

Acute Pancreatitis in Children : A Review Article

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Abstract

The incidence of acute pancreatitis (AP) in children has significantly increased in the past two decades. However, it can be associated with severe morbidity and mortality. Therefore it should be considered in every child presented with unexplained severe abdominal pain. The etiology, clinical manifestation, and course of acute pancreatitis in children are often different than in adults. Therefore the early and effective diagnosis of acute pancreatitis in children is challenging. In this review, we will discuss the etiology, clinical features and laboratory testing for the disease and also the management outlines of acute pancreatitis in children.

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Introduction

Acute pancreatitis (AP) is defined as the histological presence of inflammation of the pancreatic parenchyma. It is a reversible process characterized by the presence of interstitial oedema, infiltration by inflammatory cells and variable degrees of cellular apoptosis, necrosis and haemorrhage. Though AP is more common in adult, but its incidence has increased significantly over the past few decades, it still occurs regularly and accounts for an increasing number of hospitalizations and significant morbidity.¹

There are 3.6 to 13.2 paediatric cases per 100,000 individual per year, an incidence that approaches the incidence of disease in adults.²

Etiology of Acute Pancreatitis : The disorders associated with pancreatitis fall into several broad categories.

The different etiologies are following:

Biliary Disease : Gallstones: Gallstone pancreatitis is a common cause of AP in children than previously believed. Two factors have been suggested as the possible initiating event in gallstone pancreatitis: reflux of bile into the pancreatic duct due to transient obstruction of the ampulla during passage of gallstones or obstruction at the ampulla secondary to stone (s) or edema resulting from the passage of a stone.

Biliary sludge and microlithiasis : Biliary sludge is commonly found in 20% to 40 % of patients with AP with no obvious cause.²

Other — Other conditions causing obstruction of the ampulla that have been associated with pancreatitis include biliary ascariasis, periampullary diverticula and pancreatic and periampullary tumors.

Medications : Commonly reported associations implicate L-asparaginase, Valproic acid, Azathioprine, Mercaptopurine, and Mesalamine as triggers of pancreatitis.³

Trauma : Most often, unintentional blunt abdominal trauma causes damage to the pancreas, but child abuse can result in traumatic pancreatitis as well.

Idiopathic : After an extensive work-up for recurrent pancreatitis, approximately 13 to 34 percent of patients with acute pancreatitis are idiopathic.³

Systemic Illness : In recent studies, AP associated with systemic illnesses accounted for more than 20% of reported cases.² Of the diseases, hemolytic uremic syndrome has had the highest prevalence.³

Metabolic : Disorders that cause hypertriglyceridemia, hypercalcemia, and inborn errors of metabolism have all been associated with AP.²

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Autoimmune Pancreatitis : Autoimmune pancreatitis occurs in two forms (types 1 and 2). Type 2 seems to be more common in children and has an association with inflammatory bowel disease and other autoimmune diseases.

Anatomic Pancreatobiliary Abnormalities : Pancreatobiliary abnormalities such as pancreas divisum, abnormal junction of the common bile duct and main pancreatic duct (common channel syndrome), choledochal cysts, and annular pancreas increase the risk for AP.³

Genetic Mutations : Mutations in the cystic fibrosis gene (CFTR) have been associated with an autosomal recessively inherited pancreatitis. Pancreatitis has also been associated with low penetrance mutations in the serine protease inhibitor Kazal type 1 (SPINK1). Mutations in chymotrypsin C (CTRC) have also been identified in pancreatitis.³

Vascular Disease : Pancreatic ischemia is an uncommon cause of clinically significant pancreatitis.

Post-ERCP : AP occurs in about 3% of patients undergoing diagnostic ERCP, 5 % undergoing therapeutic ERCP, and up to 25 % undergoing sphincter of Oddi manometric studies.⁴

Other Causes : Another rare cause of recurrent pancreatitis is celiac disease, where duodenal inflammation and papillary stenosis may be the mechanisms for pancreatitis.³

Clinical Features of AP : There have been more than 28 studies characterizing children with AP in last 52 years. The common clinical presentations are following:

Abdominal pain : In pediatric studies of AP, abdominal pain is the cardinal symptom.³ The most common location of pain is in epigastric region (62%–89% of cases). However, epigastric pain is associated with back pain <10% of the time. Diffuse abdominal pain is found in 12% to 20% of patients.² The pain typically occurs acutely, without a prodrome, and rapidly reaches maximum intensity. It tends to be moderately to intensely severe and tends to last for several days. The pain tends to be steady but is exacerbated by eating or drinking, especially after taking fatty food. Patients may lean forward or even curl up in a knee-to-chest (fetal position) to decrease the pain by decreasing the stretch of the pancreas.⁵

Nausea and vomiting : The second most common symptom was nausea or vomiting, which was reported in 40% to 80% of patients.

Other symptoms: 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. In severe AP, children may initially present with shock, followed by symptoms of multiorgan failure, including dyspnea, oliguria, hemorrhage, and mental status changes.⁶

Physical examination

Mild disease presents with only mild abdominal tenderness. Severe disease presents with severe abdominal tenderness and guarding, generally localized to the upper abdomen. Hypoactive bowel sounds, accompanied by epigastric distention, may be caused by peripancreatic spread of the inflammatory process that produces a generalized ileus. About 60% of patients develop low-grade pyrexia from peripancreatic inflammation without evident infection.

Uncommon physical findings reflect specific complications

Unilateral dullness to percussion and decreased breath sounds at a lung base indicate a pleural effusion. Ecchymoses in the flanks, called "Gray-Turner's sign," indicate retroperitoneal hemorrhage from hemorrhagic pancreatitis, whereas ecchymoses in the periumbilical region, called "Cullen's sign," indicate intra-abdominal hemorrhage. Jaundice suggests choledochal obstruction from gallstone pancreatitis.⁵

Diagnosis

In order to develop the definitions that would accurately classify children with pancreatitis, a consortium named International Study Group of Pediatric Pancreatitis : In

Search for a Cure (INSPIRE) is formed. The goals of the consortium were to review available literature for consensus definitions of Acute Pancreatitis (AP), Acute Recurrent Pancreatitis (ARP) and Chronic Pancreatitis (CP).

AP requires at least two of the three criteria:⁷

1. Abdominal pain suggestive or compatible with acute pancreatitis (abdominal pain of acute onset, especially in the epigastric region),
2. Serum amylase and /or lipase activity at least 3 times greater than upper limit of normal,
3. Imaging findings compatible with acute pancreatitis.

Investigations

Biochemical test

Serum amylase : Serum amylase rises within 6 to 12 hours of the onset of AP and returns to normal within three to five days.⁸

Serum lipase : Serum lipase rises within four to eight hours of the onset of symptoms, peaks at 24 hours, and returns to

normal within 8 to 14 days.⁹

Other enzymes and products : Other pancreatic digestive enzymes that leak into the systemic circulation and are elevated in serum include trypsin, phospholipase, carboxypeptidase, carboxylester lipase, colipase, and pancreatic isoamylase.¹⁰

Other laboratory findings : Patients with pancreatitis may have leukocytosis and an elevated hematocrit from hemoconcentration due to extravasation of intravascular fluid into third spaces.

Metabolic abnormalities including elevated blood urea nitrogen (BUN), hypocalcemia, hyperglycemia, and hypoglycemia may also occur.

For determining the etiology of acute pancreatitis : All patients should have a triglyceride level, calcium level, and liver enzymes. In patients with suspicion of autoimmune pancreatitis, antinuclear antibody levels and serum IgG levels should be obtained.¹¹

Imaging

Several features may be seen on imaging in patients with AP.

Abdominal and chest radiographs

A plain abdominal X-ray may show an ileus, colon cut-off sign, sentinel loop sign, calcified gallstones, pancreatic stones, or retroperitoneal gas.⁷

A plain chest X-ray may show a pleural effusion, ARDS, or pneumonia, elevation of hemidiaphragm.

Abdominal ultrasound

It is the test of first choice for screening to diagnose AP in children and for following the clinical course. In patients with acute pancreatitis, the pancreas appears diffusely enlarged and hypoechoic on abdominal ultrasound. Gallstones may be visualized in the gallbladder or the bile duct. Peripancreatic fluid appears as an anechoic collection on abdominal ultrasound.¹²

Computed tomography (CT) scan

If performed three or more days after the onset of abdominal pain, contrast-enhanced CT scan can reliably establish the presence and extent of pancreatic necrosis and local complications and predict the severity of the disease.

Magnetic resonance imaging (MRI)

MRI can better characterize the pancreatic and bile ducts and complications of acute pancreatitis.

Magnetic resonance cholangiopancreatography (MRCP)

MRCP delineates the bile and pancreatic ducts better than CT and has a higher sensitivity in detecting choledocholithiasis.

Endoscopic retrograde cholangiopancreatography (ERCP)

ERCP with sphincterotomy is essential for the diagnosis and therapy of symptomatic choledocholithiasis.

Complications²

Local

- Inflammation
- Pancreatic edema
- Pancreatic necrosis
- Fat necrosis
- Pancreatic hemorrhage
- Pancreatic pseudocyst
- Pancreatic duct rupture
- Pancreatic duct stricture
- Thrombosis of adjacent blood vessels

Systemic

- Shock
- Sepsis
- Hypermetabolic state
- Hypocalcemia
- Hyperglycemia
- Vascular leak syndrome
- Multiorgan system failure
- DIC
- Pleural effusions
- Acute renal failure
- Splenic artery pseudoaneurysm

Management of AP

The management of acute pancreatitis traditionally has consisted of pancreatic rest (no enteral feeding), antiemetics, analgesia, fluid support, and monitoring for complications.

Abdominal pain management

Pain management requires a careful balance between adequate control and oversedation. Morphine or related opioids were used in 94% of children with AP according to the INSPPIRE physicians' questionnaire.⁷ Narcotic-sparing medications including indomethacin have shown promise in pain management in AP.¹⁰ Newer medications including intravenous acetaminophen and ke-torolac have also shown promise in reducing narcotic use following surgery in pediatric patients.¹

Intravenous Fluid (I/V) Management

Fluid resuscitation is an integral part of this care as evidenced by recently published guidelines.¹ Most commonly, crystalloid solutions are the fluid of choice for I/V resuscitation in line with efforts to favorably alter the course of AP, there is now supportive evidence for early, aggressive fluid resuscitation.

"Early resuscitation" has been defined as receiving greater than one-third of the total 72-hour intravenous fluid volume within the first 24 hours of presenting to the emergency department.¹³

Nutritional management

In patients who have mild acute pancreatitis, oral feedings can be started within 24 to 48 hours after admission. In the past,

clear liquids were started, but recent studies in adults show that regular meals can be given.¹ According to recent meta-analyses, enteral nutrition was superior to total parenteral nutrition with a lower incidence of infection and multiorgan failure, resulting in lower mortality rates and a shorter hospital stay. The only clear indications for TPN include inability to tolerate enteral nutrition due to prolonged ileus, pancreatic fistulae, or complicating abdominal compartment syndrome.¹⁴

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.⁷

Treatment of associated conditions

Gallstone pancreatitis : Early ERCP with papillotomy or surgical intervention to remove bile duct stones may lessen the severity of gallstone pancreatitis.

Cholecystectomy : Cholecystectomy should be performed after recovery in all patients with gallstone pancreatitis.

Biliary sludge : Cholecystectomy in patients who have had an episode of pancreatitis and have biliary sludge because of the high risk of recurrence.

Hypercalcemia : If present, treatment should be directed at normalizing serum calcium levels and determining the underlying etiology.

Specific treatment for severe pancreatitis : In patients with infected pancreatic necrosis, surgical drainage and pancreatectomy may be indicated.²

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. 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.¹⁵

Outcome

Outcomes in AP are similar among pediatric age groups and are not correlated with initial amylase and lipase levels. There are no existing scoring systems similar to the APACHE (Acute Physiology and Chronic Health Evaluation) or the Ranson system used in adults that can accurately predict outcome in pediatrics.¹ There are also no data, on the mortality rate of severe AP in childhood. However to reduce the mortality rate, it is important for patients with severe AP to be transferred to a medical facility with adequate monitoring and intensive care.

Conclusion

Early and effective diagnosis of AP is challenging. It is of great importance to make an early diagnosis, so that specific treatment can be offered to prevent unwanted complications and to reduce morbidity and mortality related to AP.

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