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Case Report

GESDAV

Acute acalculous cholecystitis due to *Salmonella typhi*: A case of a 12-year-old child

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ABSTRACT

Acute acalculous cholecystitis is a very rare complication of typhoid fever, and may be due to multidrug resistant and virulent forms of *Salmonella*. It is also very uncommonly found in children. A case of a 12-year-old child presenting with history of prolonged fever found to have typhoidal acalculous cholecystitis based on ultrasonographical findings is described in this report. Patient had cholecystectomy, received intravenous antibiotics and made full recovery.

KEY WORDS: Acalculous, cholecystitis, typhoid

INTRODUCTION

Acalculous cholecystitis is an acute necro-inflammatory disease of the gallbladder with a multifactorial pathogenesis. It accounts for approximately 10% of all cases of acute cholecystitis and is associated with a high morbidity and mortality [1-3]. Clinically, acute acalcular cholecystitis (AAC) is difficult to diagnose because the findings of right upper-quadrant pain, fever, leukocytosis, and abnormal liver tests are not specific. Though AAC is associated with a high mortality, early diagnosis and intervention can change this. Early diagnosis is the crux of debate surrounding AAC, and it usually rests with imaging modalities [2,3].

Salmonellosis can occur in several different forms: Gastroenteritis (the most common syndrome), enteric fever (typhoid fever and paratyphoid fever), bacteremia, chronic carrier state, and localized infections. Acute cholecystitis associated with *Salmonella typhi* is not rare in the presence of gallbladder stones. Nevertheless, its occurrence without cholelithiasis is very rare and is most commonly reported with *Salmonella* serotypes other than *S. typhi* [2,3,6].

CASE REPORT

A 12-year-old female patient, previously healthy, presented to our hospital with history of high grade fever of 4 days duration, poorly responding to antipyretics, occurring over the whole day, associated with fatigue, bone, and back pain. Patient had been admitted to an outside hospital one month prior to presentation for fever of 4 days duration, abdominal pain and diarrhea, given oral cefexime (3rd generation cephalosporin) for 2 days then admitted where she received a 10 day course of meropenem. Patient was discharged, after being a febrile for 2 days, on cefexime for 7 more days. Physical examination upon presentation was not significant except for being febrile and ill-looking. Laboratory results disclosed a white cell count of 4300 × 1000/μL with 56% neutrophils and 36% lymphocytes, hemoglobin of 11 mg/dl, and normal platelets. C-reactive protein (CRP) in serum was 14.8 mg/dl (normal ≤0.3 mg/dl) and erythrocyte sedimentation rate (ESR) was 66 mmol/h (normal 0-20 mm/h). The biochemical studies including liver and renal tests electrolyte and cholesterol panels, amylase and lipase, were normal [Table 1].

An abdominal X-ray was normal and abdominal sonography done on the same day of presentation was also normal. Serology for *S. typhi* H and O, *Brucella*, and *Rikettsia* were negative, as were stool and blood cultures.

The patient was treated with intravenous (IV) fluids, analgesics, and antipyretics. She became afebrile on the 4th day; and was discharged home on day 6 of hospitalization after being

Table 1: Biochemical studies of the patient upon presentation

SGPT	34
Total bilirubin	0.9
BUN	6
Creatinine	0.4
Amylase	46
Lipase	76
Sodium	138
Potassium	3.7
Chloride	99
Bicarbonate	25
Cholesterol	116
Triglycerides	114

SGPT: Serum glutamic-pyruvic transaminase, BUN: Blood urea nitrogen

afebrile and symptom free for around 30 h with diagnosis of viral illness. After 12 h of discharge, patient returned back to the Emergency Department due to epigastric and right hypochondrial abdominal pain, nausea, and high grade fever. She was conscious, febrile with temperature of 39°C, heart rate of 130 bpm, but no hypotension or tachypnea. On physical examination, patient had a positive Murphy's sign, severe paraumbilical and right upper quadrant tenderness with guarding upon superficial and deep palpation. There was no hepatomegaly or splenomegaly and no jaundice. She had good peripheral pulses. The laboratory tests showed mild normocytic-normochromic anemia (hemoglobin was 10 mg/dl) with 11,600 white blood cells, 72% were neutrophils. The biochemical tests were normal except for a persistent high CRP and ESR. A new abdominal sonography disclosed sludge in the gallbladder with thickened wall, no stones, with mild pericholecystic fluid. Pelvis sonography showed a prominent appendix with a rim of adjacent free fluid suggestive of early appendicitis.

The surgery and pediatrics team, after discussion, decided to start with conservative management of a suspected cholecystitis and patient was started on IV antibiotics (ceftriaxone and metronidazole). Twelve hours later, patient's abdominal pain increased in severity, she was continuously febrile, ill-looking and hypoactive so diagnostic and therapeutic laparoscopy was decided for fear of perforation and sepsis. On physical examination, patient had positive Murphy's sign and her abdomen became guarded. Laparoscopic cholecystectomy was performed preserving the appendix which was normal on endoscopic examination. Bile culture was positive for *S. typhi* after 3 days, and was sensitive to amoxicillin/clavulanate, ampicillin, ceftazidime, ceftriaxone, trimethoprin/sulfamethoxazole, and ciprofloxacin. Gallbladder pathology revealed acute necrotizing cholecystitis showing massive hemorrhagic infiltration of bladder mucosa. Patient was discharged after 10 days of IV antibiotics symptom free and was in very good shape during follow-up as an outpatient after 10 days.

DISCUSSION

Typhoid fever is a life-threatening illness caused by the bacterium *S. typhi*. Typhoid fever is still common in the developing world, where it affects about 21.5 million persons each year [4]. Gallbladder infections are common in typhoid fever; Salmonella have been isolated from gallbladders from patients with acute and chronic disease [5]. In acute typhoid fever, colonization of the gallbladder is rarely diagnosed, but it may become apparent with the onset of acalculous cholecystitis. When *S. typhi* is ingested, it reaches the intestine and multiplies in its lumen, then crosses the pass through the lymphatic system of the intestine into the blood and are carried to various organs mainly liver and spleen. Menendez *et al* [6]. proved that *S. typhi* has special affinity to the epithelium of the gall bladder where they multiply triggering a local inflammatory response. Although most bacteria are replicate in the bile extracellularly and discharged into the intestine via the bile, some infect gallbladder epithelial cells and replicate intracellularly. These cause the sloughing of damaged epithelial cells and leading to loss of epithelial integrity, inflammation, and tissue damage and eventually cholecystitis. Literature was reviewed and only few reports were found discussing cases of AAC due to *S. typhi* in children, thus they were worth mentioning.

A 20-year experience at the American University of Beirut Medical Center between 1962 and 1982 with six consecutive children suffering from acute acalculous *Salmonella* cholecystitis and four children with typhoid ileal perforation is presented in the article "Acute abdomen in *Salmonella* infection". All patients were managed surgically without mortality. Early operative intervention and prompt parenteral fluid and antibiotic administration are advised [7].

In a retrospective study analysis done in the Department of Pediatrics in Christian Medical College, Ludhiana, India, on 1995, over 15 years showed that only 11 (1.8%) out of 603 cases of typhoid had cholecystitis. Of these 11 cases only one had typical features of acute abdomen and required emergency surgery. According to this report 10 of the 11 cases were treated conservatively with ampicillin, probenecid and rest to the bowel and responded very well to this regimen. The article states: "Conventially, emergency cholecystectomy is the treatment of choice once diagnosis is established."…"Conservative management with antibiotics in cases of acute acalcular cholecystitis due to *S. typhi* has been recommended". The article also emphasized the importance of ultrasonography in diagnosis [8]. In another retrospective review (from 1970 to 1994) published by the Journal of Pediatric Surgery in 1996, 25 children with acute cholecystitis were identified, 2 of which were due to *Salmonella*. The study concluded with the importance of cholecystectomy in management of acute cholecystitis, although there may be role for nonoperative management in selected cases [9].

In the article "Acalculous cholecystitis in Nigerian children", on 2003, 16 children with acalculous cholecystitis were treated over a 9 year period, 6 of which had *S. typhi*. The organism was cultured in blood and bile in two cases, while Widal titers were significantly elevated in the other four cases. Only one child was managed nonoperatively. The necessity for early diagnosis to avoid life threatening complications was emphasized [10]. A report of three cases in the Shiraz E-Medical Journal, on 2007, presents a three year old boy, a 6-year-old girl and a 7-year-old girl with acute cholecystitis found to have *S. typhi* in biliary cultures. All three cases had negative Widal titers and were managed by cholecystectomy and IV antibiotics. The report supports urgent cholecystectomy in these cases because of

higher incidence of perforation and mortality in comparison with gallstone cholecystitis [11]. In a report published in the African Journal of Pediatric Surgery in 2007, 58 cases of children with acalculos cholecystitis managed in the National Hospital of Donka (Conakry) within a 6 year period, are presented, 38 of which were due to *S. typhi*. Thirty four patients were treated non-operatively but cholecystectomy was carried out in 24 patients. The mortality rate was 10.34% [12].

CONCLUSION

Acute acalculous *S. typhi* cholecystitis is relatively rare in children with only few reported case. In our case, with the evolving era of antibiotics, we faced a case with atypical presentation of *S. typhi* infection. Multiple courses of antibiotics received by our patient had masked the signs and symptoms of typhoid fever. Laboratory results were not conclusive in this case, and *S. typhi* infection was only diagnosed after localizing to the gallbladder causing acute acalculous cholecystitis. Ultrasonography had a major role in diagnosis and thus appropriate intervention. Early intervention with cholecystectomy and prompt IV antibiotic therapy is encouraged to prevent morbidity and mortality due to fatal complications.

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