

PROBLEM-SOLVING ARTICLE

Diagnosis and Management of Posttraumatic Pancreatitis in Children

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Summary

Traumas take a significant place in the etiology of children's acute pancreatitis. Diagnostics and treatment of posttraumatic pancreatitis (PTRP) are complex. Delayed diagnosis of pancreatitis is connected with heightened morbidity and mortality. There is a remarkable difference in the tactic of treatment between adults and children because of the anatomical physiological reasons. Special attention has to be paid to children under the age of two years. The article summarizes the literature review and the experts' conclusions from various European countries. Children who have PTRP should be concentrated in the specialized centres. It is necessary to have international cooperation of multicenters to improve the diagnostics and treatment of children PTRP.

Key words: children, pancreatitis, pancreatic trauma, posttraumatic pancreatitis, diagnostics, treatment, complications.

Abbreviations: PTRP – posttraumatic pancreatitis, US – ultrasonoscopy, CT – computer tomography, MR – magnetic resonance, ERCP – endoscopic retrograde cholangiopancreatography, SIRS - systemic inflammatory response syndrome, MODS –multiple organ dysfunction syndrome.

INTRODUCTION

Acute pancreatitis is an acute inflammation of the pancreas with variable severity from mild abdominal pain, which may go undiagnosed, to fulminant necrotizing pancreatitis and death. It is likely that there is a complete interval resolution on morphology and function as opposed to the occurrence of irreversible changes in the pancreas in cases of chronic pancreatitis. Fibrosis and infiltration of the chronic inflammatory cells can lead to exocrine or endocrine failure or both (18). In case of PTRP, especially in severe injuries with anatomical disintegration, intransient consequences of these traumas cannot be excluded; they might appear in adulthood having diseases requiring a compensatory pancreatic load. Children pancreatitis is more common than it is generally believed and can be associated with severe morbidity and mortality. The causes of an acute pancreatitis include trauma, biliary tract stone disease, choledochal cyst, ductal developmental anomalies, drugs, metabolic derangements, and infections. The cause is not apparent for about 35% of children and is called "idiopathic". Severe pancreatitis was most commonly associated with systemic disease and trauma. Numerous reports have identified an increasing trend in the diagnosis of acute pancreatitis for children and the key differences are in disease symptoms and management between infants and older children (16; 17; 21). The reasons for the increase are not entirely clear and may be multifactorial. The significance of the increase of severe infectious and systemic diseases, which have an acute pancreatitis as a complication have been mentioned (13; 17). Some publications relate it to the recent tendency to concentrate the patients in centres doing the corresponding research (21) and seeing significant correlation between the increasing

numbers of amylases/lipases tests and increasing of acute pancreatitis (16). Traumas are wide spread (15-40%) in the etiology of children's acute pancreatitis (7; 10; 12; 17; 21; 27; 28; 29). Up to 10% of children, who have a blunt abdominal cavity trauma, have pancreatic injuries, and the frequency of these cases tends to increase (15). Taking into consideration the very significant proportion of the trauma mechanism related with a bump into the bicycle's handlebar and the adoption of bicyclists' traditions of the "old Europe" in Latvia, considering our road infrastructure and drivers' intelligence, the future does not seem careless. The pancreas is located retroperitoneal to the spinal column, these 2/3 of the injury are localized in the body of the pancreas. The vulnerability of child's pancreas is common due to softer tissues and weaker anatomic protection by the anterior abdominal wall and other organs. In comparison with adults, children more frequently get an isolated pancreatic trauma, which probably indirectly indicates greater vulnerability of pancreatic tissues. Probably the fact that children in general lack primary pathology of the pancreas is crucial for better treatment results at the child's age.

Preparing this article the cognitions gained in the review of literature were discussed with the experts from Children Clinical University Hospital in Riga, Health Sciences' Paediatric Surgery Clinic of the University of Lithuania in Kaunas, Paediatric Surgery Clinic of the University of Amiens, France, Paediatric Surgery Clinic of Helios Klinikum Berlin- Buch, Berlin, Germany, where during the last 12 years altogether there have been treated over 90 patients with a pancreas trauma, more than 85 % of them are recognized as posttraumatic pancreatitis. The authors of the paper would like to express a particular gratitude for the professors V.

Barauskas (Kaunas), J. P. Canarelli (Amiens) and K. Schaarschmidt (Berlin) for sharing of their experience. Detailed research protocols about the children who have pancreas traumas have been filled in Riga during the last 2 years and the cytokine tests in 24, 48 and 72 hours after the trauma have been made to find correlations in the laboratory indicators, which along with the data of other research works (8; 9; 14; 22; 31) let recognize severe pancreatitis timely and adjust appropriate treatment tactics. Cytokines themselves do not induce pancreatitis but rather mediate the progression of pancreatitis. Pancreatic production of pro-inflammatory cytokines modulates a local injury systemic inflammatory response, and a distant organ failure, which, along with pancreatic necrosis, determines the outcome from an acute pancreatitis. Onset of cytokine production follows immediately after the onset of pancreatitis and peaks in 36 – 48 hours; cytokine antagonist therapy may represent a potential therapeutic target and therefore is of an intense interest (32).

Diagnosis. PTRP occurs in association with blunt abdominal trauma, child abuse, or penetrating wounds or after surgery. Trauma impact is necessary for the origin of PTRP; however, in less severe cases the anamnesis of the trauma might lack or it is considered to be inessential. In order not to miss out the trauma, purposeful questions shall be used including all people who take care of the child. It has to be assumed that teenagers might keep the trauma in secret. It is essential to find out the mechanism of the trauma, localization of its impact, force and duration in detail. The time of getting the trauma is important in order to apply laboratory tests in dynamics and CT the most productively. It has to be kept in mind that acute pancreatitis might develop after every seemingly insignificant abdominal trauma. Taking into consideration complicated clinical diagnostics and possible imprecision of laboratory and X-ray diagnostics, any patient of a child age having a blunt abdominal trauma, especially in case of a possible pancreatic injury, has to be hospitalized into the intensive therapy unit during the first 24 hours, where a careful monitoring and examinations in dynamics has to be performed in order to identify a more precise diagnosis, a degree of gravity of the injury and a possible necessity for surgical treatment.

Cardinal changes in the field of acute pancreatitis' diagnostics and treatment took place after the Atlanta (USA) Consensus Conference in 1992. These Atlanta criteria require that patients meet at least 2 of the following 3 parameters to qualify as having an acute pancreatitis: a typical abdominal pain, elevated amylase/lipase > 3 times the upper limit of normal, and /or confirmatory findings on cross-sectional abdominal imaging (4). After this conference the classification of an acute pancreatitis was supplemented by the term SIRS and MODS (dysfunction of more than two organs named as multi-organ failure). This conception changed the essence of treatment from treatment of local characteristics mainly in a surgical way to an early complex intensive therapy having two major aims: to

decrease the severity of SIRS ensuring the functions of all organs' systems and the adequate perfusion of all tissues and to reduce maximally the possibility to get the infection of pancreas and peri-pancreatic tissues. The main conclusion of the new strategy – to a large extent the condition of the patient is not so severely threatened by necrosis, purulence or exudate as a body reaction to this pathological condition. However, the experience gained in the treatment of adults cannot be completely applied to children. Difference in age, developmental stages, and environmental exposures for children may influence the presentation of children who have an acute pancreatitis.

Acute pancreatitis in children usually presents with the sudden onset of mid-epigastric pain continuous and dull in nature (80-95%). Diffuse abdominal pain was reported into for 12-20% of patients. The typical radiation of the pain to the back observed in adults is missing in 60-90% of children (13, 20, 28). Pain is associated with anorexia, nausea and vomiting (40-80%) (25, 28, 29). In severe disease, the child is irritable and assumes a flexed position. For nonverbal children, irritability was a common presenting complaint and may be a surrogate for complaints of pain in this age group. The abdomen may be distended with guarding and rigidity present (29-37%) (3, 11). In very severe cases a child may present with shock, respiratory distress or multi -organ failure or unexplained jaundice or ascites. In the cases of necrotizing or hemorrhagic pancreatitis, hemorrhage may dissect from the pancreas along the tissue planes, presented as ecchymosis either in the flanks (Grey-Turner sign) or at the umbilicus (Cullen's sign). The ecchymoses typically take 1 to 2 days to develop and are observed among children very rarely in comparison with adults. When necrosis, abscess or pseudocyst develop, the presentation may be with a mass in the epigastrium. The most common mass was an abdominal pseudocyst (80% of masses) (28). More than a half of children under the age of two have a high temperature, which is not typical for other age groups. There is no single definitive diagnostic test available. Elevated amylase/lipase levels are helpful in the diagnosis, although normal serum amylase/lipase levels do not exclude pancreatitis from the differential diagnostic opportunities. The degree of serum amylase/lipase elevation does not correlate with the severity of the disease. Serum amylase level may be normal in the first 24 hours; peak between 24 and 72 hours and in uncomplicated cases, remain elevated for 2 to 5 days. Serum lipase levels are usually elevated in pancreatitis in 1 – 2 hours and remain elevated for longer time than amylase (~7 days). In addition, peak lipase levels were about 5 times higher than amylase levels for the children who have an acute pancreatitis. However, it does not mean that the amylase test is dispensable, because about 10% of patients who have an acute pancreatitis had only elevated amylase. Lipase is elevated in 100 % of patients for children under the age of two, but amylase was elevated in only about 40% to 60%. This discrepancy may be attributed to developmental

differences in the expression of the pancreatic enzymes during the first few months of life (12; 20). Both enzymes may be elevated in cases of other illnesses as well. Hyperamylasemia or hyperamylasuria may be caused by salivary inflammation or trauma; intestinal disease including perforation, ischemia, necrosis, inflammation or result from reduced renal clearance. Other laboratory abnormalities that may be present in an acute pancreatitis include hemoconcentration, coagulopathy, leukocytosis, hyperglycemia, glucosuria, hypocalcemia, elevated γ -glutamyl transpeptidase and hyperbilirubinemia.

Imaging of the abdomen is important as a part of the evaluation of the patient who has an abdominal trauma. Plain abdominal radiographs may reveal an isolated loop of intestine in the vicinity of the inflamed pancreas, the so-called "sentinel loop" for the patient who has pancreatitis. Other findings, suggesting pancreatitis, include local spasm of the transverse colon with proximal dilation known as the "colon cut-off" sign. Plain chest roentgenograms should be performed for all patients who have an acute pancreatitis to look for evidence of pleural effusion and pulmonary edema. US is the most useful investigation and may show an increased pancreatic size and a decreased echogenicity. It may also show a peripancreatic fluid collection. It does not subject children to ionizing radiation and it is widely available. The 2 main disadvantages of ultrasound are that it is operator- dependent and an overlying bowel gas or an obese abdomen can obscure the pancreas. Contrast enhanced dynamic CT scan is the imaging modality of choice: it shows the size, the texture of the inflamed pancreas, a peripancreatic fluid collection, abscess, a pseudo cyst, a ductal dilatation, calcification and perfusion defects or the pancreas to differentiate interstitial pancreatitis from a necrotizing pancreatitis. If in abdominal trauma CT is performed early (< 12 hours after the trauma), the obtained results can be insufficient because the time is needed to visualize the changes of the soft tissues (26; 30). If necessary, CT scan can also be used for interventional procedures for the diagnosis or the drainage of fluid collections. CT is generally recommended to evaluate pancreatitis for several days (72 hours) into the diagnosis when a pancreatic necrosis is suspected clinically. Some research make doubt about the efficiency of computer tomography in diagnostics of the children pancreatitis indicating only 60% of sensitivity and stressing the risk of radiation (12, 20, 29). The practise of choosing US over CT is reasonable for the children till 2 years of age because there is a greater risk of long-term complications with ionizing radiation for young children (5). MR and ERCP have become more essential in the diagnostics and treatment of PTRP because they provide information about the condition of the pancreatic duct. MR reduces children exposure to ionizing radiation. ERCP is useful in the treatment of pancreas pseudocysts, but it disposes patients to the risk of increasing morbidity (pancreatitis 3-14 %, intra-abdominal fluid collection infection risk 10 %) (6, 24). Several scoring systems are used for adults, but there is

no a universally accepted scoring system for predicting severity for children acute pancreatitis. DeBanto et al. developed a new scoring system for children, using age (<7 years), weight (<23 kg), admission WBC count (> 18,500), admission LDH (>2000 IU/L), 48-h trough Ca 2+, 48-h trough albumin, 48-h fluid sequestration, and 48-h rise in blood urea nitrogen. If each criterion is assigned a value of 1 point, then the outcome of patients, with 0-2 points was 8,6 % severe and 1,4 % mortality; with 2-4 points, 38,5% severe and 5,8 % mortality; and with 5-7 points, 80 % severe and 10% mortality. They showed a better sensitivity versus Ranson and Glasgow scores (70% vs 30% and 35%, respectively) and a better negative predictive value (91% vs 85% and 85%) (33). A pleural effusion is highly specific in predicting a severe pancreatitis. The severity of the acute pancreatitis may increase obesity.

Management. PTRP treatment among children is a complex measure where the age of children, injuries, caused by the trauma and possible damages of other organs, SIRS, MODS have to be taken into consideration. They have to be placed in the intensive therapy unit, the tests of blood gases, serum electrolytes, creatinine, calcium, glucose intake and output, sometimes also central venous pressure monitoring have to be done. If the severity of the trauma requires a surgical treatment or it has made due to the doubts of the diagnosis, the tissues of pancreas have to be treated maximally carefully. Hemostasis of the pancreas tissues by coagulation has to be abstained; it has to be done by absorptive 5-0 monofilament stitches. Although the efficiency of octreotid application is still being discussed, we tend to apply it in the cases when we perform a direct impact on pancreases tissues. We consider that reduction of pancreatic secretion can decrease the risk of pancreatic fistula development or facilitate their faster closure.

A supportive care with a particular emphasis on the measures that prevent hypoxemia and an insure adequacy of fluid resuscitation is a critical component in the care of patients who have an acute pancreatitis. It is recommended that supplemental oxygen should be administered during the first 24 – 48 hours, especially if narcotic agents are used to control the pain. A supplemental oxygen should be continued until the clinician is fully satisfied that there is no further threat of hypoxemia. The key features in treating of the patients who have an acute pancreatitis are aggressive fluid replacement with crystalloid solution, preferably physiological saline solution (for its higher osmolarity when compared to Ringer Lactate), in aliquots of 20 mL/kg every 20 -30 minutes, with frequent subsequent evaluations, until the signs of dehydration are reversed at the physical exam and parameters such as diuresis (above 1 mL/kg/hour), the heart rate, a pulse and a capillary refill are normalized. Hypovolemia caused by the third space losses, vomiting, diaphoresis, and a greater vascular permeability compromises the microcirculation of the pancreas and is a major contributor to the development of the necrotizing pancreatitis. The second

important consequence of hypovolemia is an intestinal ischemia. There is an evidence that ischemia increases an intestinal permeability to bacteria, the products of bacteria, and endotoxins. The translocation of bacteria is an important cause of the secondary pancreatic infection. The translocation of bacterial products and endotoxins are also potent stimulants of the cytokine release and increases in a nitric oxide that contribute both to an ongoing pancreatic injury and also to the organ failure (particularly respiratory failure) (1). The parenteral analgesics should be started even in a mild pancreatitis because pain can be extreme. Opioids may be necessary; however, the use of maximum doses of medicaments should be avoided, due to the occurrence of nausea and vomiting, besides the contraction of the digestive sphincters. Tramadol can be used at 1 mg/kg/dose up to four times a day, diluted in a saline solution and in minimum infusion duration of 20 minutes. Nutrition is critically important for the patients who have pancreatitis. Nasogastric suction is only used for the patients who have ileus or a severe vomiting, for a symptomatic relief. Most published guidelines recommend jejunal feeding for 1 to 2 days after the developing of the severe pancreatitis, but there may be a role for slow, continuous nasogastric tube feedings. The total parenteral nutrition is generally not recommended unless a patient proves intolerant to enteral feeding. The studies have shown that some antibiotics like cefuroxime, ciprofloxacin and imipenem cross a blood pancreatic barrier and are found in high level in pancreas and within the necrotic pancreatic tissue (19; 23). It has been shown that in severe acute pancreatitis, i.v. antibiotic prophylactic therapy for 10 – 14 days can reduce the incidence of septic complications. Surgery is indicated if diagnosis is doubtful, if patient develops infected necrosis or in sterile necrotising pancreatitis; if patient deteriorates in spite of adequate medical management or if there is pancreatic abscess. An infected pancreatic necrosis needs debridement and a multiple drainage of lesser sac.

In children, only a small percentage of patients were reported to have severe complications, as opposed to adults. A multiorgan dysfunction or a pancreatic necrosis went on to develop for fewer than 6% of children. Early –onset complications primarily include multi-organ dysfunction or shock. Two major organs involved are the lungs and kidneys. An acute respiratory distress syndrome, pneumonia, or pulmonary effusion can develop for a patient. A renal failure has also been observed. Pseudo-cysts were formed for 10 % to 20 % most often associated with a traumatic etiology. Small pseudo-cysts not causing any symptoms can be managed conservatively. Most pseudo-cysts resolve over the course of six weeks. Pseudo-cysts that persist beyond six weeks, those larger than six centimetres, required some degree of surgical intervention. Mortality of acute pancreatitis for children ranged from 0% to 11 %. The reasons for a lower rate of death among children than among adults may include the virtual absence of an alcoholic pancreatitis, an etiology known to carry

a much higher rate of mortality. In addition, adults may have lost important protective mechanisms with age that children have retained. Discovering of these potential protective mechanisms may help to elucidate treatments for both adult and paediatric patients with pancreatitis (2).

CONCLUSIONS

The frequency of PTRP among children tends to increase. It is related to the increase of traumas.

The diagnostics and treatment of children PTRP is complicated. The age group of children under the age of two has to be distinguished as being very different from older children and adults. The early diagnosis and the proper management can contribute to better outcomes for patients and prevent immediate and late related complications.

Children PTRP becomes complicate more frequently than an acute pancreatitis of other etiology by formation of pseudo-cysts, which can resorb spontaneously, it can be successfully treated by a transcutaneous drainage controlled by US or CT or an endoscopic drain to the stomach.

Children who have a pancreas trauma and PTRP have to be concentrated in specialized clinics. A high quality care, a constant monitoring of experienced gastroenterologists and children surgeons have to be ensured in the children intensive therapy unit.

In order to improve the diagnostics and treatment of children PTRP and precisely adapt the adult algorithms for the children in corresponding age groups, it is necessary to have a prospective international cooperation of multicenters.

Conflict of interest: None

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