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THE ROLE OF ACUTE PANCREATITIS IN PEDIATRIC BURN PATIENTS

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Abstract

Few publications recognize acute pancreatitis (AP) as a complication after large burn injuries, consequently the incidence and outcome of post-burn AP in children is not well defined. The aim of this study was to determine the incidence, morbidity, and mortality relating to AP in a pediatric burn population; and to correlate clinical diagnosis with autopsy findings to determine the incidence of unrecognized pancreatitis. Records of 2,699 patients with acute burns were reviewed. AP was defined as abdominal pain and/or feeding intolerance in addition to a three-fold elevation of amylase and/or lipase. One-hundred twenty-seven burned children served as the control cohort. To assess the presence of autopsy confirmed AP in pediatric burn patients; we evaluated autopsy reports of 78 children who died from burns, looking for reported evidence of pancreatic inflammation, and fat/parenchymal necrosis. Our data show that AP in children has a low incidence post-burn. The study included 2,699 patients of which 13 were suffering AP (13/2699 = 0.05%). Mortality is significantly higher for the AP group vs. the control group, $p < 0.05$. Autopsy reports established 11 of 78 patients with evidence of pancreatitis, resulting in an incidence of 0.17 % for pancreatitis at autopsy. Although it has low incidence, AP is associated with increased mortality in severely burned pediatric patients, which underlines the importance of increased vigilance in the evaluation and treatment of pancreatitis in burned children.

Keywords

pancreatitis; pediatrics; burn

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1. INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory disorder of the pancreas caused by an intracellular activation of pancreatic digestive enzymes. Its presentation ranges from mild, self-limiting disease to a fulminant illness that may rapidly lead to multiple-organ failure and death. Clinically, it is characterized by steady, acute abdominal pain of varying severity, often radiating from the epigastrium to the back, together with nausea and vomiting [1]. Serum amylase activity is usually elevated, but it can be transient. Typically, amylase levels rise 2 to 12 hours after the onset of symptoms and then decline. In general, serum lipase is thought to be more sensitive and specific than serum amylase in the diagnosis of AP, it might remain elevated longer than amylase, and also it remains normal in some non-pancreatic conditions that increase serum amylase including macroamylasemia, parotitis, and some carcinomas [2]. Although elevated levels of amylase has been associated with burns, in the past AP was almost never diagnosed as a complication in burn patients. It presents with non-specific clinical manifestations and may be overlooked in severely burned patients due to burns on the abdomen, use of narcotics and sedations, and being on a ventilator [3,4]. Publications that recognize AP as a complication after large burn injuries in adults and children are limited. Wilson et al. [5] reported one case of a 5-year-old boy that 40 days after a 50% total burn surface area (TBSA) full thickness burn, presented signs and symptoms of AP, confirmed by an elevated serum lipase, elevated urine amylase, and an abdominal CT that reported a swollen pancreas. To our knowledge post-burn pancreatitis in children has not been further described. Therefore, the incidence and outcome of post-burn AP in children is essentially unknown.

The aim of the present study was to determine the incidence, morbidity and mortality relating to AP in a pediatric burn population. A secondary aim was to correlate clinical diagnosis with autopsy findings and determine the incidence of unrecognized pancreatitis in pediatric burn patients.

2. PATIENTS AND METHODS

A total of 2,699 patients with acute burn injuries were admitted to Shriners Hospitals for Children, Galveston, Texas, from 2000 to 2008. The records and laboratory data were reviewed. AP was defined as clinically documented abdominal pain and/or feeding intolerance in addition to at least a three-fold elevation of amylase and/or lipase, considering normal value for amylase 50–120 U/L and lipase 10–150 U/L. Amylase and lipase levels were checked as part of our routine measurements including nutritional and liver panels. It is routine of our hospital to check nutritional, renal, and pancreatic levels twice weekly. Even though pancreatitis is rare, we implemented this as a practice. We increased the frequency if the diagnosis of pancreatitis was made. Patients' age, gender, ethnicity, TBSA burn, third-degree burn, burn mechanism, and ICU length of stay (LOS) were documented. In order to determine the relevance of AP on morbidity and mortality, 127 burned children admitted to our institution in the same period were randomly selected from children matched by age and burn size in which AP did not develop, served as the control cohort.

To assess the presence of autopsy confirmed AP in pediatric burn patients; we evaluated autopsy reports of all children who died from burns in the same period (2000 to 2008) which were 78 children. We looked for reported gross and microscopic evidence of parenchymal inflammation, fat necrosis, and parenchymal necrosis in the pancreas.

The study was approved by the Institutional Review Board of the University of Texas Medical Branch and informed written consent was obtained from patients, parents, or legal guardians prior to enrollment.

2.1 Statistical Analysis

Unpaired Student t-tests and Chi-square test were used to compare differences in the variables, where appropriate. Data were expressed as percentages or means $\pm$ standard deviation, where appropriate. Log-rank analysis was used for Kaplan Meier survival curve. Significance was accepted at $P < 0.05$.

3. RESULTS

Our data show that pancreatitis in children has a low incidence post-burn. In the present study, we included 2,699 patients admitted with acute burn injuries, of which 13 were clinically diagnosed as suffering from AP ($13/2699 = 0.05\%$) with an average onset of 40 ± 39 days post-burn. Patient demographics such as age, gender distribution, TBSA burn, third-degree BSA, or burn mechanism were similar in the pancreatitis and control groups (Table 1). The average time from burn to hospital admission was 6 to 7 days for both groups. Although not statistically significant, the length of ICU stay was longer for patients with pancreatitis when compared with the control group (60 ± 57 and 29 ± 20 days, respectively). Multi-organ failure was diagnosed in 6 (46%) of the pancreatitis patients and in 28 (22%) of the controls, sepsis was present in 3 (27%) of the pancreatitis patients and in 22 (17%) of the controls. Statistical analysis resulted in no significant difference for both variables.

Survival was studied through a Kaplan-Meier survival curve with Log-rank analysis that showed mortality is significantly higher for the pancreatitis group when compared with the control group, $p < 0.05$ (Figure 1).

Evaluation of 78 autopsy reports from 2000 to 2008 established eleven patients with evidence of inflammation, fat necrosis, and parenchymal necrosis in the pancreas, resulting in an incidence of 0.17 % for pancreatitis at autopsy. The majority of patients who had pancreatitis at autopsy had clinical signs including abdominal pain, nausea/vomiting, and tube feeding intolerance, but there were some patients who did not, indicating that there were patients suffering from subclinical acute pancreatitis episodes.

4. DISCUSSION

AP is defined as an abrupt inflammation of the pancreas. Depending on its severity, it can have adverse complications and high mortality despite treatment. Treatment varies from conservative measures, such as NPO and IV fluid hydration, to admission to the ICU or even surgery (often requiring more than one intervention) to deal with complications of the disease process [1]. AP is highly variable in clinical presentation and severity, common initial manifestations which include abdominal pain, vomiting, and fever accompanied by increased pancreatic enzymes and radiologic signs of edema of the pancreas in ultrasound or computed tomography [6–8].

In general, it is difficult to estimate the true incidence of AP in the pediatric population because most of the literature consists of a small series of patients or case reports. In 1968, Kirksey et al. [9] reported 12 cases of pancreatitis in their series of 1,291 unselected burn patients (0.9%).

Our study in pediatric patients also demonstrates a low incidence of AP post-burn (0.05%). Ryan et al. [10], in a retrospective review of adult patients with large burns, reported that 40% of the patients developed hyperamylasemia or hyperlipasemia temporally associated with emerging infections, and in most cases related to symptoms of pancreatitis. In addition, inhalation injury, associated trauma, and escharotomy were identified as risk factors for pancreatitis. The difference of the incidence of AP between our study and this study could

be explained by the difference in the populations studied. While in adults, a high percentage of the AP is related to either alcohol intake or gallstones, in children the etiology is unknown in about 25 percent of the cases. Trauma, structural anomalies, multisystem disease, drugs and toxins, and viral infections account for most identified causes [11,12]. In our study, none of the patients had a recognizable cause for acute pancreatitis. However, this is a small sample size, and we consider that to obtain significant conclusions this should be studied in a larger database.

If a patient develops symptoms and signs of pancreatitis, our practice is to make the patient NPO and we place a nasoduodenal feeding tube beyond the second portion of duodenum to provide nutrition. We believe by doing so, we rest the pancreas by decreasing the activity, inflammation, and stress in the organ, while delivering adequate amounts of nutrition. If the patient's symptoms worsen or pancreatic enzymes rise, we will change to total parenteral nutrition (TPN). We believe that our patient population develops pancreatitis due to mesenteric ischemia and reperfusion, and that enteral feeding will increase reperfusion and thus microcirculation. We do not routinely administer TPN.

The analysis of autopsy reports during the same period of time demonstrated an incidence of 0.17% of AP; this confirms that some patients that had pathologic changes compatibles with AP were not diagnosed during the clinical course of the disease. This provides emphasis to the statement that AP could be an easily missed diagnosis in burn patients, maybe because of the variable clinical presentations such as being on a ventilator, having abdominal burn, and the use of sedation and analgesia and other drugs that can mask the symptoms. The study established that when acute pancreatitis is clinically diagnosed the risk of death is increased. We further believe that acute pancreatitis is at times missed as a diagnosis in pediatric burn patients; and it is important to increase vigilance in order to obtain an early diagnosis. We believe that feeding intolerance and clinical instability of the patient along with abdominal pain and nausea/vomiting could be a sign of pancreatitis and diagnostic test should be initiated.

The aim of this study was to determine morbidity and mortality when pancreatitis is diagnosed. We may have missed sub-clinical AP in the control cohort because they had no clinical signs. Therefore, we propose that it is important to diagnose AP to obtain adequate diagnosis and adequate treatment to improve poor outcome associated with AP. In our study, one patient that presented with marked elevation in amylase and lipase up to three days before death had an autopsy that did not report changes compatible with AP. Although these test are nonspecific and elevations of these enzymes have been reported in patients in whom pancreatitis cannot be identified at autopsy [3], presumably this can be due to a very small focus of pancreatic necrosis.

The pathogenesis of AP is not fully understood. There is experimental evidence that ischemic injury to the pancreas during episodes of hypotension may initiate pancreatitis as well as exacerbate it [13]. Also, clinical studies have shown the association of pancreatic ischemia with the development of AP [14,15]. Thermal injury is associated with poor peripheral and visceral perfusion during the early post-burn period. In an experimental animal model of smoke inhalation injury, Schenarts et al. [16] demonstrated that the blood flow decreased in the ileum, spleen, and pancreas. At the present time, acute intestinal necrotizing ischemia is a well-known complication in severe burned patients [17].

In conclusion, AP has not been clinically recognized as a complication in pediatric burns. Although it has low incidence, AP is associated with increased mortality in severely burned pediatric patients, which underlines the importance of increased vigilance in pre-mortem

evaluation and treatment of pancreatitis in burned children, particularly the determination of associated risk factors is warranted.

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Figure 1.
*Significant difference in pancreatitis vs. control, $p < 0.05$.

Table 1

Demographics for burn patients and controls.

Demographics	Control (n=127)	Pancreatitis (n=13)	p-value
Age	10 ± 4	12 ± 4	ns
Gender (M/F)	91 / 36	10 / 3	ns
TBSA	61 ± 13	66 ± 23	ns
Third BSA	47 ± 23	55 ± 31	ns
Flame %	84	77	ns
Electrical %	7	8	ns
Electrical/Flame %	9	15	ns
Length of ICU Stay (days)	29 ± 20	60 ± 57	ns
Pancreatitis Onset (days)		40 ± 30	ns
Survival %	87	69	*p<0.05

TBSA=total body surface area. Data presented as means ± s.d. or as percentages.

* Significant difference in survival in pancreatitis vs. control groups, p<0.05.