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Episode of Familial Mediterranean Fever-Related Peritonitis in the Second Trimester of Pregnancy Followed by Acute Cholecystitis: Dilemmas and Pitfalls

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Female, 33
Final Diagnosis: Acute cholecystitis after Familial Mediterranean Fever-related peritonitis
Symptoms: Acute abdomen • fever
Medication: Colchicine
Clinical Procedure: Laparoscopic cholecystectomy and adhesiolysis in the second trimester of pregnancy
Specialty: Surgery

Objective: Rare co-existance of disease or pathology

Background: Differential diagnosis of acute abdomen in pregnant patients is one of the greatest challenges for the clinician. Occurrence of Familial Mediterranean Fever (FMF) paroxysm of peritonitis and acute cholecystitis during pregnancy is a unique clinical entity that leads to serious diagnostic and therapeutic dilemmas.

Case Report: We present the case of a 33-year-old Armenian patient at 16 weeks' gestational age with a history of FMF, who was admitted twice within 1 month with acute abdomen. The first episode was attributed to FMF and successfully treated conservatively with colchicine. The second episode was diagnosed as acute cholecystitis and led to emergent laparoscopic cholecystectomy and lysis of peritoneal adhesions from previous FMF attacks. The patient presented an uneventful postoperative clinical course and had a normal delivery of a healthy infant at the 39th week of gestation.

Conclusions: Pregnant patients with acute abdomen should be evaluated with open mind. To the best of our knowledge, this is the first published report of the coexistence of 2 different causes of acute abdomen during pregnancy. Meticulous history and thorough physical, laboratory, and radiologic examination are the keys to reach a correct diagnosis. Treatment of pregnant patients with acute abdomen should be individualized. Administration of colchicine should be continued during conception, pregnancy, and lactation in patients with FMF history. Laparoscopic intervention in pregnant patients with surgical abdomen such as acute cholecystitis is the optimal method of treatment.

MeSH Keywords: Abdomen, Acute • Cholecystitis, Acute • Familial Mediterranean Fever • Laparoscopy • Pregnancy Trimester, Second

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/896017

Background

Pregnancy is a dynamic state that induces changes in maternal anatomy and physiology. Abdominal pain and discomfort, nausea, and emesis are common symptoms related to obstetric or non-obstetric causes. The incidence of acute abdomen in pregnancy is 1 in 500–635 cases. Acute appendicitis and cholecystitis are the 2 most frequent diagnoses leading to hospitalization and surgery among pregnant patients [1–4].

Familial Mediterranean Fever (FMF) is an autosomal recessive, systemic, autoinflammatory disease that affects the serous membrane. It mainly presents in patients of Mediterranean descent as recurrent, self-limiting episodes of aseptic peritonitis accompanied by fever that last for 24–72 hours. Colchicine is the "gold-standard" medication and it prevents FMF attacks and systemic amyloid deposition. The course of disease during pregnancy may vary from clinical remission to high-frequency attacks of acute abdominal pain [5–8].

Occurrence of 2 different causes of acute abdomen in pregnancy is a unique clinical entity which leads to serious diagnostic and therapeutic dilemmas. We present herein the case of a patient we treated who had FMF-related peritonitis and acute cholecystitis during the second trimester of pregnancy.

Case Report

We present the case of a 33-year-old gravida 2, parity 1, Armenian patient at 16 weeks' gestational age who was referred to our surgical department with symptoms and signs of acute abdomen. She had a history of both FMF treated with colchicine (1 mg/day per os) and cholelithiasis with episodes of biliary colic that had started 6 months ago. FMF had been diagnosed in childhood and manifested with approximately 1 attack of peritonitis every 5 years. The first pregnancy of the patient had been uneventful, without paroxysms of FMF.

The patient presented at this time with generalized abdominal pain, nausea, and fever up to 38.5°C. Physical examination revealed tenderness throughout the abdominal wall and especially periumbilically, as well as absence of bowel movement. Laboratory findings indicated an increase in C-reactive protein (CRP: 16.8 mg/dl with normal range 0–0.5 mg/dl), mild anemia (hematocrit: 31.5% with normal range 37–47%, hemoglobin: 10.5 gr/dl with normal range 11.5–16.5 gr/dl) and normal white blood cell counts (9.93 K/μl with normal range 4.0–11.0 K/μl) with a "left shift" (neutrophils 84% with normal range 40–75%, lymphocytes 12% with normal range 20–40%) [9]. Biochemical markers of liver function and serum and urine amylase levels were all within normal limits. Obstetric examination showed a 16-week-old fetus with normal heart sounds, and absence of uterine contractions. Ultrasound scanning of the upper abdomen revealed a normal gallbladder containing sludge and gallstones smaller than 5 mm. Moreover, the celiac aorta presented no abnormalities on triplex scanning and there were no signs of pericarditis on echocardiography. Finally, she was admitted to our department with the diagnosis of FMF-related peritonitis.

The patient was treated conservatively with bowel rest, intravenous administration of fluids, analgesics, and continuation of the treatment with colchicine (1 mg/day per os). She had a good clinical response and symptoms of peritonitis retreated within 48 hours, and fever along with CRP values decreased to normal. Consequently, she was discharged on the fourth day after admission.

However, the patient presented again 10 days later with symptoms of acute abdomen and fever (T=38.7°C) and was readmitted. Palpation revealed generalized abdominal sensitivity and rebound tenderness, but the most prominent clinical sign was a positive Murphy's sign. Results of obstetric examination were normal and revealed a healthy fetus. Since the patient had a history of symptomatic cholelithiasis and a similar episode of abdominal pain that was treated as a paroxysm of FMF had occurred recently but there was a quick clinical remission, differential diagnosis pointed to acute cholecystitis as a possible cause of acute abdomen. Blood test results were similar to those of the first admission, apart from a more elevated value of CRP (20.2 mg/dl). We performed a MRI of the upper and lower abdomen without intravenous contrast because it crosses the placenta and enters the embryo circulation, as well as a magnetic resonance cholangio-pancreatography (MRCP) due to the complex history and clinical condition of the patient [1,2,10]. The gallbladder appeared to be dilated, measuring 11 cm in its longitudinal dimension, filled with sludge and multiple small gallstones. The findings were indicative of gallbladder hydrops. The intra- and extra-hepatic biliary tract was normal, without dilation and without gallstones (Figure 1). There were not pathologic findings from the rest of the abdominal and pelvic organs.

The patient was treated conservatively until the correct diagnosis was established, with bowel rest, hydration, intravenous antibiotics (Cefuroxime 1.5 gr ×3, Metronidazole 500 mg ×3) and analgesics (paracetamol 1g) as well as an increased dose of colchicine (1.5 g/day per os). However, there were no signs of clinical improvement, since fever up to 38°C and right upper-quadrant abdominal pain persisted. Based on the MRI findings and the clinical condition of the patient, we suspected that hydrops could proceed to empyema of the gallbladder, which would be hazardous for the coexisting pregnancy. Moreover, considering the FMF history and the lack of clinical response despite the increased dosage of colchicine, we

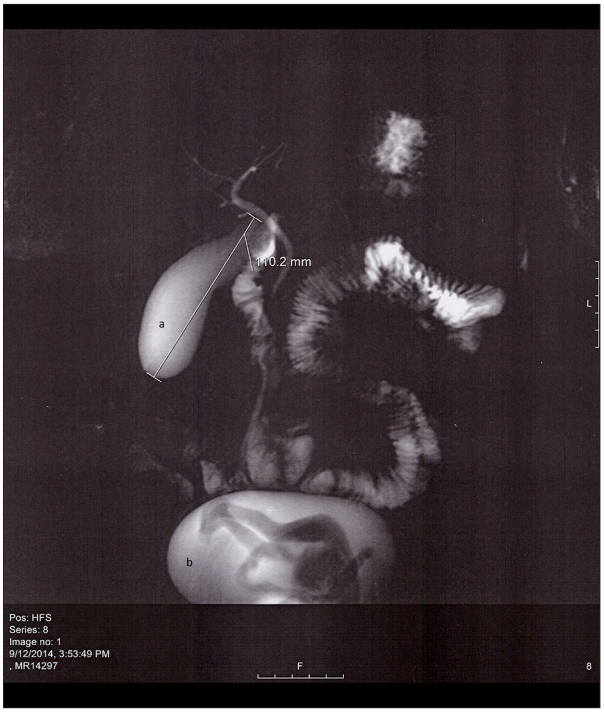

Figure 1. MRCP image. (a) Distended gallbladder (hydrops) measuring 11 cm in its longitudinal dimension. (b) Uterus containing a fetus at the 16th week of gestation.

decided to perform a diagnostic laparoscopy 48 hours after the second admission.

Pneumoperitoneum was established at 12 mmHg through a supra-umbilical incision using the Hassan technique and the patient was placed in 30° anti-Trendelenburg and 30° left lateral position. Exploration of the abdominal cavity revealed a distended gallbladder with presence of pseudomembranes at the gallbladder wall. Moreover, there were extended peritoneal adhesions between the liver and the anterior abdominal wall, characteristic of previous episodes of FMF related peritonitis (Figure 2). The lower abdomen and pelvis did not present any pathologic findings. We decided to perform a laparoscopic cholecystectomy and lysis of the right hypochondriac adhesions. Both procedures were laborious due to thickened and inflammatory tissues. The gallbladder was retrieved through the umbilical port using a laparoscopic specimen retrieval bag. Specimen from the resected adhesions was also sent for biopsy. Peritoneal irrigation with 10 liters of normal saline 0.9% was performed and a drain was placed below the liver bed. The operation was completed within 60 minutes and was uneventful for both the patient and the fetus.

The pathology report of the gallbladder showed chronic hyperplastic cholecystitis with serosal foci of suppuration infiltrating the gallbladder wall. Moreover, biopsy of the specimen from the adhesions indicated acute purulent peritonitis.

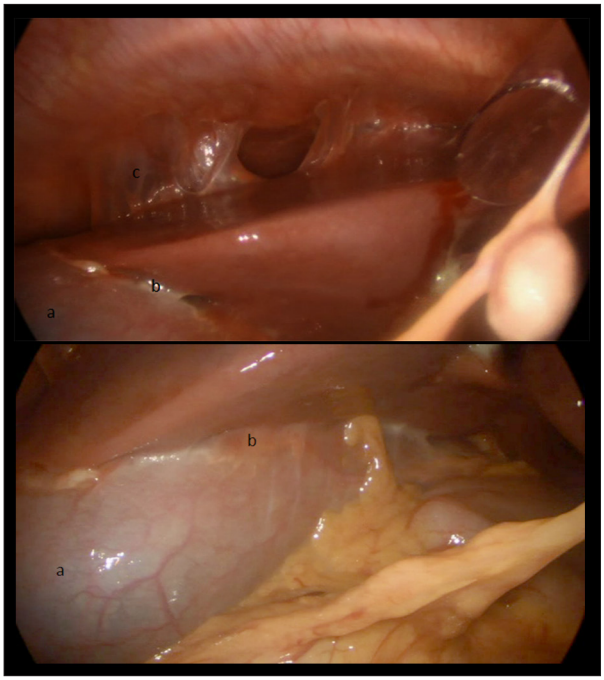

Figure 2. Intraoperative photos. (a) Distended gallbladder (hydrops). (b) Pseudomembranes at the gallbladder wall. (c) Peritoneal adhesions between the upper surface of the liver and the right hypochondriac region, characteristic of previous episodes of FMF-related peritonitis.

Postoperatively, the patient and the fetus had a stable and uncomplicated clinical course. She was discharged on the third postoperative day afebrile and without abdominal pain. Colchicine was prescribed in the initial dose (1 mg/day per os). The patient did not present any other episode of acute abdomen during pregnancy and had a normal delivery of a healthy infant at the 39th week of gestation.

Discussion

Evaluation of a pregnant patient with acute abdomen is one of the greatest challenges for the clinician. Delay in diagnosis can be harmful for both the mother and the fetus. Apart from obstetric causes, diseases of the gastrointestinal, hepatobiliary, genitourinary, vascular, and hematologic system should be included in the differential diagnosis. Acute cholecystitis is reported in 0.2–0.5 per 1000 pregnancies. Pregnancy is a risk factor for gallstone disease due to increased levels of serum estrogen and progesterone, leading to high saturation of bile with cholesterol and bile stasis [1,2,4,11].

Familial Mediterranean Fever is a chronic disease that should be diagnosed and treated properly early after onset of symptoms to prevent possible complications and exclude other causes of acute abdomen. FMF may cause female infertility

due to abdominopelvic adhesions from recurrent peritonitis attacks or ovarian amyloid deposition. FMF episodes of peritonitis during pregnancy may cause uterine contractions and are also associated with recurrent miscarriage, premature rupture of membranes, cesarean delivery, and low birth weight [6,7,12].

In our case we treated a pregnant patient with 2 subsequent episodes of acute abdomen. She had a history of both FMF receiving colchicine and symptomatic cholelithiasis. Dilemmas arose regarding correct diagnostic approach and treatment. After excluding obstetric causes of abdominal pain and acute cholecystitis according to ultrasound evaluation, the first episode was considered to be a FMF peritonitis attack and was successfully treated conservatively. Thorough history, clinical, laboratory, and imaging investigation helped us establish the diagnosis. FMF-related peritonitis is aseptic, self-limiting, and retreats after 48–72 hours. Although it resembles acute surgical abdomen, surgery is contraindicated, especially in cases of coexisting pregnancy [5,7,12].

Colchicine is the "gold-standard" treatment of FMF and should be administered orally in a minimal dose of 1 mg/day in adults to prevent FMF attacks. When the attacks are not controlled, the dose may be increased to 2 mg/day. Colchicine treatment of FMF patients is beneficial and should be continued during conception, pregnancy, and lactation [5–8,12].

Nevertheless, symptoms of acute abdomen soon relapsed. We were unsure whether it was another episode of FMF or a different cause of acute abdomen. Clinical examination excluded obstetric pathology and revealed a positive Murphy's sign. History of gallstone disease pointed to acute cholecystitis as a probable diagnosis. In order to achieve a faster and precise diagnosis due to the complex history and the pregnancy of the patient, we immediately performed abdominal MRI and MRCP [1,2,10]. We wanted to exclude occult pathology from the hepatobiliary tract that was not detected with ultrasound scanning during the previous admission of the patient.

Indeed, abdominal MRI and MRCP showed elements of gallbladder hydrops. Therefore, we had to deal with a clinical entity that could lead to septic complications, such as gallbladder empyema, and jeopardize the mother and the fetus. Since there was no clinical improvement after 48 hours of conservative treatment with increased dose of colchicine and antibiotics, we decided to proceed immediately to laparoscopic intervention. According to the guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), laparoscopic surgery is permitted in pregnant patients with symptomatic cholelithiasis and is safe in all trimesters of pregnancy [1,11,13]. In our case, symptoms of acute abdomen retreated after laparoscopic cholecystectomy and adhesiolysis and the pregnancy proceeded uneventfully.

Finally, the pathology report suggested that peritoneal adhesions that had been formed due to the inflammatory response in previous FMF attacks may have been contaminated during the episode of acute cholecystitis, leading to local purulent peritonitis. According to the literature, FMF does not affect the hepatobiliary system and there is no association between FMF and acute cholecystitis. There is only 1 case – an 8-year old girl with a previous history of FMF – that presented with symptoms of acute cholecystitis and underwent cholecystectomy, with a pathology report suggesting polyarteritis nodosa involving the hepatobiliary system [14].

Conclusions

Pregnant patients with acute abdomen should be evaluated with an open mind and all possible scenarios should be taken into account. Precise history and thorough physical, laboratory, and radiologic examination are the keys to reaching the correct diagnosis. Treatment should be individualized, and must be effective and safe for both the patient and the fetus. Administration of colchicine should be continued during conception, pregnancy, and lactation in patients with FMF history. Laparoscopic intervention in pregnant patients with surgical abdomen is the optimal method of treatment. To the best of our knowledge, this is the first reported case of a pregnant patient with FMF-related peritonitis and successive acute cholecystitis.

Statement

There were no sources of financial support or conflicts of interest regarding this article.

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