cost, and their quality of life decreased. About 25% patients with acute pancreatitis had recurrence^[1]. We reviewed the clinical data of acute pancreatitis patients in our hospital for 3 years, and evaluated the relative factors that affected the recurrence in 77 patients.

MATERIALS AND METHODS

Clinical data

From 1997 to 2000, 245 acute pancreatitis patients (based on clinical diagnosis and classification standard of pancreatitis, 1997, Chinese Medical Association^[2]) were admitted to our hospital. According to the different causes, classification and clinical stages, the patients received different treatments. Routing treatments included: intravenous fluid resuscitation, anti-shock, water maintenance, electrolyte and acid-base balances, fluid replenishment, fast, naso-gastric decompressing, using somatostatin, parenteral nutrition, pain relief, using wide-spectrum antibiotics and serum albumin. In clinical observations and follow-up, 77 acute pancreatitis patients had recurrence. Of them, 32 were men and 45 were women, and the average was 58.04 ± 15.43 years. The average follow-up time was 26 mo (12-60 mo).

Diagnosis standard of recurrent acute pancreatitis

After conservative or operative treatment, the clinical syndromes and signs of acute pancreatitis disappeared, serum and uric amylase returned to normal. Other laboratory tests such as blood leukocyte counting, liver functions, renal functions, blood sugar, etc., were normal, and there were no uncomfortable complaints after refeeding. After that, if the patients had acute pancreatitis syndromes or signs with elevating serum and uric amylase again, they were diagnosed as recurrent acute pancreatitis.

Classification of recurrent acute pancreatitis

Biliary pancreatitis: Clinical jaundice with elevated serum bilirubin, direct bilirubin/total bilirubin > 50%, the dilation of intra-hepatic and extra-hepatic bile duct (the diameter more than 1 cm) by image examinations such as B-ultrasound,

computer tomography (CT), endoscope retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP).

Alcohol-induced pancreatitis: An average of 80 g alcohol taken daily for more than 5 years or an excess alcohol taken immediately before the acute attack.

Hyperlipidemia pancreatitis: The levels of serum lipid, especially the triglyceride was obviously elevated.

Idiopathy pancreatitis: No remarkable findings in his or her disease history, clinical manifestations, laboratory and image examinations.

Refeeding recovery

The naso-gastric tube was removed when clinical syndromes and signs were disappeared. Then the patients were allowed to drink water for 1-3 d. If there were no discomforts, the patients were told to eat non-fat fluid and non-fat semi-fluid diets gradually, and at last to eat low-fat semi-fluid diets. The total calorie of non-fat fluid diets was 510 kcal/d, containing 2.7% protein, 0.6% lipid, 96.7% carbon hydrate. The total calorie of non-fat semi-fluid diets was 1 500 kcal/d, containing 8.2% protein, 1.6% lipid, 90.2% carbohydrate. The total calorie of low-fat semi-fluid diets was 1 600-1 800 kcal/d, containing 15.5% protein, 17.6% lipid and 66.9% carbohydrate respectively.

Analysis of relative factors

The clinical data of each patient were recorded in detail. The possible factors related to recurrent acute pancreatitis were calculated, including age more than and equal 60 years or less than 60 years; etiology, biliary pancreatitis; bile duct obstruction; levels of serum amylase, three times more than normal values; acute hepatic function injury manifested as high levels of serum glutamic-pyruvic or serum glutamic-oxalacetic transaminase with or without elevated serum bilirubin; severe systemic infection; local complications of acute pancreatitis such as acute fluid accumulation, necrosis, pseudocyst, abscess formation.

Statistical analysis

χ^2 test was used for univariate analysis, and logistic regression for multivariate analysis by SPSS. $P < 0.05$ was considered statistically significant.

RESULTS

Status of recurrent acute pancreatitis

The recurrent rate of acute pancreatitis in this study was 31.43% (77/245). Of the 77 relapsed patients, 56 (72.73%) had two relapses, 19 (24.67%) had three relapses, and each one (2.60%) had four and five relapses. Forty-seven (61.04%) had their recurrence in hospital, and 30 (38.96%) after discharge. Seventeen had recurrence in 1 year after discharge, nine in 1-3 years, and four 3 years after discharge.

Etiology and classification of recurrent acute pancreatitis

Of the 77 recurrent acute pancreatitis patients, 48 had biliary pancreatitis, 3 had alcohol-induced pancreatitis, 3 had hyperlipidemic pancreatitis, and 21 had idiopathy pancreatitis. No trauma, post-operative and drug-induced

pancreatitis were found. With the clinical diagnosis and classification standard by Chinese Medicine Association, 13 patients were confirmed to have severe acute pancreatitis in 77 recurrent acute pancreatitis patients. Of them, five had pancreas necrosis, five pseudocyst, one pancreatogenic encephalopathy and two respiratory failure.

Laboratory tests of recurrent acute pancreatitis patients

Of the 77 recurrent patients, 61 had their serum or uric amylase three times higher than the values of upper limit of normal. Fifty-three had the leukocyte counting more than 10.0×10^9 , 47 the glucemia more than 6.1 mmol/L, 37 with acute hepatic function injury, and 32 the serum calculi less than 2.2 mmol/L.

Analysis of relative factors of recurrent acute pancreatitis

The univariate analysis indicated that the recurrence of acute pancreatitis in treatment period was associated with local complications of pancreas, obstructive jaundice and hepatic function injury ($P = 0.022 < 0.05$, $P = 0.012 < 0.05$ and $P = 0.002 < 0.05$, respectively). Multivariate analysis showed that there was no single factor related to recurrent acute pancreatitis (Table 1).

Table 1 Relative factors of recurrent acute pancreatitis

Relative factors	Total cases (n)	Recurrent (%)	Univariate analysis P	Multivariate analysis P
Age ≥ 60	101	37 (36.63)	0.142	0.423
Male	109	32 (29.36)	0.532	0.569
Biliary	162	48 (29.36)	0.397	0.215
Obstructive jaundice	58	26 (44.83)	0.012	0.144
Amylase elevation	167	48 (28.74)	0.185	0.194
Liver injury	127	51 (40.16)	0.002	0.257
Systemic infection	12	5 (41.67)	0.642	0.082
Local complication	18	10 (55.66)	0.022	0.091

DISCUSSION

Recurrent acute pancreatitis represents a challenging clinical problem because of its high recurrent rate^[1,3]. Of the 245 patients with acute pancreatitis in this study, 77 (31.43%) had relapses. Of the 77 recurrent patients 47 (61.04%) had relapse in hospital, suggesting that acute pancreatitis is easy to relapse. Gullo *et al*^[1], reported that 288 (27%) had recurrence in the total of 1 068 acute pancreatitis patients, and alcohol was the most frequent factor. Pelli *et al*^[4], found that 46% alcohol-induced acute pancreatitis patients had recurrence, 80% of them had relapses during the first 4 years. We analyzed 30 recurrent acute pancreatitis patients after discharge by follow-up, 50% patients had recurrence in 1 year after discharge, one-third patients in 1-3 years and 13% patients 3 years after their discharge.

Some factors were probably related to recurrent acute pancreatitis^[4-6]. Theoretically, if the causes of acute pancreatitis existed, they could make the acute pancreatitis to relapse repeatedly. For example, biliary pancreatitis could recur, while the choledocholithiasis was existed or small gallstones went to the common bile duct from cholecyst duct^[7-9]. In

hyperlipidemia pancreatitis a high level blood viscosity in patients would make the pancreas microcirculation abnormal and acute pancreatitis could relapse. Somogyi *et al*^[3], suggested the causes of recurrent acute pancreatitis could be categorized into: (1) toxic-metabolic acute pancreatitis such as alcohol, hypertriglyceridemia, hypercalcemia and medications; (2) mechanical obstructive acute pancreatitis such as choledocholithiasis (microlithiasis), periampullary/ampullary obstruction (diverticulum, cyst, polypus, tumor, stenosis and infection), pancreatic duct obstruction (tumor, non-neoplastic stricture), congenital malformations (annular pancreas); and (3) miscellaneous acute pancreatitis such as vascular (hypotension, vasculitis, hypercoagulable state, embolism), infections (cytomegalovirus, tuberculosis, Coxsackie virus, mumps, human immunodeficiency virus, parasites), tropical pancreatitis, cystic fibrosis. Of the 77 recurrent acute pancreatitis patients in this paper, 8 (10.39%) belonged to toxic-metabolic pancreatitis, 48 (62.34%) mechanical pancreatitis, and 21 (27.27%) miscellaneous pancreatitis. In our country, alcohol-induced pancreatitis was fewer. Although a lot of drugs could induce acute pancreatitis, but it was mainly limited in case reports. Recent years, hyperlipidemia pancreatitis was emphasized^[10]. Therefore, it is suggested that acute pancreatitis patients should do serum lipid tests routinely in order to find their causes and reduce relapse. Biliary pancreatitis could be properly diagnosed by using B-ultrasound, CT, ERCP and MRCP. But for idiopathy pancreatitis, the causes were difficult to find and it could have a higher recurrent rate^[11-13].

Univariate analysis indicated that patients with local complications such as acute fluid accumulation, necrosis, pseudocyst, abscess formation had a tendency to recur, which should be responsible for the changed pancreas structure. Levy *et al*^[14], reported that patients with higher Balthazar's CT scores had abdominal pain recurrence more often than the others^[14], indicating that the acute pancreatitis patients with obstructive jaundice and hepatic function injury are easy to relapse. We previously studied acute pancreatitis patients with hepatic function injury and found that the liver was a common organ that could be affected by acute pancreatitis. It is known that acute pancreatitis is a systemic disease. Patients with obstructive jaundice and hepatic function injury meant that the systemic infection was uncontrolled, and so it was easy to relapse^[15]. Multivariate analysis showed that there was no single factor related to recurrence during treatment, indicating that the recurrence of acute pancreatitis probably is a result of multiple factors acting together.

In our study, the symptoms and signs, serum amylase, blood glucose, blood calculi, liver function tests, local and systemic complications and mortality of recurrent acute pancreatitis patients were not different from those of primary acute pancreatitis^[1].

So far there is no report that the refeeding in acute pancreatitis patients was associated with their relapsing. Naso-gastric decompression, parental nutrition, using

histamine H₂-receptor antagonists and somatostatin were not found to have any relations with relapsing of acute pancreatitis^[14]. But in our studies two-thirds of the patients relapsing in hospital were associated with refeeding, and the most were after refeeding of non-fat fluid diets. To prolong the fast time properly by using parenteral or enteral nutritional support therapies and to pay attention to the levels of serum amylase and lipase of patients can decrease the risk of recurrence after refeeding in patients with acute pancreatitis.

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