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TOPIC HIGHLIGHT

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Acute pancreatitis in children and adolescents

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Abstract

In this Topic Highlight, the causes, diagnosis, and treatment of acute pancreatitis in children are discussed. Acute pancreatitis should be considered during the differential diagnosis of abdominal pain in children and requires prompt treatment because it may become life-threatening. The etiology, clinical manifestations, and course of acute pancreatitis in children are often different than in adults. Therefore, the specific features of acute pancreatitis in children must be considered. The etiology of acute pancreatitis in children is often drugs, infections, trauma, or anatomic abnormalities. Diagnosis is based on clinical symptoms (such as abdominal pain and vomiting), serum pancreatic enzyme levels, and imaging studies. Several scoring systems have been proposed for the assessment of severity, which is useful for selecting treatments and predicting prognosis. The basic pathogenesis of acute pancreatitis does not greatly differ between adults and children, and the treatments for adults and children are similar. In large part, our understanding of the pathology, optimal treatment, assessment of severity, and outcome of acute pancreatitis in children is taken from the adult literature. However, we often find that the common management of adult pancreatitis is difficult to apply to children. With advances in diagnostic techniques and treatment methods, severe acute pancreatitis in children is becoming better understood and more controllable.

Key words: Acute pancreatitis; Children; Pathophysiology; Etiology; Diagnosis; Treatment

Core tip: The etiology, manifestations, and course of acute pancreatitis in children are often different than in adults, and these differences should be highlighted. The etiology of acute pancreatitis in children is drugs, infections, trauma, or anatomic abnormalities. The diagnosis of acute pancreatitis is based on clinical symptoms, serum pancreatic enzyme levels, and imaging studies. Treatments in adults and children are similar. With advances in diagnostic techniques and treatments, severe acute pancreatitis in children is becoming better understood and more controllable.

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INTRODUCTION

Acute pancreatitis is not necessarily a rare disease, even in children and adolescents (hereinafter referred to as "children"), and may be life-threatening if it is severe[1,2]. Therefore, acute pancreatitis should always be considered during the differential diagnosis of abdominal pain in children, and appropriate treatment should be started promptly when necessary. However, many treatment regimens are based on consensus conferences and evidence in adults, so a search for the cause and appropriate treatment in children is often difficult[3,4]. This paper discusses the causes, diagnosis, and treatment of acute pancreatitis in children, including a review based on our own experiences.

Table 1 Etiology of childhood acute pancreatitis

Congenital anomalies, periampullary obstruction
Choledochal cyst, abnormal union of the pancreaticobiliary junction, gallstone, cholecystitis, pancreatic divisum, tumor, ascaris aberrant
Infectious
Mumps, measles, coxsackie, echo, lota, influenza, epstein-barr virus, Mycoplasma, salmonella, gram-negative bacteria
Drugs
L-asparaginase, steroid, valproic acid, azathioprine, Mercaptopurine, mesalazine, Cytarabine, Salicylic acid, indomethacin, tetracycline, chlorothiazide, isoniazid, anticoagulant drug, borate, alcohol
Trauma
Blunt injury, child abuse, ERCR, After surgery
Systemic disease
Reye syndrom, systemic lupus erythematosus, polyarteritis nodosa, Juvenile rheumatoid arthritis, sepsis, multiple organ failure, Organ transplantation, hemolytic-uremic syndrome, henoch-schoenlein purpura, kawasaki disease, inflammatory bowel disease, chronic intestinal pseudo-obstruction, gastric ulcer, anorexia nervosa, food allergy, cystic fibrosis
Metabolic
Hyperlipoproteinemia (I, IV, V), hypercalcemia, diabetes, α1 antitrypsin deficiency
Nutrition
Malnutrition, high-calorie infusion, vitamin A and D deficiency
Others
Familial, idiopathic

ERCP: Endoscopic retrograde cholangiopancreatography.

Table 2 Cause of acute pancreatitis in children and adolescents

Ref.	Location	Cases	Etiology (%) Systemic	Biliary[1]	Anatomic[2]	Trauma	Familial	Metabolic[3]	Drugs	Others[4]	Idiopathic
Lopez[50]	United States	274	48	10	NA	19	NA	0.7	5	0.4	17
DeBanto *et al*[1]	United States	301	3.5	10.5	1.5	13.5	5.5	4	11	16.5	34
Werlin *et al*[8]	United States	180	14	12	7.5	14	3	5.5	12	24	8
Nydegger *et al*[4]	Australia	279	22.2	5.4	NA	36.3	NA	5.8	3.2	2.2	25.1
Suzuki *et al*[19]	Japan	135	8.9	30.4	25.9	9.6	NA	NA	11.1	3.7	10.4
Lantz *et al*[2]	United States	211	3.3	11.8	5.2	7.6	0.9	6.2	19.9	13.8	31.3

All studies contained more than 100 cases. NA: Not available. [1]Gallstone, biliary sludge, choledochal cyst; [2]Abnormal union of the pancreaticobiliary junction, pancreatic divisum; [3]Diabetic acidosis, hyperlipidemia, organic acidemias, hypercalcemia; [4]Associated viral infection, postendoscopic retrograde cholangiopancreatography, alcohol, autoimmune, cystic fibrosis, post-surgery.

ETIOLOGY

Alcohol and gallstones are the etiology of acute pancreatitis in many adults, and although some differences exist based on sex and ethnicity, these two etiologies account for more than 60% of cases of acute pancreatitis in adults[5,6]. However, the etiology in children is often drugs, infections, trauma, and anatomic anomalies such as choledochal cysts and abnormal union of the pancreatobiliary junction (Table 1)[1,4,7,8]. Table 2 shows the incidence of acute pancreatitis by etiology. There is a considerable difference in the etiology of acute pancreatitis in Western and Asian children[9].

Drugs

Among drugs used in childhood and adolescence, L-asparaginase (ASNase), steroids, and valproic acid often cause pancreatitis as an adverse reaction. In particular, ASNase, a key drug used in treatment of childhood leukemia, is associated with a higher incidence of pancreatitis as compared to other drugs, ranging from 2%-16% when mild cases are included[10-12]. A characteristic of pancreatitis associated with ASNase, in addition to clinical symptoms of abdominal pain and tenderness, is the early absence of elevated serum amylase levels in about half of patients[13,14]. This phenomenon is attributed to inhibition of protein synthesis by ASNase[14]. Therefore, when acute pancreatitis is suspected based on clinical findings, even in the absence of serum amylase elevation, acute pancreatitis must always be considered in the differential diagnosis, and it is important not to miss the opportunity for early treatment. Azathioprine and mesalazine can also cause pancreatic toxicity, so if serum pancreatic enzyme levels increase during the treatment of inflammatory bowel disease, drug-related pancreatitis must also be considered[15].

Infectious disease

Mumps is often encountered in daily clinical practice, but few patients develop pancreatitis that requires additional treatment. Pancreatitis as a complication is reported in 0.3%-15% of patients when mild cases are included[16]. Abdominal symptoms such as pain and tenderness may occur before the clinical onset of mumps (4-8 d after viral infection) and often spontaneously resolve in about 1 wk. In addition, pancreatitis may occur without parotid

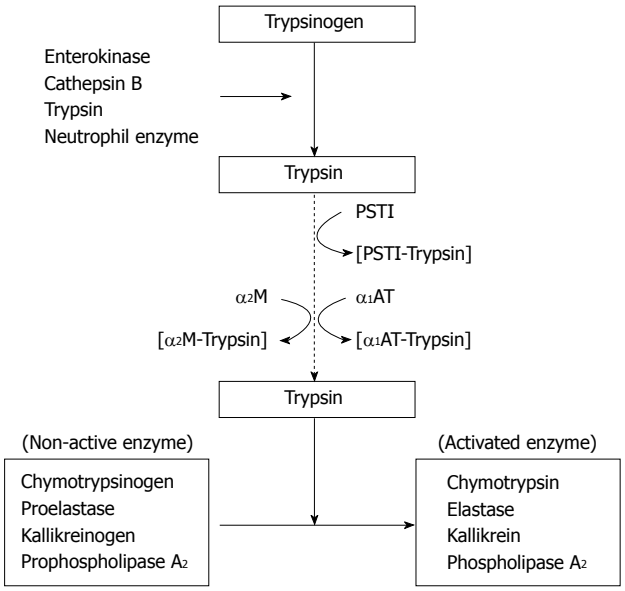

Figure 1 Suppression mechanisms for pancreatic enzyme activation. PSTI: Pancreatic secretory trypsin inhibitor; α2M: α2-macroglobulin; α1AT: α1-antitrypsin.

gland swelling in a few patients. When pancreatitis of unknown etiology occurs, testing for the mumps virus is recommended. Two deaths have been reported to date, so although rare, possible serious infection must be kept in mind[17].

Pancreatitis associated with mycoplasma infection is broadly classified into two types: early onset type during early infection (days 1-3) and late-onset type after respiratory tract symptoms have occurred (days 7-14). The mechanism in the former is thought to be direct invasion of mycoplasma into the pancreas, and in the latter, pancreatic injury caused by autoantibodies to acinar cells[18]. The prognosis in pancreatitis due to mycoplasma is generally good.

Congenital anomalies

Among anomalies of the pancreatobiliary system, choledochal cyst is the most common cause of acute pancreatitis[1,2,4,19]. In fact, many choledochal cysts are discovered because of symptoms of acute pancreatitis. In children with acute pancreatitis in whom the etiology is unclear, ultrasonography, endoscopic retrograde cholangiopancreatography (ERCP), or magnetic resonance cholangiopancreatography (MRCP) should be performed[20,21]. Most choledochal cysts, with the exception of Todani classification type Ⅱ (bile duct diverticulum) and type Ⅲ (choledochocele), are associated with abnormal union[22]. The sphincter of Oddi is usually most thickened in the duodenal muscularis mucosa; however, in abnormal union, because this sphincter surrounds a common channel after union of the main pancreatic duct and common bile duct, there is communication between the ducts during sphincter contraction[23]. Therefore, reflux of bile into the pancreatic duct, a protein plug in the common channel, or gallstone impaction is probably involved in the onset of pancreatitis.

PANCREATITIS CAUSED BY GENETIC MUTATIONS

Hereditary pancreatitis is due to autosomal dominant inheritance with about 80% penetrance. A relationship between a mutation in the cationic trypsinogen gene (protease serine 1, *PRSS1*) and hereditary pancreatitis was identified in 1996[24]. In 2000, a mutation in the serine protease inhibitor gene (*Kazal* type 1: *SPINK1*) was reported to be related to chronic idiopathic pancreatitis of unknown cause[25]. Patients with hereditary pancreatitis due to a *PRSS1* gene mutation or relapsing pancreatitis due to a *SPINK1* gene mutation can develop pancreatic exocrine insufficiency and diabetes in the future, and they are a high-risk group for pancreatic cancer[26-28]. The cause of these complications like cancer, as in chronic pancreatitis due to other etiologies, involves hyperplasia and metaplasia of the pancreatic duct epithelium due to recurrent or chronic inflammation. *K-ras* gene mutations also play a role[29]. Diabetes or pancreatic cancer developing in childhood cases has not been reported.

Recently, variants in *CPA1,* which encodes carboxypeptidase A1, were implicated in early onset pancreatitis in children up to 10 years old. The mechanism by which *CPA1* variants confer increased pancreatitis risk may involve misfolding-induced endoplasmic reticulum stress rather than elevated trypsin activity[30].

Other causes

In malignant lymphoma, lymphoma invasion near the head of the pancreas may compress the pancreatic duct and lead to acute pancreatitis[31]. In addition, in solid pseudopapillary neoplasms, intratumoral hemorrhage due to trauma can cause transient tumor enlargement, leading to pancreatic duct obstruction and acute pancreatitis[32].

PATHOPHYSIOLOGY

To understand the pathophysiology of acute pancreatitis, knowledge about the inhibitory mechanisms of activation of pancreatic enzymes under physiological conditions is necessary. In normal pancreatic acinar cells, lysosomes containing cathepsin B, which are involved in intracellular and extracellular digestion, and zymogen granules containing digestive proenzymes, such as trypsinogen, are released; and these inactive proenzymes remain inactivated[33,34]. In addition, even if trypsin is aberrantly activated in the pancreas for some reason, its activity is blocked by pancreatic secretory trypsin inhibitor (PSTI). Moreover, if trypsin leaks into the blood, the endogenous trypsin inhibitors α1-antitrypsin (α1AT) and α2-macroglobulin (α2M) bind to trypsin and suppress its activity (Figure 1)[35]. Anatomically, the sphincter of Oddi located in the duodenal ampulla of Vater prevents reflux of duodenal fluid into the pancreatic duct. Pancreatic duct pressure is also usually higher than bile duct pressure, so there is no bile reflux into the pancreatic duct[23].

Excessive stimulation of pancreatic exocrine secre-

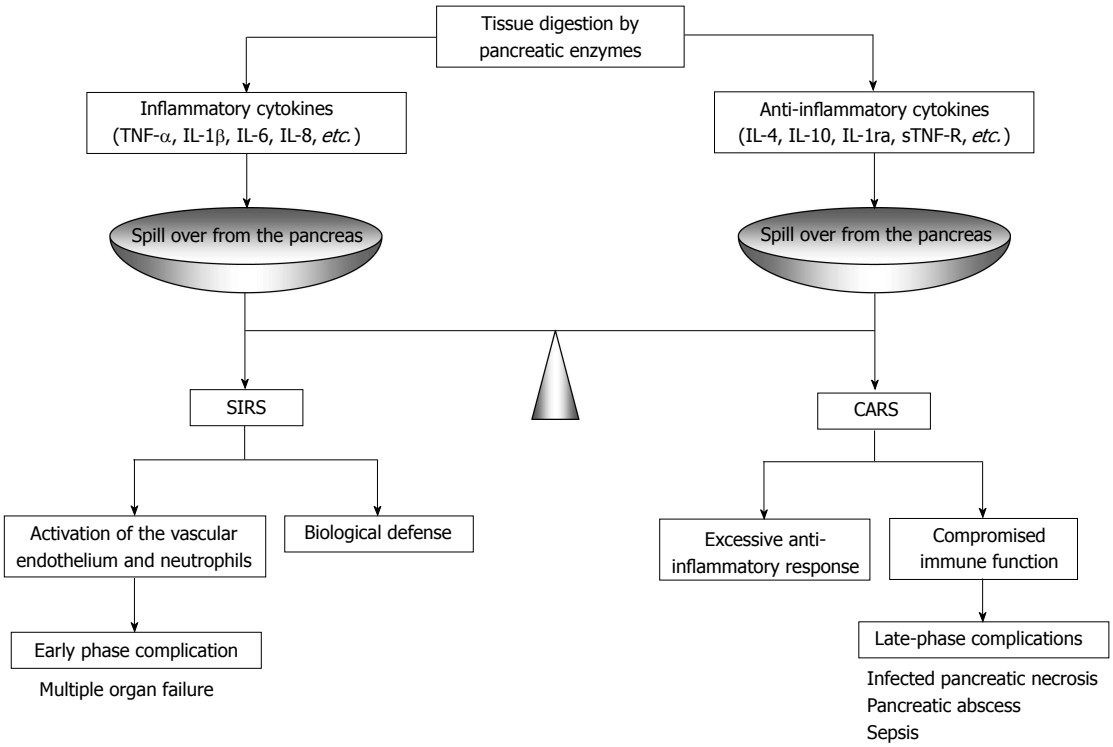

Figure 2 Compensatory anti-inflammatory response syndrome and systemic inflammatory response syndrome during acute pancreatitis. TNF: Tumor necrosis factor; IL: Interleukin; sTNF-R: Soluble tumor necrosis factor receptor; CARS: Compensatory anti-inflammatory response syndrome; SIRS: Systemic inflammatory response syndrome.

tions can cause reflux of pancreatic juices and enterokinase, pancreatic duct obstruction, and inflammation. These conditions can disrupt the above-mentioned defense mechanisms, activate trypsin beyond the ability for trypsin inactivation, and increase attacking factors, thus leading to acute pancreatitis[36]. Enterokinase is the most efficient activator, but trypsin itself, lysosomal enzymes (cathepsin B) in pancreatic acinar cells, and neutrophilic enzymes are also activators[34,36]. In experimental models of early acute pancreatitis, blockage of secretion has been suggested as the initiating event, leading to the accumulation of zymogen granules within acinar cells. This event is followed by a co-localization of digestive enzymes and lysosomal enzymes within vacuoles and, finally, an activation of enzymes that cause acute intracellular injury[37]. The activation of zymogen protease in pancreatic acinar cells is thought to play an important role in the development of acute pancreatitis[36,38].

Mild pancreatitis mainly involves the pancreas and local surrounding lesions. It is generally reversible, and about 6 mo after clinical remission, the pancreas recovers its normal morphology and function. In severe pancreatitis, vasoactive substances such as histamine and bradykinin are produced in large amounts with trypsin activation. As this vasoactive process increases, third spacing of fluids and shock due to hypovolemia may occur. In addition, leakage of activated enzymes from the pancreas causes secondary cytokine production. These cytokines trigger the systemic inflammatory response syndrome (SIRS)[39,40]. SIRS results in hyperactivation of macrophages and neutrophils throughout the body and the release of tissue injury mediators; multiorgan failure, including shock, circulatory failure, and acute respiratory distress syndrome (ARDS), may occur[41-43].

Meanwhile, as a biological defense response, anti-inflammatory cytokines and cytokine antagonists are induced to prevent prolongation of SIRS. This predominance of cytokine antagonists is called compensatory anti-inflammatory response syndrome (CARS)[44]. Because CARS inhibits new cytokine production, susceptibility to infection is increased, and infection of vital organs can occur. As a result of infection, endotoxins in the blood stimulate neutrophil aggregation in distal organs, tissue injury mediators are released, and distal organ failure occurs (Figure 2).

CLINICAL DIAGNOSIS AND ASSESSMENT OF SEVERITY

The diagnosis of acute pancreatitis is in principle based on clinical findings, biochemical tests, and imaging studies. Both a differential diagnosis and assessment of severity are necessary. The etiology of acute pancreatitis in children often differs from that in adults, and differences in the clinical manifestations and course may occur. Therefore, the diagnosis should be made keeping in mind specific features of the disease in children and after obtaining a past medical and family medical history (Figure 3).

Clinical manifestations

More than 90% of adults with acute pancreatitis report

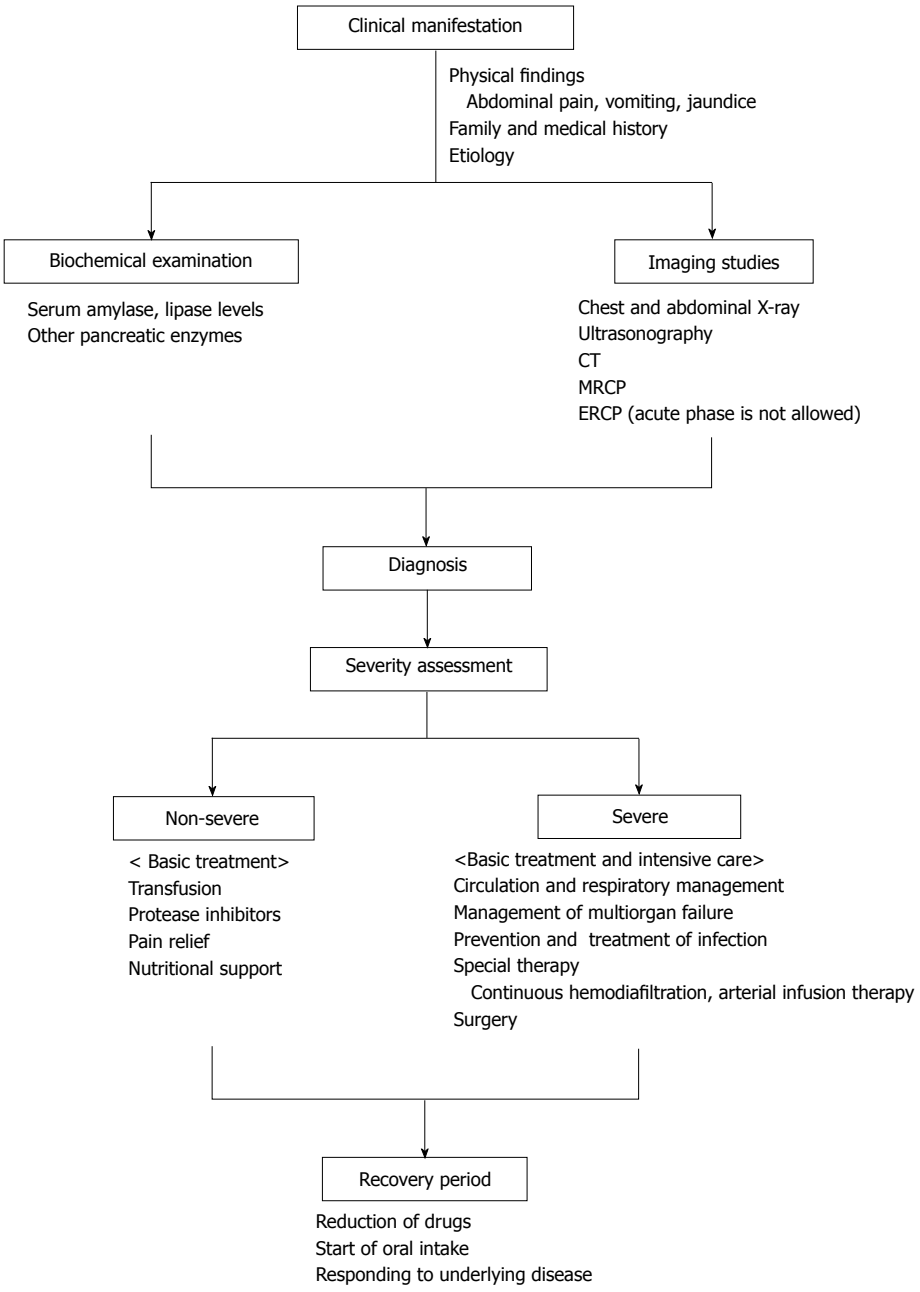

Figure 3 Clinical diagnosis of acute pancreatitis. CT: Computed tomography; ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography.

abdominal pain[45,46]. Abdominal pain is also an important early symptom in children. Weizman *et al*[47] reported that all 61 of their pediatric patients with acute pancreatitis initially had abdominal pain. Ziegler *et al*[48] also reported abdominal pain in 40 of 49 patients (82%). Table 3 shows the initial symptoms by age in our series of 135 children with acute pancreatitis[19]. In older children, the frequency of abdominal pain as a first symptom was similar to that in adults, whereas in younger children, vomiting was an important clinical symptom[49]. However, very young children and those with mild pancreatitis sometimes have non-specific abdominal pain. The location, characteristics, and triggers of abdominal pain, as well as physical examination of the abdomen, are important clues in the diagnosis of acute pancreatitis.

Other symptoms may include jaundice, fever, diarrhea, back pain, irritability, and lethargy. Jaundice and clay-colored stools suggest an abnormality of the biliary system such as a choledochal cyst, and there may be a palpable abdominal mass[8]. Infants and toddlers cannot verbalize abdominal pain, but vomiting, irritability, and lethargy are common[48]. In severe acute pancreatitis, children may initially present with shock, followed by symptoms of multiorgan failure, including dyspnea, oliguria, hemorrhage, and mental status changes[1].

Laboratory investigations

The prompt measurement of serum amylase is useful for

Table 3 First symptoms and chief complaints by age *n* (%)

	Age, yr			
	1-5 (*n* = 53)	6-10 (*n* = 47)	11-17 (*n* = 35)	Total (*n* = 135)
Abdominal pain	46 (86.8)	39 (83.0)	32 (91.4)	116 (85.9)
Fever	21 (39.6)	21 (44.7)	10 (28.6)	52 (38.5)
Vomiting	29 (54.7)	16 (34)	6 (17.1)	51 (37.8)
Jaundice	9 (17)	2 (4.3)	0	11 (8.1)
Back pain	0	1 (2.1)	5 (14.3)	6 (4.4)
Pale stool	3 (5.7)	1 (2.1)	0	4 (3)
Diarrhea	0	1 (2.1)	2 (5.7)	3 (2.2)
Loss of consciousness	1 (1.9)	1 (2.1)	1 (2.0)	3 (2.2)
Others	5 (9.5)	2 (4.2)	2 (5.8)	9 (6.6)

a diagnosis of acute pancreatitis[50]. However, elevated levels are also seen in gastrointestinal diseases such as pancreatobiliary tract obstruction and perforative peritonitis, as well as in salivary gland disease and renal failure. Therefore, low disease specificity is a problem. Serum lipase has a sensitivity of 86.5%-100% and specificity of 84.7%-99.0% for diagnosing acute pancreatitis[51]. Thus, its sensitivity is higher compared to serum amylase. In severe pancreatitis, serum lipase levels 7 times higher than normal have been reported within 24 h after onset of pancreatitis[52]. The degree of elevation and serial changes, however, generally do not correlate with disease severity[53]. In acute pancreatitis due to ASNase or valproic acid, which is fairly common in children, serum amylase may not be elevated[13]. Therefore, other serum pancreatic enzymes should also be measured.

Imaging

When acute pancreatitis is suspected, plain chest and abdominal X-rays are essential. A plain chest X-ray may show a pleural effusion, ARDS, or pneumonia. Although these findings are not specific for acute pancreatitis, they are important for the assessment of disease severity. A plain abdominal X-ray may show an ileus, colon cut-off sign, sentinel loop sign, calcified gallstones, pancreatic stones, or retroperitoneal gas. This information is important in assessing the clinical course of acute pancreatitis and is necessary for a differential diagnosis to rule out other diseases such as gastrointestinal perforation[54,55].

Ultrasonography is a convenient and non-invasive test. It is the test of first choice for screening to diagnose acute pancreatitis in children and for following the clinical course. The ultrasound diagnosis of acute pancreatitis is based on pancreatic morphology, appearance of the pancreatic parenchyma and pancreatic duct, and extrapancreatic findings[56,57].

CT scanning together with ultrasonography is essential for diagnosing acute pancreatitis. CT is useful to evaluate any extrapancreatic lesions, monitor the clinical course, and assess severity. In particular, CT is superior for early assessment of acute pancreatitis when ultrasound findings are nonspecific because of abdominal gas[56,58].

Pancreatitis in children is often caused by pancreatobiliary tract anomalies such as a choledochal cyst or abnormal union of the pancreatobiliary junction. Therefore, ERCP should be performed in pancreatitis of unknown cause. MRCP imaging has also improved and is useful in searching for a cause of acute pancreatitis in children[59]. In particular, MRCP should be performed before ERCP to detect any pancreatobiliary tract disease in children with initial onset of acute pancreatitis of unknown cause. However, in younger children, abnormal union of the pancreatobiliary junction is often difficult to delineate[21].

Severity assessment

Rapid and accurate assessment of severity is useful for selecting appropriate initial treatment and predicting the prognosis. In 2002, DeBanto *et al*[1] were the first to suggest a scoring system for predicting the severity of acute pancreatitis in children. This system is modified from the Ranson and Glasgow systems and consists of the following eight parameters: age (< 7 years old), weight (< 23 kg), white blood cell count at admission (> 18500 cells/μL), lactic dehydrogenase at admission (> 2000 U/L), 48-h trough Ca^{2+} (< 8.3 mg/dL), 48-h trough albumin (< 2.6 g/dL), 48-h fluid sequestration (> 75 mL/kg per 48 h), and 48-h rise in blood urea nitrogen (> 5 mg/dL). They set the cutoff for predicting a severe outcome at three criteria. However, this scoring system is not exact for Asian children[18]. Lautz *et al*[2] also reported that DeBanto pediatric scores have limited ability to predict acute pancreatitis severity in children and adolescents in the United States. Recently, we reported the usefulness of a new severity assessment that modified the acute pancreatitis severity scoring system of the Ministry of Health, Labour and Welfare of Japan (JPN score) for use in children[60,61]. The parameters of the pediatric JPN score were as follows: (1) base excess ≤ -3 mEq or shock (systolic blood pressure cutoffs according to age group); (2) PaO_2 ≤ 60 mmHg (room air) or respiratory failure; (3) blood urea nitrogen ≥ 40 mg/dL [or creatinine (Cr) ≥ 2.0 mg/dL] or oliguria (< 0.5 mL/kg per h); (4) lactate dehydrogenase ≥ 2 × the value of the upper limits; (5) platelet count ≤ $1 \times 10^5/mm^3$; (6) calcium ≤ 7.5 mg/dL; (7) C-reactive protein ≥ 15 mg/dL; (8) number of positive measures in pediatric SIRS score ≥ 3; and (9) age < 7 years old or/and weight < 23 kg. The cutoff for predicting a severe outcome was set at three criteria.

The CT severity index has proven to be very useful in adults[62]. Recently, Lautz *et al*[58] also reported that the CT severity index was superior to a clinical scoring system for identifying children with acute pancreatitis at heightened risk for developing serious complications.

TREATMENT

The initial treatment for acute pancreatitis is to withhold oral intake of food or fluid to allow the pancreas to rest (*i.e.*, prevent stimulation of pancreatic exocrine secretions). Fluid and electrolyte supplementation, enzyme inhibition therapy, and treatment to relieve pain and

prevent infection are provided. It is important to gradually permit liquid and food intake at a suitable time while continuing treatment. This treatment strategy is based on a consensus conference and evidence accumulated in adult patients. The basic pathogenesis of acute pancreatitis does not greatly differ between adults and children, and the treatment selected for children should be similar to that in adults.

Infusion of extracellular fluid

Because fluid leaks into the surrounding tissue due to inflammation associated with acute pancreatitis, adequate infusion to supplement extracellular fluid is needed during initial treatment. In severe cases, increased vascular permeability and decreased colloid osmotic pressure causes extravasation of extracellular fluids into the surrounding tissue and retroperitoneum and then into the peritoneal cavity and pleural cavity, thus leading to large losses in circulating plasma volume[63]. This acute circulatory impairment causes a rapidly deteriorating condition in early acute pancreatitis.

DRUG THERAPY

Analgesics

Pain in acute pancreatitis is often intense and persistent, and pain control is required. Appropriate use of analgesics can effectively reduce pain, but this should not interfere with making a diagnosis or providing other treatments[64-66]. The analgesics used include pentazocine, metamizole, and morphine.

Antibiotics

In mild cases of acute pancreatitis, the incidence of infectious complications and mortality rates are low, and prophylactic antibiotics are usually not necessary. However, even in mild cases, antibiotics should be considered if severity increases or complications like cholangitis develop. In severe cases, antibiotics can reduce infectious pancreatitis complications and improve the prognosis[67]. Drugs should be selected with good tissue distribution to the pancreas.

Pancreatic protease inhibitors and octreotide

The Santorini Consensus Conference in 1997 concluded that gabexate mesilate did not contribute to reduced mortality rates in acute pancreatitis[68]. However, in severe acute pancreatitis, continuous infusion of large doses of gabexate mesilate may decrease complications and mortality rates[69]. Similar efficacy in children has been reported, but no clear evidence exists[70]. Protease inhibitors may be a part of combined modality therapy (especially to improve hemodynamic status), but judicious administration is advised in severe cases.

Octreotide was introduced in the early 1980s and offers several advantages over somatostatin, such as a much longer half-life and the option for either subcutaneous or intravenous administration[71]. Octreotide is a powerful inhibitor of exocrine pancreatic secretion and cholecystokinin production[72]. Several studies have evaluated the effect of octreotide on the incidence of clinical pancreatitis after ERCP and postoperative complications such as pancreatic duct fistula following pancreaticoduodenectomy and pancreatic transplantation[73,74]. Effectiveness in reducing complications in acute pancreatitis has not been demonstrated[75]. However, at the case report level, octreotide has been effective in treating pancreatic pseudocysts as a complication in acute pancreatitis and in preventing and treating drug-related pancreatitis due to ASNase, a key drug used to treat lymphocytic leukemia in children[76-78]. As a somatostatin derivative, the most common adverse effect of octreotide is abdominal distention, but adverse effects such as failure to thrive are unlikely if octreotide is given for only 2-6 wk.

NUTRITIONAL SUPPORT

In severe pancreatitis, the early initiation of enteral nutrition reduces the incidence of infections and leads to shorter hospital stays[79]. An enteral feeding tube is placed in the duodenum or in the jejunum past the ligament of Treitz[80]. This type of nutrition is recommended to reduce stimulation of exocrine pancreatic secretion.

Control of abdominal pain and serum pancreatic enzyme levels should be considered in deciding when to resume oral intake. If serum pancreatic enzymes are decreasing, overall status is good, and abdominal pain has subsided, liquid intake can be started. If serum amylase and lipase levels are approximately less than two times the upper normal limits, a fat-restricted diet should be started[81]. Energy and fat intake can gradually be increased with careful monitoring.

Specific treatment for severe pancreatitis

In patients with infected pancreatic necrosis, surgical drainage and pancreatectomy may be indicated. Specific treatments such as continuous hemodiafiltration to remove humoral mediators and continuous regional arterial infusion of a protease inhibitor and antibiotics have been effective in adults[82,83]. These specific treatments have also been effective and lifesaving in children[84,85]. Although there is no universally acceptable scoring system for predicting the severity of childhood acute pancreatitis, consideration should be given to early transfer of severe patients to a medical center where intensive treatment is available.

Endoscopic treatment and surgery

Anatomic anomalies such as abnormal union of the pancreatobiliary junction are an indication for surgery. In patients with outflow tract obstruction of pancreatic juices caused by ampulla of Vater anomalies or pancreatic divisum, endoscopic sphincterotomy is effective.

Infectious complications should be clinically suspected if fever or signs of inflammation recur during the course of acute pancreatitis. Symptoms often become

prominent 2 wk or more after the onset of pancreatitis. The definitive diagnosis of infected pancreatic necrosis can be made by CT- or ultrasound-guided local fine-needle aspiration and bacteriologic cultures[86,87]. However, this procedure may be difficult in children. Therefore, worsening blood test results, positive blood cultures, positive blood endotoxins, elevated serum procalcitonin levels, and CT findings of the pancreas may serve as clues to a diagnosis of infected pancreatic necrosis[88].

Patients whose general condition is stable can be conservatively treated with antibiotics and observed, but if their condition does not improve, a necrosectomy is required. Necrosectomy early in pancreatitis is associated with a high mortality rate, so it should ideally be performed after the patient's hemodynamic status and general condition have stabilized[89]. Percutaneous necrosectomy, endoscopic transgastric necrosectomy and laparoscopic pancreatic necrosectomy have recently been reported as less invasive treatments in adults and a few children[90-92]. Pancreatic abscesses generally require percutaneous, endoscopic, or surgical drainage.

Pancreatic pseudocysts are cysts that develop due to injury of the pancreatic duct and extravasation of fluid. These occur 4 wk or later after the onset of pancreatitis. Treatment is indicated for pseudocysts if their size does not decrease, if they are accompanied by abdominal pain, or if there are complications of infection or hemorrhage. Endoscopic ultrasound-guided transgastric puncture and drainage can safely be performed in these cases[93,94].

CONCLUSION

Currently, our approach to acute pancreatitis in children mainly depends on physician experience and knowledge gained from acute pancreatitis in adults. Acute pancreatitis in children tends to be considered a difficult disease, even by pediatric gastroenterologists. However, with recent advances in diagnostic techniques and treatment methods, unfamiliar and difficult diseases are becoming controllable diseases once they are better understood. In order to improve treatment outcomes in patients with childhood acute pancreatitis, future studies focusing on developing a scoring system for predicting the severity of acute pancreatitis and identifying the potential effective treatment modalities for children should be conducted.

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