Keep Acute Pancreatitis in Mind: A Disease with an Insidious Presentation in Childhood: Review

Çocukluk Çağının Sinsi Bir Hastalığı: Akut Pankreatiti Akılda Bulundurun

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ABSTRACT The aim of the study is to perform a literature review of acute pancreatitis in childhood in Turkey in terms of how they are diagnosed, treated and survived. By using Medline/Pubmed and Turkish Medical databases, a computed review was performed. Thirty two children with acute pancreatitis reported by Turkish authors were analyzed. The median age of 17 boys and 14 girls diagnosed as acute pancreatitis was 7 years. The most common etiologic factors were drug or toxin intake and viral infections. The most frequent symptoms were abdominal pain, nause and/or vomiting. Diagnosis mainly based on elevated serum amylase. Ultrasound was used in 18 of the patients with a moderate predictive value. Many of patients were treated conservatively whereas only 15.6% of patients were operated. Fatal outcome was 9.4% due to concomitant metabolic disorders, infections or multiple organ failure. Acute pancreatitis proceeds with nonspecific symptoms which represent diagnostic challenges. That is why the misdiagnosis is generally unavoidable. As the disease carries significant morbidity and mortality, clinicians should be more suspicious while evaluating children with nonspesific abdominal symptoms.

Key Words: Pancreatitis; child; disease management

ÖZET Bu çalışmanın amacı, Türkiye'de, çocukluk çağında akut pankreatit tanısı almış olguları, nasıl tanı aldıkları, tedavi edildikleri ve hastalıklarının seyirleri açısından gözden geçirmektir. Medline/Pubmed ve Türk Tıp Dizini veri tabanları kullanılarak, belirlenen konu başlıkları taranmıştır. Türk hekimleri tarafından rapor edilen 32 akut pankreatitli hastaya ulaşılmış ve verileri gözden geçirilmiştir. Akut pankreatit tanısı almış 17 erkek ve 14 kız çocuğunun ortanca yaşı 7'dir. Hastalığa en sık sebep olan etiyolojik faktörler ilaç ve toksin alımı ve viral enfeksiyonlardır. En sık görülen belirtiler karın ağrısı, bulantı ve/veya kusmadır. Tanı esas olarak serum amilaz düzeylerine bakılarak konulmuştur. Ultrason, 18 hastada kullanılmış ve hastalığın tanısında orta derecede yardımcı olarak bulunmuştur. Hastaların %15.6'sı ameliyat edilirken, büyük çoğunluğu destek tedavisi ile takip edilmiştir. %9.4 oranında hasta, eşlik eden metabolik hastalıklara, enfeksiyonlara veya çoklu organ yetmezliğine bağlı olarak kaybedilmiştir. Akut pankreatit, nonspesifik belirtilerle seyreden ve tanısal güçlüklere yol açabilen bir hastalıktır. Bu nedenledir ki yanlış tanılandırılması kaçınılmazdır. Hastalık belirgin morbidite ve mortaliteye sahip olduğu için, klinisyenlerin nonspesifik karın belirtileri olan çocukları değerlendirirken daha çok şüpheci olmaları gerekmektedir.

Anahtar Kelimeler: Pankreatit; çocuk; tedavi yaklaşımları

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Acute pancreatitis (AP) is the acute inflammation of the pancreas causing a variable clinical severity. Although the disease is uncommon in pediatric age group, it is important in the differential diagnosis of acute or reccurent abdominal pain with an unknown etiology.

In contrast to adults, AP in childhood has a wide spectrum of etiological factors like infections, trauma, metabolic diseases, congenital anomalies, drugs and toxins. It is usually presented with sudden onset of epigastric pain radiating to back, nausea, vomiting and anorexia. The most frequent physical examination finding is tenderness at the epigastrium with decreased bowel sounds. An elevated serum amylase (especially isoamylase isoenzyme), urine amylase, amylase creatinine clearance ratio are good (but not the best) indicators for pancreatitis. Abdominal ultrasound (US) and computed tomography (CT) scans are the imaging methods of choice in delineating the pancreas. The treatment is largely supportive. Avoiding surgery is essential, unless any specific circumstances for surgery occur.[1-4]

Because of the wide spectrum of etiological factors for pancreatitis, we believe that children are more prone to the disease. As it has nonspesific symptoms and signs, it can be overlooked by the clinicians.

The aim of this study is to analyze the pediatric cases of AP in the Turkish population in terms of how they are diagnosed, treated and survived.

MATERIAL AND METHODS

A computed literature review for AP in childhod was performed. "Pancreatitis", "acute necrotizing pancreatitis" and "pancreatic pseudocyst" were selected as medical heading subject (MeSH) terms and Medline/Pubmed search was done with these terms. Then the search was limited with language (English) and age (all children 0-18 years) and the 2896 pubmed articles in English medical literature were reviewed. Acute pancreatitis in the pediatric age group reported by the Turkish authors was selected. A similar search was made through Turkish Medical Data Base and 87 articles in Turkish medical literature and their references were reviewed. Acute pancreatitis in the pediatric age group was selected. The achieved 24 articles and 32 patients were analyzed (Table 1).

RESULTS

The reviewed literature revealed limited number of published articles well-matched with the requested properties. Most of the articles were case reports (27/32). There were one review of acute pancreatitis including 5 "acute pancreatitis" cases and one review of pancreas pseudocysts including 1 "acute pancreatitis" case.[5,6] Three review articles investigating the complication of either a disease (mumps) or a drug usage (L-asparaginase) were found to represent "acute pancreatitis" cases.[7-9]

The findings of thirty two patients were revised. The mean age at the diagnosis was 7 years (ranging fom 6 months to 18 years). Male to female ratio was 1.2:1 (17 boys and 14 girls; the gender of one case was not mentioned). The etiologic factors of the patients included drugs and toxins in 28.1% (9/32), viral infections in 21.8% (7/32), idiopathic in 12.5% (4/32), systemic disorders in 12.5% (4/32), metabolic disorders in 9.4% (3/32), parasitic infestations in 9.4% (3/32), sepsis in 3.1% (1/32) and concomitant anatomic malformation in 3.1% (1/33). The most common symptoms were abdominal pain (84.4%-27/32), vomiting (46.9%-15/32) and nausea (21.9%-7/32). Two patients admitted with seizures and coma (6.2%) and 2 patients with anorexia (6.2%) accompanying the abdominal pain and vomiting. Diagnosis was mainly based on elevated serum amylase level (90.6%) and serum lipase level (21.9%). High urine amylase level in 5 patients (15.6%), high amylase creatinine clearance level in 3 patients (9.4%), and high periton fluid amylase level in 2 patients (6.2%) were found during the evaluation. US scan was used for diagnosis of 18 patients in which 14 of them revealed pathologic findings like pancreatic inflammation, edema, peripancreatic exudation, or pseudocyst formation. Computed tomography scan was performed in 9 patients and 7 patients with pancreatic inflammation or pseudocyst formation were diagnosed. Three patients with acute abdominal findings underwent laparotomy. Two of them were diagnosed AP perioperatively and one with no perioperative findings was diagnosed AP postoperatively with laboratory and radiological findings. One child was operated with the suspicion of a pancreatic tumour and diagnosed postoperatively. One child was diagnosed at autopsy. Conservative treatment was the choice of therapy in most of the

TABLE 1: Children with acute pancreatitis reported by Turkish authors.

Age	Gender	Additional Disorder	Etiology	Diagnosis	Prognosis	
Hicsönmez[5]	4	M	-	Idiopathic	Perioperatively	Well
	4	M	-	Idiopathic	CF- LF	Operated for PP; well
	7	F	-	Ascariasis?	CF- LF	Well
	7	F	-	Mumps	CF- LF	Well
	9	M	-	Sepsis	CF- LF	Died because of MOF
Karaguzel[6]	5	F	-	Idiopathic	CF- LF- RF	Operated for PP and pancreatic fistula; well
Say[7]	*	M:F= 3:2	-	Mumps	CF-LF	Well
			-	Mumps	CF-LF	Well
			-	Mumps	CF-LF	Well
			-	Mumps	CF-LF	Well
			-	Mumps	CF-LF	Well
Cetin[8]	9	M	ALL	L-asparaginase	LF	Well
Bay[9]	NM	M	ALL	L-asparaginase	NM	Well
Kalkanoglu[10]	16	M	Tyrosinemia type I	Porphyrin metabolite accumulation	CF- LF	Well
Coskun[11]	2	F	Glutaric acidemia type II	Organic acidemia	At autopsy	Died Autopsy: Hemorrhagic AP
Kuskaya[12]	14	F	-	Cephtriaxone and biliary pseudolithiasis	CF- LF- RF	Well
Fidan[13]	16	F	-	Malathion	LF	Well
Saka[14]	16	M	-	L-arginin	CF- LF	Well
Kuyucu[15]	2	M	-	Meglumine antimoiate	CF- LF- RF	Well
Ertekin[16]	5	F	-	Hepatitis A	CF- LF- RF	Well
Bulbul[17]	13	F	Partial lipodystrophy, MPGN	-	CF- LF- RF	Died because of infection
Ozmen[18]	18	F	-	Hydatid cyst	CF- LF- RF	Reoperated 11 times; well
Soyer[19]	3	F	HSP	-	CF- LF-RF	Well
Malbora[20]	5	M	ALL (B cell)	-	CF- LF- RF	Well
Ozel [21]	8	F	Duodenal duplication cyst	-	CF- LF- RF	Operated for duplication cyst; well
Harputluoglu[22]	17	F	-	Organophosphate intoxication	CF- LF- RF	Well
Karabulut[23]	5	M	ALL	L-asparaginase	CF- LF- RF	Well
Inalhan[24]	6	M	-	Idiopathic reccurent	CF- LF- RF	Well
Zeytunlu[25]	17	NM	-	Hydatid cyst	CF- LF- RF	Operated for hydatid cyst; well
Cay[26]	14	M	-	Eosinophilic pancreatitis	Postoperatively	Well
Onal[27]	6m	M	Type I hyperlipoproteinemia	Lipid deposition	RF	Well
Ozaydın[28]	11	M	Epilepsy	Valproic acid	Postoperatively with LF-RF	Well

MPGN: Membranoproliferative glomerulonephritis, ALL: Acute lymphoblastic leukemia, HSP: Henoch-Schonlein Purpura CF: Clinical findings, LF: Laboratory findings, RF: Radiological findings, PP: Pancreatic pseudocyst, MOF: Multiple organ failure, AP: Acute pancreatitis, NM: Not mentioned in the text,
*: 1 child between 1-4 years, 2 children between 5-6 years, 2 children between 7-9

patients (84.4%-27/32) including bowel rest, iv fluids, antibiotic usage, and treatment for etiologic factors like discontinuing the medications, using antidotes for the taken drugs. The 2 of the remaining 5 patients, which were diagnosed perioperatively, has undergone necrosectomy. One was diagnosed as eosinophilic pancreatitis after surgery and one was diagnosed as acute pancreatitis after a ne-

gative laparotomy whereas one was operated correction of an anatomic malformation. Four patients from the conservatively treated group developed pancreatic pseudocyst (PP) and 2 of them have undergone surgery. External drainage and cystogastrostomy were performed for these children. Three of the patients were died because of the primary metabolic disorder, infection or multiple organ failure while having therapy for the primary problem. The survived 29 patients did well after their treatment for pancreatitis. Only two patients suffering from abdominal pain in the long term follow up suggested reccurency with a ratio of 6.2% for the whole series.

DISCUSSION

AP is supposed to be the most common pancreatic disorder in the pediatric age group. There is a limited data about the disease in the literature and it is difficult even to estimate the prevalance and the incidence of pancreatitis in the childhood.[1]

There is a wide spectrum of etiological factors related with the disease. Benifla et al, in a literature data analysis of 589 children with pancreatitis, reported the most common causes as idiopathic pancreatitis (23%), trauma (22%), structural anomalies (15%), multisystem disease (14%), drug and toxins (12%), viral infections (10%), hereditary (2%) and metabolic disorders (2%).[3] Werlin et al, in a series of 214 pancreatitis attacks of 180 children, reported that the vast majority of the etiological factors were trauma, biliary tract disease, multisystem disease, drug intake and idiopathic.[4] In this series, the most common causes of AP were drug and toxin intake and viral infections. The high ratio of drug and toxin related pancreatitis in this series, as not befitting the literature, was the reason of single case reports composing the vast majority of this review. Trauma, however is one of the most common causes for the disease, was not seen as a single cause of pancreatitis in this series. Karaguzel et al. reported 10 children with PP.[6] Pseudocsyts were seen as a result of a blunt trauma in 8 children, AP in 1 child and unknown etiology in 1 child. The 60% of this group of children were told to have high serum and urine amylase levels. Only the patient having PP as a reason of acute pancreatitis was included to this series. If five of the children having PP with high levels of serum and urine amylase levels were accepted as PP related to posttraumatic pancreatitis and added to this series, the ratio of trauma as an etiological factor would be as high as 13.5% and would be half amount of drugs and toxins' ratio.

Abdominal pain, nause and/or vomiting were the most common clinical symptoms of this series. The pain however emphasized variable, is the most common symptom in large series of AP.[3,4] As the typical one radiating to back cannot be differed by children, it is often told as a tummy ache. Vomiting, being more visible than nause is in fact most realistic symptom of the disease.

Elevated serum amylase with an estimated sensitivity of 85% and specifity of 40% and elevated urine amylase with an estimated sensitivity of 93% and specifity of 75% are used in the diagnosis of the disease.[1] In this series the diagnosis were mainly based on elevated serum amylase. Elevated serum lipase, however having higher sensitivity and spesicifity, was used only in 6 patients for diagnosis. Plasma immunoreactive cationic trypsin, pancreastic elastase I and phospholipase A_2 are the diagnostic tests with a higher sensitivity and corralates with the severity of the disease. But these tests are not used routinely in many of the clinics.[1,2]

US is the most frequently used and the least invasive radiological technique to determine the changes in pancreatic tissue in terms of size, shape and echogenity. Eighteen patients in this series have had US scan in which 77.7% revealed positive signs for AP. CT is often used for managing not only the pancreas but also the adjacent tissues and the complications related to AP. It was performed only in 9 patients with a predictive value of 77.7%. Endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiopancreatography or percutaneous cholangiogram, however not used routinely, can be performed to rule out anatomic malformations and biliary strictures.[1,2]

Benifla et al reported that 16% of the patients in their series were diagnosed perioperatively.[3] In this series 3 patients with acute abdomen findings were undergone laparotomy in which 2 of them diagnosed during laparotomy and necrosectomy were performed.

Conservative treatment was the choice of therapy in most of the patients (84.4%). In this series most of the patients were basically treated for AP whereas the rest, for their primary metabolic and systemic problems. Surgical intervention was needed in 4 of these patients as they have developed PP however 2 of them have undergone surgery. The fatal outcome of this series was 3.1%. This was lower than the reports of Benifla et al.[3] The rate for reccurency was reported in 9% of the children by the same authors, being more common with idiopathic pancreatitis and congenital anomalies. In the long term follow up, the reccurence was seen in two patients with idiopathic pancreatitis with a reccurent rate of 6.2% for this series.

The literature review resulted limited articles about AP by the Turkish authors. It raised the question about the disease being overlooked in Turkey. The disease however carries significant morbidity and mortality, diagnosis at its early steps avoids the later trouble.

Acute pancreatitis is an abdominal catastrophe representing diagnostic challenges for all age groups. Even though the disease is considered to occur less frequent in childhood, it probably is more common than considered. Because of the variable etiological factors and nonspesific clinical features of AP, misdiagnosis is generally unavoidable. We recommend the clinicians to keep in mind the high possibility of misdiagnosis and to be more suspicious while evaluating the children with nonspecific abdominal symptoms.

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