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Acute Necrotizing Pancreatitis in Children

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Abstract

Objective—Necrotizing pancreatitis is very rare in children. In this case series, we describe the etiologic factors, course, and outcome of acute necrotizing pancreatitis in children.

Study Design—We performed a retrospective study of children with necrotizing pancreatitis diagnosed over the last 21 years at Yale New Haven Children's Hospital. Computed tomography (CT) scan criteria were used to diagnose necrotizing pancreatitis and to assess severity index. Charts were reviewed to collect demographic data, etiology, details of hospital stay, complications, and outcome.

Results—Eight children (mean age 12.8 years; range 4 to 20.7 years) had necrotizing pancreatitis. Etiologic factors were medications, diabetes, gallstones, and alcohol. All patients had a prolonged hospitalization (9 to 40 days; mean 18 days) and five patients required admission to the pediatric intensive care unit. During the hospital stay, patients developed complications involving the respiratory, hematological, renal, metabolic, and circulatory systems. All patients had aggressive supportive medical therapy and none required surgical intervention. There were no deaths attributable to pancreatitis. Late complications following hospital discharge occurred in six patients and included pseudocysts, transient hyperglycemia, diabetes, and pancreatic exocrine insufficiency. The CT severity index correlated with the risk of complications.

Conclusions—Acute necrotizing pancreatitis has a variable etiology in children. CT scan is useful for the diagnosis and assessment of severity. Necrotizing pancreatitis in children is associated with severe acute and late complications and requires intensive medical therapy.

Keywords

Pancreatitis; necrosis

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Introduction

Acute pancreatitis is an inflammatory disorder of the pancreas characterized by abdominal pain, vomiting, and an increase in pancreatic enzymes. Recent studies indicate an increase in the prevalence of acute pancreatitis in children. [1,2] In the majority of cases, acute pancreatitis resolves with bowel rest and does not result in severe complications in children. It can rarely be complicated by the development of necrosis.

Acute necrotizing pancreatitis is a serious condition associated with high morbidity and mortality rates in adults. [3] It is diagnosed by a lack of enhancement of the pancreas on a Computed Tomography (CT) scan with intravenous contrast.[4] Necrotizing pancreatitis is well described in adults [3–5] , but the pediatric literature is very limited. It has been estimated that necrotizing pancreatitis occurs in less than 1 % of children with acute pancreatitis. [6] From five large pediatric series in the United States, pancreatic necrosis was observed in only 3 out of 1014 children. [2,7–10] There are a few case reports of necrotizing pancreatitis in children [11–15], however the data are limited regarding etiology, course, and outcome. We reviewed our experience of children with acute necrotizing pancreatitis in our hospital over the last 21 years and report the etiologic factors, clinical features, course, and outcome.

Methods

We searched the radiology database at Yale New Haven Hospital from 1991 to 2012 for reports of all abdominal CT scans performed in children up to 21 years of age. All reports were searched for specific terms including pancreatitis, necrosis, and necrotizing pancreatitis. The CT scans reporting necrosis of the pancreas were retrieved and reviewed by an experienced radiologist (KB).

Pancreatic necrosis was defined as a lack of enhancement of the pancreas on the contrast-enhanced CT scan. [3] As per the guidelines of American College of Gastroenterology, necrotizing pancreatitis was defined as necrosis involving more than 30% of the whole pancreas and/ or necrosis of more than a 3 cm area of the pancreas. [4]

We graded the severity of pancreatic necrosis and inflammation seen on the CT scan , using the guidelines of the United Kingdom Working Party on Acute Pancreatitis. [5] The guidelines assign 0 for no necrosis , 2 for necrosis of less than 1/3 of the pancreas, 4 for necrosis of more than 1/3 but less than ½ of the pancreas, and 6 for necrosis of more than ½ of the pancreas. The inflammation grade is 0 for normal pancreas, 1 for edematous pancreatitis, 2 for edema plus mild extrapancreatic changes, 3 for severe extrapancreatic changes including one fluid collection, and 4 for multiple or extensive extrapancreatic collections. [5] The overall CT severity index (range 0 to 10) is the sum of the inflammation grade and necrosis score, and is correlated with a risk of complications in the adult population. [5]

After the diagnosis of necrotizing pancreatitis was established by CT scan criteria, hospital charts were reviewed for demographic data, medical history, presenting features, hospital course, biochemical and radiological data, and outcome. Charts were specifically reviewed for systemic complications observed during the hospital stay. Following hospital discharge, clinical outcome was assessed by collecting data from imaging studies and clinic visits for

complications such as pseudocyst and pancreatic insufficiency in the form of diabetes and steatorrhea.

This study was approved by the Human Investigation Committee of Yale University.

Results

Over the last 21 years at Yale New Haven Hospital, we identified nine patients who had contrast-enhanced CT scans showing necrosis of more than 30% of the pancreas and/ or more than 3 cm area of the pancreas. One patient was excluded because he received his initial care at a different hospital and details were not available. The demographic data of eight children with necrotizing pancreatitis are shown in Table 1.

All patients presented with severe acute abdominal pain and vomiting. Except for patient 8 who had gallstone pancreatitis in the past, no patients had past or family history of acute pancreatitis. The co-morbid conditions and possible etiologic factors are shown in the Table 1. The etiology was unclear in patient 5 who was on tacrolimus and prednisone following bone marrow transplantation. The etiology in other children was determined from the physician's notes. Patient 3 had diabetic ketoacidosis as a first presentation of diabetes, based on a high hemoglobin A1C, and this was thought to have caused the pancreatitis. Patient 8 had a history of alcohol abuse and had excess alcohol intake on the night prior to admission.

As shown in Table 1, all patients had significant elevations of amylase and lipase ; more than 3 times upper limits of normal. The hematocrit was low, ranging from 22 % to 30 % except for patient 3 who had a high hematocrit of 47 %. Patient 5 had leucopenia (white blood cell count of 300/ul) on admission due to recent medications. All other seven patients had leucocytosis on admission (white blood cell count 15,500 to 31,800/ul ; mean 22,800/ ul). C-reactive protein was measured in four patients and was found to be extremely high (mean 132 mg/L with a range from 40 to 262 mg/L ; normal < 3 mg/L). Serum albumin was checked in seven patients and was found to be low (mean 2.3 g/dl with a range from 1.8 to 2.9; normal 3.5 to 5 g/dl). Serum calcium was low in all patients with a mean value of 7.7 mg/dl (range 7.2 to 8; normal 8.8 to 10.2 mg/dl). CT scans showed variable degrees of inflammation and necrosis on admission (Table 2). Patients 3 and 5 had more than a 3 cm area of necrosis, but less than 33% of the pancreas (necrosis score 2). Patients 2, 6, 7, 8 had necrosis between 33 to 50% of the pancreas (score 4). Patients 1 and 4 had necrosis of more than 50% of the pancreas (score 6). Figure 1 shows the CT scan of pancreatic necrosis seen in patient 4.

All patients required fluid resuscitation on admission. Five patients were admitted to the pediatric intensive care unit for 2 to 8 days (mean 5 days). All patients received narcotic analgesics, intravenous fluids, and were kept nil per os (NPO) strictly for 1 to 11 days (mean 7.5 days). Overall, the hospital stay ranged from 9 to 40 days (mean 18 days).

All patients needed intensive supportive treatment for various complications observed during the hospital stay (Table 2). Respiratory complications were common and were treated with oxygen (5 patients) , positive airway pressure (1 patient), and drainage of bilateral

pleural effusions (1 patient). One patient required fluid resuscitation and vasopressor support for 2 days for circulatory failure. Two patients required fresh frozen plasma transfusions for disseminated intravascular coagulation. Four patients required insulin therapy for persistent hyperglycemia during the hospital stay. Other complications such as ascites and pleural effusions resolved with albumin and diuretics. Two patients had persistent oliguria, but did not develop renal failure. Sepsis was suspected in six patients who received antibiotics, however the cultures were negative. Splenic vein thrombosis in patient 1 resolved without the need for anticoagulation therapy. Six out of the eight patients received total parenteral nutrition via central line for 5 to 18 days (mean 10.5 days) and one patient received nasojejunal feeds for 7 days. No patient died during the hospital stay.

All patients had close follow up after hospital discharge and the mean duration of follow up was 43 months (range 4 to 118 months). Two patients required insulin therapy for persistent hyperglycemia for up to 1 month following hospital discharge. Four patients had pseudocysts ranging in size from 2.5 cm to 5.8 cm on imaging studies, and all resolved without any intervention. Patient 4 developed diabetes and steatorrhea which was confirmed by low fecal elastase (value < 15 mcg/g ; normal >200 mcg/g). His CT scan showed severe pancreatic atrophy (figure 2) in the same location of necrosis four months following discharge. He is doing well on insulin and pancreatic enzyme therapy at the last follow up visit, 22 months after the development of necrotizing pancreatitis. To our knowledge, none of the patients had recurrence of pancreatitis during the follow up period. Patient 7 expired due to an unrelated cause of cerebral hemorrhage, 11 months following hospital discharge for pancreatitis.

Discussion

We report the etiology, hospital course and outcome of acute necrotizing pancreatitis in children. There were multiple etiologic factors for necrotizing pancreatitis in our patients. It is always difficult to ascribe an etiology for pancreatitis in children with co-morbid conditions receiving multiple medications as seen in our patients. In two patients, diabetes and minocycline were thought to be etiologic factors since both have been reported to cause acute pancreatitis in the literature.[1,16] In one patient, the cause was unclear as several possible etiologic factors associated with acute pancreatitis were present, including prednisone, tacrolimus, and bone marrow transplant. [1,9] Gallstones, alcohol, valproate and asparaginase are definite causes of acute pancreatitis that were seen in our other patients. Previous cases of necrotizing pancreatitis in children have been reported with the use of valproate[15] , L asparginase [12,14] , *mycoplasma pneumonia* [11], and Crohn's disease [13].

The initial presentation of necrotizing pancreatitis in our patients was similar to that of acute non-necrotizing pancreatitis. Our patients had abdominal pain, vomiting, and elevated pancreatic enzymes. Levels of pancreatic enzymes do not correlate with severity of pancreatitis [12] and do not help differentiation between acute mild pancreatitis and necrotizing pancreatitis. We observed leucocytosis, hypoalbuminimia, and hypocalcemia in our patients. In a large study of children with acute pancreatitis, these features have been shown to indicate severe pancreatitis.[7] We assessed CT scan grading of severity of inflammation and necrosis proposed by the UK guidelines for the management of acute

pancreatitis.[5] A high CT severity index (7 to 10) is associated with a 92% risk of complications and 17% mortality in adults. [5] We also observed severe complications and worse outcomes in two patients with a high severity index of nine and a relatively uneventful course in a patient with a low severity index of four.

Acute pancreatitis without necrosis usually does not lead to complications in children. The hospital course of necrotizing pancreatitis in our patients was remarkable for multiple systemic complications as reported in adults. [3–5] All children were very ill and required prolonged stay (mean 18 days) in the hospital. Hospital stay in our patients was much longer than that reported in children with acute pancreatitis without necrosis (median 5 to 9 days) in three large pediatric series. [8–10] None of our patients had surgical intervention and all received intensive medical supportive therapy. In recent years, treatment of necrotizing pancreatitis has shifted away from early surgical debridement (necrosectomy) to aggressive medical care except for patients with infected necrosis. [3,4] In addition to acute complications, we observed late complications including pseudocysts, pancreatic atrophy, exocrine and endocrine pancreatic insufficiency as has been reported in adults . [3] One of our patients developed severe pancreatic atrophy and has ongoing exocrine and endocrine pancreatic insufficiency requiring insulin and pancreatic enzyme therapy. All other patients eventually had a satisfactory outcome.

It is not clear why acute pancreatitis progresses to necrotizing pancreatitis in some patients. Antioxidant enzyme gene polymorphism and glutathione depletion have been associated with severity of acute pancreatitis in adults and it may mediate the progression from mild to severe pancreatitis. [17] However, hereditary (familial) pancreatitis is least likely to cause necrotizing pancreatitis in adults.[3] It has also been suggested that a combination of intravascular volume depletion, inflammation, and high hematocrit leads to blockage of pancreatic blood flow and necrosis.[6] All of our patients had depletion of intravascular volume and inflammation, but did not have high hematocrit except for one patient.

In summary, we report the etiology, clinical course, and outcome of acute necrotizing pancreatitis in children. The etiology is varied and initial presentation is similar to that of acute pancreatitis without necrosis. The diagnosis of necrotizing pancreatitis is important since the morbidity associated with acute pancreatitis increases markedly when necrosis is present. Contrast-enhanced CT scan is invaluable for the diagnosis and assessment of severity. Aggressive supportive medical therapy and prolonged hospital stay are necessary for children with acute necrotizing pancreatitis and associated complications. Follow up is also necessary to assess outcome and delayed complications of necrotizing pancreatitis.

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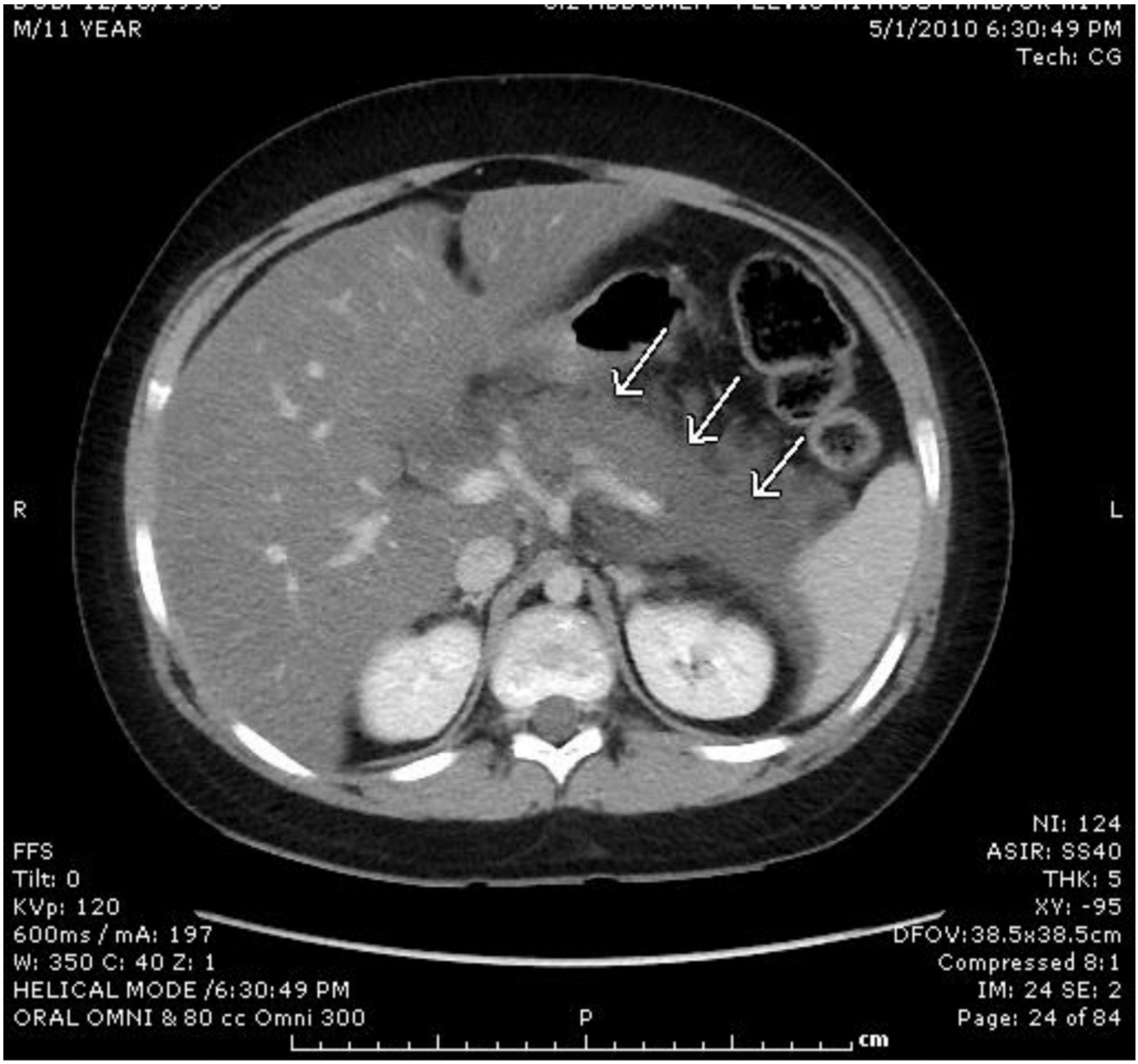

Figure 1.

CT scan of patient 4 showing extensive necrosis (> 80%) of the body and tail of the pancreas (arrows) on admission.

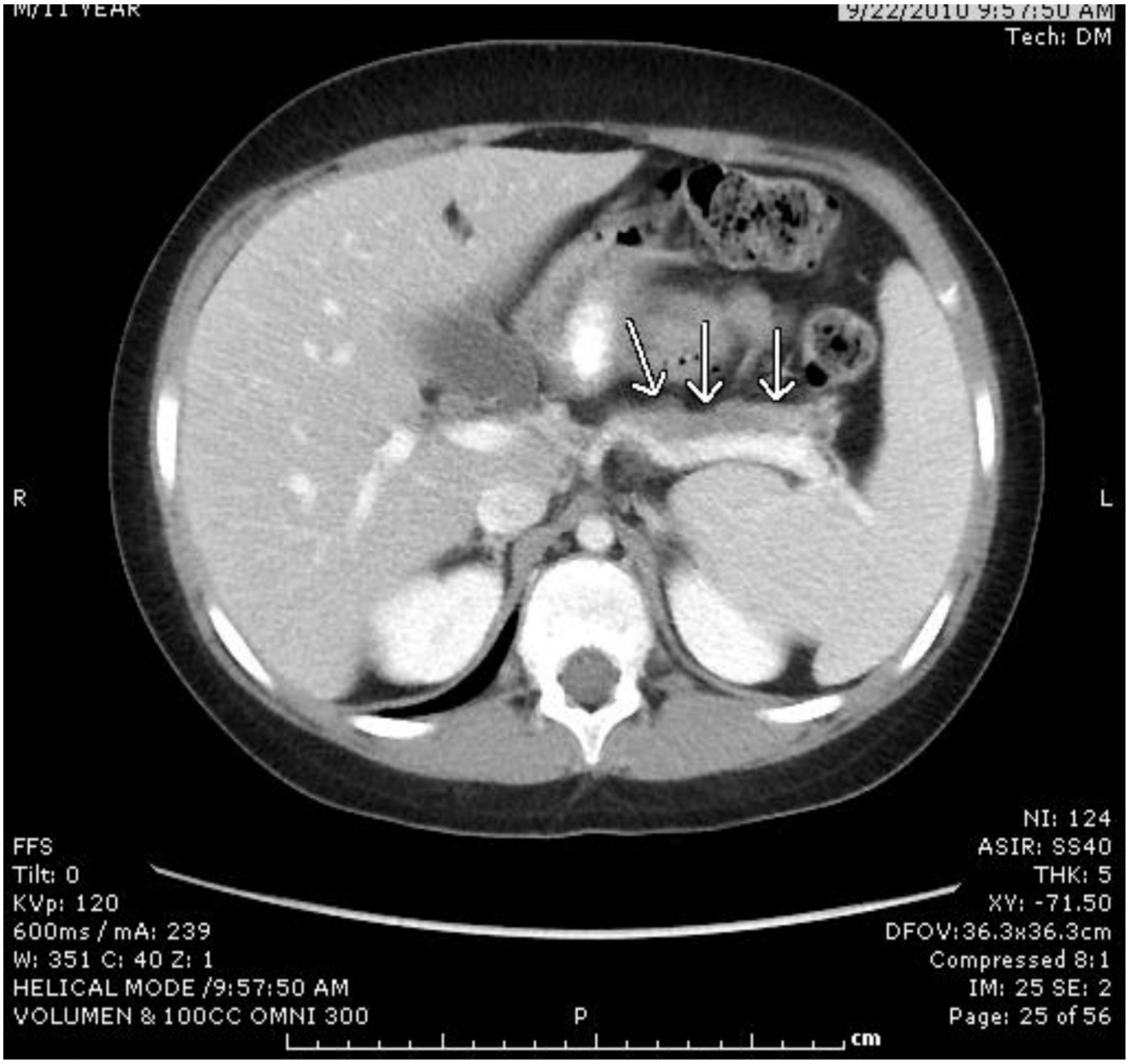

Figure 2.

CT scan of patient 4 showing extensive atrophy of the body and tail of the pancreas (arrows) at a follow up visit 4 months following necrotizing pancreatitis.

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Table 1

Demographic data, co-morbid conditions, etiology, and peak serum pancreatic enzyme levels in children with necrotizing pancreatitis.

Patient	Age (yr)	Sex	Co-morbid condition	Possible Etiology	Amylase (Normal 28-100 U/L)	Lipase (Normal < 60 U/L)
1	12.9	F	Rett syndrome, seizure disorder	Minocycline	2210	2070
2	17.4	F	Nil	Gall stone	1730	5280
3	13.8	F	Diabetes	Diabetes	854	3166
4	11.5	M	Acute lymphoblastic leukemia	Asparginase	581	3010
5	4.1	M	Sanfilipo syndrome, s/p bone marrow transplant	Unclear	1170	4180
6	4	F	Seizure disorder	Valproate	319	1190
7	17.8	M	Acute lymphoblastic leukemia	Asparginase	441	2510
8	20.7	M	History of gall stone and cholecystectomy	Alcohol	499	1690

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Table 2

CT scan severity index (necrosis score + inflammation grade = severity index[5]) and the acute complications and outcome of children with necrotizing pancreatitis. (DIC- Disseminated Intravascular Coagulation)

Pt	Necrosis Score	Inflamm. grade	Severity Index	Acute complications	Outcome
1	6	3	9	Circulatory failure, pleural effusion, respiratory distress, ascites, hyperglycemia, splenic vein thrombosis	Transient hyperglycemia
2	4	2	6	Atelectesis	Pseudocyst
3	2	4	6	Atelectesis	Pseudocyst
4	6	3	9	Bilateral pleural effusions, ascites, respiratory distress, oliguria, hyperglycemia	Pseudocyst, Diabetes, Exocrine insufficiency
5	2	2	4	Oliguria, hyperglycemia	Unremarkable
6	4	2	6	Respiratory distress, bilateral pleural effusions, ascites, DIC	Unremarkable
7	4	2	6	Respiratory distress, bilateral pleural effusions, hyperglycemia, ascites, DIC	Transient hyperglycemia
8	4	2	6	Bilateral pleural effusions, respiratory distress, ascites	Pseudocyst