A Case Report of Acute Abdominal Pain From a Rare Infectious Etiology

Global Pediatric Health
Volume 5: 1–5

DOI: 10.1177/2333794X18783876
journals.sagepub.com/home/gph
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Received January 24, 2018. Accepted for publication May 20, 2018.

Introduction

Abdominal pain is the most common presenting symptom in the pediatric population. Gallbladder disease is not a frequent cause of abdominal pain in this group. Cholecystitis is defined as inflammation of gall bladder with or without evidence of gallstones. Acute acalculous cholecystitis (AAC) is a rare entity in the adult population. Incidence of acalculous cholecystitis in adults was reported as 2% to 15% in previous studies.[1-3] However, AAC accounts for 30% to 50% cases of cholecystitis in the pediatric population.[4,5] Acalculous cholecystitis occurs mostly in critically ill patients with surgery, trauma, burns, mechanical ventilation, after prolonged fasting, and in those patients receiving total parenteral nutrition.[6-9] systemic and local infections (sepsis, Epstein-Barr virus [EBV], hepatitis A virus, and enteric fever)[10-16] and systemic noninfectious diseases (systemic lupus erythematosus, leukemia)[17,18,19] have been described in association with AAC in children of various ages. We present a rare infectious cause of AAC.

Clinical Presentation

A 10-year-old Caucasian girl with history of vesicoureteral reflux grade 3 bilaterally, was transferred from an outside hospital with abdominal pain. The patient was complaining of right upper quadrant (RUQ) abdominal pain 5 days prior to admission with worsening into the evening. The pain continued despite Tylenol and Motrin. It was described as achy, 7/10 in intensity, and was in the RUQ without radiation. There were no aggravating factors, and the pain had no association with food intake. She felt better when she was resting. She had an episode of diarrhea on the same day of pain onset and one episode of nonbilious/non-bloody vomiting 2 days prior to admission. Associated symptoms included a fever with a temperature of 100.4°F from 4 days prior to admission; she was responsive to treatment with Tylenol and Motrin. She developed a rash on the same day of fever onset. The rash first appeared on her neck and later spread to her face, upper, and lower extremities. The rash was not itchy or painful.

Her mother took her to urgent care 4 days prior to admission. She was sent home with reassurance and with a diagnosis of viral illness. She had poor appetite and decreased oral intake for 5 days before the admission. Her mother was concerned that she was still having abdominal pain, poor appetite, and rash. She took the patient to her pediatrician; who performed a rapid streptococcal antigen test (negative), and streptococcal throat culture was sent and was subsequently negative. She was provisionally diagnosed with scarlet fever and was started on amoxicillin therapy. Of note, there were no known sick contacts at home or school. She completed 2 days of amoxicillin, did not show any improvement, and so her mother took her to an outside hospital.

Vitals at the outside hospital were temperature 37.4°C, heart rate 149/minute, blood pressure 106/57 mm Hg, respiratory rate 22/minute, and SpO_2 96% on room air. Complete blood count showed white blood cells 12.2 k/mm^3 (with 70% neutrophils, 14% lymphocytes, and 9% monocytes), hemoglobin 13.3 g/dL, hematocrit 38.9%, platelets 439,000/mm^3, serum sodium 138 mmol/L, potassium 3.5 mmol/L, chloride 102 mmol/L, carbon dioxide 27 mmol/L, blood urea nitrogen 6 mg/dL, creatinine 0.45 mg/dL, serum glucose 106 mg/dL, calcium 10 mg/dL, total protein 7.2 g/dL, and albumin 3.7 g/dL. Alkaline phosphatase was high at 402 U/L, aspartate aminotransferase (AST) 37 U/L, alanine aminotransferase (ALT) was high at 111 U/L, Total bilirubin was high with total 2.2 mg/dL, and direct bilirubin was not available. Lipase was mildly elevated at 284 U/L. Urinalysis with microscopy showed specific gravity 1.014, bilirubin 1+, ketones +, urobilinogen 1, glucose −, nitrite −, LE

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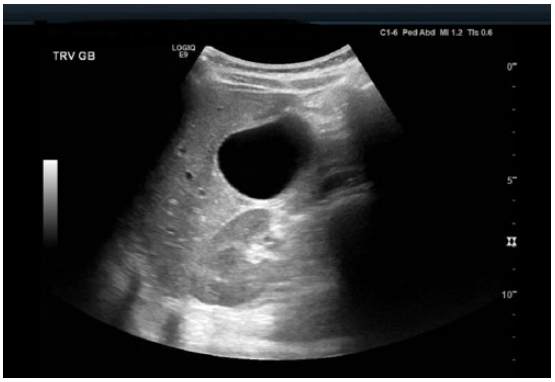

Figure 1. Gallbladder distension with mild pericholecystic fluid on ultrasound.

trace, red blood cells 3 to 10/high-power field (HPF), white blood cells 3 to 10/HPF, and epithelial cells 6 to 30/HPF.

Abdominal ultrasound showed a prominent gallbladder that was distended measuring up to 4.6 cm in short axis. No gallstones, gallbladder wall thickening, or pericholecystic fluid were noted. She received intravenous (IV) famotidine 10 mg, normal saline bolus at 20 cc/kg once, IV Zofran 4 mg, and was transferred to our tertiary care emergency department for further management.

In our emergency department, vitals were temperature 36.9°C, heart rate 96/minute, respiratory rate 22/minute, blood pressure 101/68 mm Hg. Abdominal X-ray showed moderate retained stool on the right and left colon with a nonobstructive bowel gas pattern. C-reactive protein was mildly elevated at 16.39 mg/L, erythrocyte sedimentation rate was mildly high at 36 mm/h, and direct bilirubin was 1.3 mg/dL.

Abdominal ultrasound (Figure 1) was repeated, which showed distention of the gallbladder measuring 4.3 cm in maximum transverse dimension that was stable when compared with the earlier study. Gallbladder wall hyperemia was noted on Doppler, and gallbladder wall thickness was at the upper limits of normal measuring 3 mm without evidence of biliary stone. There was mild pericholecystic fluid. A small amount of free fluid in the right lower quadrant was noted. The appendix was not visualized.

She was started on maintenance IV fluids and was sent to 23 hours observation unit.

In the observation unit, the patient was hemodynamically stable and remained afebrile. She was noted to have an erythematous macular rash all over the body (Figure 2). She had conjunctival injection in both eyes with clear discharge. Symmetric tonsillar enlargement with mild erythema (2+) was noted. There were no tonsillar exudates. She had tenderness over the RUQ with a positive Murphy's sign on admission. There were no organomegaly or palpable masses. The rest of the examination was normal. She was kept NPO (nil per os) initially, started on IV ceftriaxone, and was continued on IV fluids

Laboratory tests were repeated on the day of discharge and showed the following: lipase 310 U/L, bilirubin 0.9 mg/dL, AST 44 U/L, ALT 89 U/L, C-reactive protein 9 mg/L, and erythrocyte sedimentation rate 27 mm/h.

Infectious Diseases consultation recommended evaluating for possible infectious causes of acalculous cholecystitis. Cytomegalovirus immunoglobulin Ig G and IgM (negative), anti-streptolysin O titer (negative), hepatitis panel (negative), infectious mononucleosis screen (negative), EBV serology panel (negative). Parvovirus B19 IgM was negative. Respiratory virus polymerase chain reaction panel was negative. Liver enzymes were retested, with the results AST 53 U/L and ALT 98 U/L. Diet was advanced slowly and the patient tolerated well without vomiting, diarrhea, or return of abdominal pain. Infectious Diseases consultation also recommended *Mycoplasma* IgG and IgM antibody testing. *Mycoplasma pneumoniae* IgM was positive. *M pneumoniae* IgG was negative. The patient was discharged home with oral azithromycin therapy. She followed-up in gastroenterology clinic a few weeks after discharge, where she was completely asymptomatic. ALT, AST, bilirubin, and lipase were repeated and were within normal limits. Her repeat ultrasound was normal with no signs of cholecystitis.

Diagnosis

Acute acalculous cholecystitis secondary to *Mycoplasma pneumoniae* infection.

Discussion

AAC has been seen in multiple bacterial, viral, and parasitic infections in previously healthy children. Ischemia/reperfusion of gall bladder is the central pathogenetic pathway in critically ill patients, which can be caused by various mechanisms such as hypovolemia, hypotension, vasculitis, or sepsis.[9,10,20] Pathogenesis of cholecystitis in healthy children remains unclear. Various mechanisms have been proposed, such as biliary stasis due to dehydration and/or poor gall bladder emptying, and changes in bile canalicular proteins, which can ultimately cause changes in composition and concentration of bile. These characteristic changes in bile can injure the mucosal wall, inducing inflammation.[21]

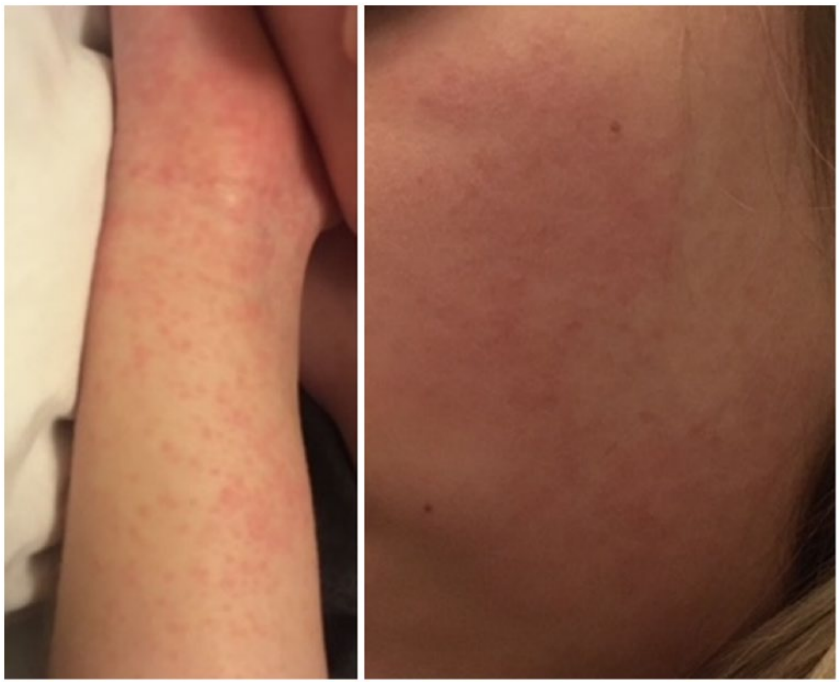

Figure 2. Macular rash over patient's forearm and face.

Table 1. Sensitivity of Each Ultrasound Finding in Detecting AAC, Shown in Different Studies.

Ultrasound Findings	Imamoglu et al[24]	Becker et al[23]	Dietch et al[38]
Gallbladder wall >3.5 mm	100%	90%	80%
Gallbladder distension	50%	27%	—
Pericholecystic fluid	41%	63%	—
Intraluminal sludge	50%	72%	—

Abbreviation: AAC, acute acalculous cholecystitis.

AAC is difficult to diagnose clinically. Clinical features in patients with AAC lack specificity. These features include RUQ abdominal pain, vomiting, fever, localized tenderness, and in half of the cases a palpable RUQ mass. Laboratory tests may reveal leukocytosis, raised acute phase reactants, hyperbilirubinemia, and mild hypertransaminasemia.

Abdominal ultrasound is the most commonly used and reliable diagnostic test. Ultrasound criteria to diagnose AAC are (1) gallbladder wall thickness >3.5 mm, (2) pericholecystic fluid, (3) gallbladder distension, (4) intraluminal debris or sludge, and (5) subserosal edema, along with no evidence of gallstones.[22-24] Each criterion varies in sensitivity and specificity (Table 1). There is no certain number of criteria defined to diagnose/confirm AAC. Computed tomography scan confirms the ultrasound findings of AAC. Ultrasound findings in our patient met 2 criteria among all, including gallbladder distension and pericholecystic fluid. Gallbladder wall thickness was upper limits of normal at 3 mm.

Differential diagnosis in our initially febrile patient included all the possible infectious causes for acalculous cholecystitis; EBV and scarlet fever being highest in the list because of fever and rash in clinical presentation. Acalculous cholecystitis has been described in various infections including bacteria (*Streptococcus pyogenes*, *Staphylococcus aureus*, *Escherichia coli*, *Brucella abortus*, *Brucella melitensis*, *Campylobacter jejuni*, *Coxiella burnetii*, *Leptospira borgpetersenii*, *Leptospira interrogans*, *Mycobacterium tuberculosis*, *Mycobacterium avium complex*, *Salmonella typhi*, *Salmonella paratyphi B*, *Salmonella enteritidis*, and

Vibrio cholerae),[25-28] yeasts (*Candida albicans*),[29,30] viruses (hepatitis A virus, hepatitis B virus, EBV, cytomegalovirus, and flavivirus), and parasites (*Plasmodium falciparum*, *Plasmodium vivax*, *Ascaris lumbricoides*, and *Echinococcus granulosus*).[31]

Mycoplasma pneumoniae is not a frequent infection associated with AAC. Based on the literature obtained from PubMed and Google Scholar, the very first case was reported in 1992. Horii et al described a patient with AAC with *Mycoplasma* infection in Japan.[32] Six more cases were reported in a recent article in 2017. In their study group of a total 147 patients with AAC, 9% died and 29% needed intensive care unit care. Clinical details about the patients with *Mycoplasma* infection were not available in this study.[33] *Mycoplasma pneumoniae* primarily affects the respiratory system. Other systems such as central nervous system, cardiovascular system, and urogenital system can be affected. Other manifestations include polymorphous mucocutaneous eruptions (including classic and atypical Stevens-Johnson syndrome), hemolytic anemia, thrombocytopenic purpura, and hemophagocytic syndromes. Gastrointestinal manifestations of *Mycoplasma* have been reported in the literature; these include gastroenteritis, hepatitis, and pancreatitis.[34-36] The pathogenesis of AAC in *Mycoplasma* remains unknown. Biliary stasis, which has been proposed as primary pathogenetic mechanism in other previously healthy children with various infections, may also be applicable in the pathophysiology of *Mycoplasma* infections causing gallbladder inflammation.

AAC in critically ill children is treated by cholecystostomy or cholecystectomy due to high mortality.[37] In healthy children, conservative treatment with antibiotics, IV fluids, and bowel rest is recommended. Cholecystectomy or cholecystostomy is indicated if there is progressive clinical deterioration or persistent tender mass, and/or increasing gall bladder distention on ultrasound. Our patient's symptoms improved with a short course of oral antibiotics active against *Mycoplasma* infection. No surgical intervention was needed. Laboratory tests and ultrasound did not show any signs of cholecystitis at 3-week follow-up.

Author Contributions

RDB: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

EM: Contributed to conception and design; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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