A Five Year Review of Pancreatitis among Filipino Children

Ma. Charina B. Dizon, Germana V. Gregorio and Elizabeth G. Martinez

Section of Pediatric Gastroenterology, Hepatology and Nutrition, College of Medicine and Philippine General Hospital, University of the Philippines Manila

ABSTRACT

Background. Pancreatitis is uncommon in childhood and there is presently no study among Filipino children.

Objective. To determine the clinical features and outcome of pancreatitis among Filipino children.

Method. Review of medical records of all patients diagnosed to have pancreatitis based on standard criteria from 2005 to 2009.

Results. A total of 23 children (mean age: 12 years; 13 male, 10 female) were included, 21 with acute and two with chronic pancreatitis. Twenty one (91%) presented with abdominal pain and two with jaundice. Nine had idiopathic pancreatitis. In 14 patients, the etiology was identified: bile duct obstruction (7), trauma (2), drugs (2), infection (2) and hypertriglyceridemia (1). Only four of 20 patients with ultrasound examination showed an enlarged pancreas. Complications were pseudocyst formation (6), pancreatic abscess (4), diabetes mellitus (2) and hypocalcemia (1). Of the 23 patients, eight required surgery: pancreatic debridement (4), choledochal cyst excision (2), cholecystectomy (1) and Whipple's procedure (1). All pseudocysts resolved spontaneously. One patient with pancreatic tumor declined surgery and another with pancreatitis due to choledochal cyst died of sepsis.

Conclusions. In our study, severe abdominal pain was the most frequent presenting symptom of childhood pancreatitis. Sixty percent had an identifiable cause for pancreatitis. A favorable outcome was observed.

Key Words: bile duct obstruction, severe abdominal pain, pancreatic pseudocyst

Introduction

Acute pancreatitis (AP) is an inflammation of the pancreas as a result of the sudden release of activated pancreatic enzymes leading to digestion of the pancreatic parenchyma and other regional tissues with associated rise in pancreatic enzyme levels in the blood.[1] Pancreatitis may either be acute or chronic. Two of the following three criteria based on the Atlanta classification are used in the diagnosis of acute pancreatitis: (1) acute abdominal pain and tenderness in the upper abdomen; (2) elevated levels of pancreatic enzymes in blood, urine, or ascitic fluid at least three times the upper limit of normal; and (3) presence of abnormal imaging findings in the pancreas that are associated with acute pancreatitis.[2] Chronic pancreatitis is considered if imaging studies demonstrate pancreatic calcifications, ductal stones or intraductal changes regardless of amylase and lipase levels.[3]

The clinical features and treatment depend on the severity of the disease. Pancreatitis can have severe complications and high mortality despite treatment. The disease is frequently reported in adults[4] but rarely in children and requires a high index of suspicion for diagnosis. In the Philippines, there are several published reports of pancreatitis in adults[5,6] but none in children. A survey of the cases at the Philippine General Hospital, a tertiary referral medical center, showed only a total of five cases from 2000 to 2004, but thereafter, an increase in frequency was observed.

The objective of this study is to determine the clinical features and outcome of pancreatitis among Filipino children.

Methods

A review of medical records was done on all children diagnosed to have pancreatitis by the Section of Pediatric Gastroenterology, Hepatology and Nutrition of the Philippine General Hospital between 2005 to 2009. A patient was diagnosed to have acute pancreatitis in the presence of two of the following three criteria:[2] (1) typical clinical manifestation (severe abdominal pain, anorexia, nausea and vomiting); (2) increased serum concentration of pancreatic enzymes 3–4 times above normal limits; and (3) sonographic or radiologic evidence of pancreatic inflammation. In the presence of pancreatic calcification, pancreatic duct changes or abnormalities on imaging studies, chronic pancreatitis is considered. Patients with multiple episodes or recurrent pancreatitis were only recorded for their initial presentation.

The patients' clinical features, treatment and outcome were recorded and analyzed. Work-up for the potential etiology of the pancreatitis was also noted in each case.

Corresponding author: Germana V. Gregorio, MD, PhD
Department of Pediatrics
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila, Philippines 1000
Telephone: +632 5269167
Email: germana1@hotmail.com

Infectious causes that were ruled out included tuberculosis, mumps and hepatitis B; these have been reported to cause pancreatitis. A detailed inquiry into the drugs the patient may have taken and that may have caused pancreatitis was also made. When possible, an initial ultrasound of the upper abdomen was done to look for sonographic evidence of pancreatitis. Computerized tomography of the abdomen and magnetic resonance cholangiopancreatography were requested only when indicated. A diagnosis of idiopathic pancreatitis was made only when identifiable causes of pancreatic inflammation had been excluded.

Results

A total of 23 patients were included of whom 21 had acute and two had chronic pancreatitis. Mean age at initial presentation was 12 (range two to 18) years with slightly more males (56%). The majority (61 %) were over 10 years old. Twenty one (91%) patients presented with severe diffuse abdominal pain, 19 with associated vomiting; while two—one with choledochal cyst and another with pancreatic tumor—had jaundice as an initial presentation. Three of the 21 patients with severe abdominal pain were initially diagnosed to have ruptured acute appendicitis and underwent an exploratory laparotomy. The diagnosis of pancreatitis was confirmed based on elevated serum amylase and lipase levels and a CT scan of the abdomen showing an inflamed pancreas. Other signs and symptoms according to the age group are presented in Table 1.

Table 1. Presenting signs and symptoms of 23 children diagnosed with pancreatitis according to age group

Sign/Symptom	Age (years)			n (%)
	< 5	5-10	11-18	
Abdominal pain	1	7	13	21(91)
Vomiting	2	6	11	19 (83)
Anorexia	0	3	5	8 (35)
Weight loss	0	0	5	5 (23)
Nausea	0	1	3	4 (18)
Jaundice	1	0	1	2 (9)
Diarrhea	0	1	0	1 (4)
Fever	0	1	0	1 (4)

The mean initial serum amylase and lipase levels were 3,516 IU/L (range: 108 to 54,774, nv: 27–131) and 1708 (range: 146 to 28,523, nv:10–220), respectively.

Thirty nine percent (9 cases) of our patients had no recognized cause for pancreatitis and were considered idiopathic. Biliary obstruction (7 cases, 30%) was commonly seen causing pancreatitis that included choledochal cyst (3), stone (2) and pancreatic tumor (2). Two cases each of traumatic, drug-, and infection-induced pancreatitis were seen. The traumatic pancreatitis cases were due to blunt bicycle and motorcycle injuries; the possible drug-induced cases were associated with use of amphetamine and L-asparaginase (for treatment of acute lymphoblastic leukemia); the infections were associated with disseminated tuberculosis. One 16-year-old obese (BMI=35) female had hypertriglyceridemia as a risk factor for necrotizing pancreatitis. She subsequently developed insulin-dependent diabetes mellitus.

Ultrasound as an imaging study was done in all but the three cases whose initial assessment was acute abdomen; immediate surgery was done in these cases. Of the 20 in whom ultrasound was performed, normal findings of the pancreas were noted in six, and pancreatic enlargement and inflammation of the peripancreatic fat in four. The pancreas could not be visualized in two patients. Sonography also revealed the presence of choledochal cyst (3), pseudocyst (2) pancreatic head mass (2) and gallstones (1). Twelve patients had computerized tomography of the abdomen and six had magnetic resonance cholangiopancreatography. Of the patients who had further imaging studies, two were diagnosed to have chronic pancreatitis based on the presence of pancreatic duct stones.

The most common complication was formation of pseudocyst observed in six patients (Figure 1) with one having both a pancreatic and mediastinal pseudocyst. All resolved spontaneously. Other complications observed were pancreatic abscess (4), development of malnutrition (2), diabetes mellitus (2), hypocalcemia (1) and fungal infection (1).

All patients were managed conservatively with bed rest, complete restriction of oral intake and gastric decompression until abdominal pain resolved, maintenance of fluid and electrolyte balance and total parenteral nutrition as needed. Antibiotic treatment was given only for specific indications. In addition, eight patients had surgical interventions for the following: debridement of necrotizing pancreatitis (4), choledochal cyst excision (2), cholecystectomy for cholelithiasis (1) and Whipple's procedure for a pancreatic head mass (1). One patient developed a pancreatic fistula after pancreatic necrosectomy. The fistula spontaneously closed. Endoscopic retrograde cholangiopancreatography (ERCP) was only utilized in one patient as MRCP was suggestive of a possible pancreatic divisum (Figure 2). However, the ERCP showed a filling defect, possibly stones at the pancreatic duct, thus a stent was inserted (Figure 3). He was eventually asymptomatic after two weeks.

Twenty one of the 23 patients were discharged improved. One patient with pancreatic tumor went home against medical advice and another who underwent external drainage of choledochal cyst died of sepsis. A nine-year-old boy at the time of initial presentation and in whom an infectious, autoimmune and structural cause of the pancreatitis could not be identified developed three further episodes in the last three years. Three previous MRCPs done during the episode of pancreatitis showed no pancreatic or bile duct lesions. This patient was considered as having an acute relapsing pancreatitis.

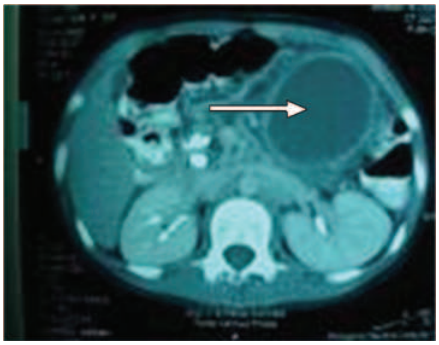

Figure 1. CT scan plate of a 12-year-old female who presented with chronic abdominal pain and weight loss. This plate shows a single pseudocyst which eventually resolved. An MRCP was eventually done and showed pancreatic stones.

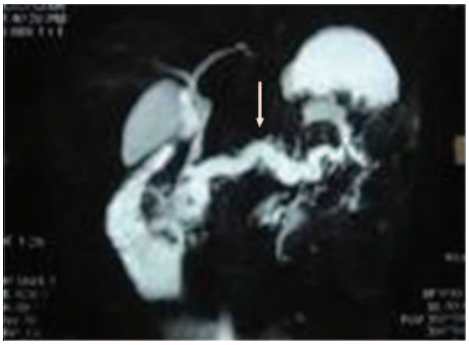

Figure 2. MRCP plate of a 13-year-old male who presented with recurrent abdominal pain showing dilated duct and an apparent filling defect.

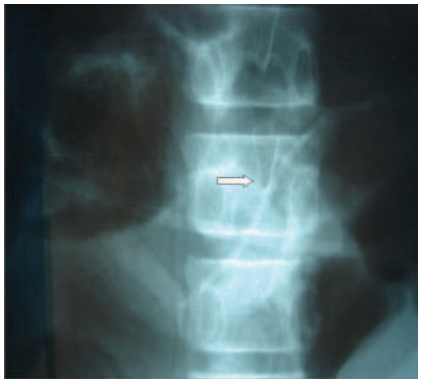

Figure 3. ERCP plate showing a stent inserted on main pancreatic duct

Discussion

The present study reports for the first time a series of Filipino children afflicted with pancreatitis, a disease commonly reported only in adults.[7,8] Over a five-year period, we showed an increased number of children referred with the disease to our Section from five to 23 cases from 2000 to 2004 and 2005 to 2009. This may mean a true increase or an improved awareness of the disease. Five of these patients were confined in other institutions in Metro Manila but were primarily referred and managed by the consultants of the Section; thus, we could not estimate the incidence of the disease in our center.

In agreement with Werlin's study[9] conducted at the Children's Hospital of Wisconsin, Milwaukee, severe abdominal pain was the most common symptom observed in children with pancreatitis but was seen at a higher frequency (91%) in our series as compared with their study (68%). The study was also a chart review of pancreatitis in children over a six-year period but in a larger number of patients. The main difference between that study and the present study is that biliary tract obstruction was the most common identified cause in our patients whereas systemic disorders were more common in Werlin's study (45/180, 25%). These disorders included hemolytic uremic syndrome, connective tissue disorders, malignancy and transplantation of the bone marrow and other solid organs. Their patients did not initially present with symptoms related to pancreatitis but instead with symptoms related to the primary diagnoses. Other factors such as simultaneous use of several drugs and surgical procedures may have complicated their clinical course.

Ultrasound of the abdomen for screening was done in the majority of our patients but only four of the 20 cases were noted to have pancreatic enlargement or an inflamed pancreas. Our experience is in agreement with previous reports[10] that indicate that ultrasound has low sensitivity in the diagnosis of pancreatitis, although it is a useful tool in supporting the diagnosis and for monitoring patients for complications like pseudocyst formation. Further imaging studies like computerized tomography of the abdomen and magnetic resonance cholangiopancreatography were done only in our patients when indicated. We performed CT scan in 12 of our patients and all showed evidence of pancreatitis and other associated conditions. MRCP was useful in demonstrating the presence of pancreatic stones in two cases. These additional radiologic exams were requested to further define the biliary obstruction, the extent of pancreatic involvement and the complications of pancreatitis, particularly pseudocyst and abscess.

Similar to the report by Nydegger from Australia,[11] most of our patients had idiopathic pancreatitis. It might well be that advanced molecular or genetic studies will identify the etiology of pancreatitis in these patients. The effect of yet unknown environmental toxins may also trigger pancreatitis in a genetically predisposed individual. Of interest is the presence of disseminated tuberculosis that caused pancreatitis in two of our patients. One of the two had associated pleural effusion and was on anti-tuberculosis

treatment for one month at the time of diagnosis; thus, drug-induced pancreatitis due to intake of isoniazid and rifampicin[12] could not be excluded. This patient developed mediastinal and pancreatic pseudocysts; these resolved spontaneously. The other patient was diagnosed with disseminated tuberculosis on the basis of pulmonary findings and acid fast bacilli positive vaginal discharge was not being treated with anti-TB drugs at the time of diagnosis of pancreatitis. The tubercular involvement of the pancreas may have occurred as a result of direct extension, lymphohematogenous dissemination, reactivation of a previous abdominal focus or immune reaction to generalized tuberculosis.[13,14]

In our series, the most common complication observed was pseudocyst formation (26%), in agreement with a previous report done in Taiwan and India which reported frequencies of 23 and 41%, respectively.[15,16] Pseudocyst is a localized collection of peripancreatic fluid surrounded by non-epithelialized fibrous or granulation tissue. Pseudocysts arise secondary to rupture or obstruction of pancreatic ducts. Fortunately, none of our six patients with pseudocyst required surgical intervention. The pseudocysts ranged in size from 4 to 12 cm^3. All had spontaneous resolution from one to three months after initial detection of pseudocysts. It has been suggested that pseudocysts related to non-traumatic pancreatitis are more likely to require surgical interventions than those secondary to trauma.[17] We had four cases of non-traumatic and two of traumatic pancreatic pseudocyst; the small number of patients in our study does not allow us to make any definite conclusion.

We limit the use of total parenteral nutrition while patients are on nothing per orem. Once the abdominal pain abates, it is our practice to start patients on enteral feeding, usually after 72 hours from admission. The initial feeding consists of a low fat diet (1 gm/kg/day) that is gradually increased as tolerated by the patient. It has been shown that enteral compared with parenteral nutrition decreases the risk of infectious complications and mortality among patients with severe acute pancreatitis.[18] However, the exact mechanism of the favorable effect of enteral nutrition remains unclear. It has been postulated that enteral nutrition enhances gut barrier function, preventing the endotoxemia and subsequent bacterial translocation that plays a pivotal role in the development of infectious complications during severe acute pancreatitis.[19,20,21]

Conclusion

In this study, severe abdominal pain was the most common presenting symptom of acute or chronic pancreatitis. The diagnosis should be considered in an acutely ill child with abdominal complaints on the basis of clinical, biochemical and radiologic features. Sixty percent of patients had an identifiable cause for the pancreatitis. A favorable outcome was observed. Early diagnosis, close monitoring and timely intervention are mandatory to decrease the morbidity and mortality.

References

1. Lopez MJ. The changing incidence of acute pancreatitis in children: a single-institution perspective. J Pediatr. 2002;140(5):622–4.
2. Bollen TL, van Santvoort HC, Besselink MG, et al. The Atlanta Classification of acute pancreatitis revisited. Br J Surg. 2008:95(1);6–21.
3. Koizumi M, Takada T, Kawarada Y, et al. JPN Guidelines for the management of acute pancreatitis: diagnostic criteria for acute pancreatitis. J Hepatobiliary Pancreat Surg. 2006;13(1):25–32.
4. Gislason H, Horn A, Hoem D, et al. Acute pancreatitis in Bergen, Norway: a study on incidence, etiology and severity. Scand J Surg. 2004;93(1):29–33.
5. Leopoldo ZE, de Castro CM, Gutierrez MT. Acute pancreatitis among Filipinos. Fil Fam Phy. 1979;17(2):1–13.
6. Chua JD. A study on the clinico-epidemiological correlates of acute pancreatitis in the Philippine General Hospital from 1982–1986. Acta Med Philipp. 1992;28(2):112–25.
7. Goldacre MJ, Roberts SE. Hospital admission for acute pancreatitis in an English population, 1963–98: database study of incidence and mortality. Brit Med J. 2004;328(7454):1466–9.
8. Eland IA, Sturkenboom MJ, Wilson JH, et al. Incidence and mortality of acute pancreatitis between 1985 and 1995. Scand J Gastroenterol. 2000;35(10):1110–6.
9. Werlin SL, Kugathasan S, Frautschy BC. Pancreatitis in children. J Pediatr Gastroenterol Nutr. 2003;37(5):591–5.
10. Silverstein W, Isikoff MB, Hill MC, et al. Diagnostic imaging of acute pancreatitis: prospective study using CT and sonography. Am J Roentgenol. 1981;137(3):497–502.
11. Nydegger A, Heine RG, Ranuh R, et al. Changing incidence of acute pancreatitis:10-year experience at the Royal Chilrden's Hospital, Melbourne. J Gastroenterol Hepatol. 2007:22(8):1313–6.
12. Badalov N, Baradarian R, Iswara K, et al. Drug-induced acute pancreatitis: an evidence-based review. Clin Gastroenterol Hepatol. 2007;5(6):648–61.
13. Avasthi R, Chaudhary SC, Jain P. Disseminated tuberculosis manifesting as chronic pancreatitis. Indian J Tuberc. 2008 Oct;55(4):214–6.
14. Pramesh CS, Heroor AA, Gupta SG, et al. Pancreatic tuberculosis: an elusive diagnosis. HPB. 2003;5(1):43–5.
15. Yeung CY, Lee HC, Huang FY, et al. Pancreatitis in children--experience with 43 cases. Eur J Pediatr. 1996;155(6):458–63.
16. Das S, Arora NK, Gupta DK, et al. Pancreatic diseases in children in a north Indian referral hospital. Indian Pediatr. 2004;41(7):704–11.
17. Teh SH, Pham TH, Lee A, et al. Pancreatic pseudocyst in children: the impact of management strategies on outcome. J Pediatr Surg. 2006;41(11):1889–93.
18. Petrov MS, van Santvoort HC, Besselink MG, et al. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis of randomized trials. Arch Surg. 2008;143(11):1111–7.
19. Ammori BJ, Leeder PC, King RF, et al. Early increase in intestinal permeability in patients with severe acute pancreatitis: correlation with endotoxemia, organ failure, and mortality. J Gastrointest Surg. 1999;3(3):252–62.
20. Nagpal K, Minocha VR, Agrawal V, et al. Evaluation of intestinal mucosal permeability function in patients with acute pancreatitis. Am J Surg. 2006;192(1):24–8.
21. Windsor JA, Fearon KC, Ross JA, et al. The role of serum endotoxin and antiendotoxin core antibody levels in predicting the development of multiple organ failure in acute pancreatitis. Brit J Surg. 1993;80(8):1042–6.