

Underlying Appendicitis Leading to Chorioamnionitis in Preterm Rupture of Membranes

Jennifer Gibbs, DO, Firas Bridges, MD, John J. Vullo, DO, & Anthony Sampino, DO

Department of Obstetrics & Gynecology and Department of General Surgery,
Good Samaritan Hospital Medical Center, West Islip, NY

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Background: PPROM complicates 3% of pregnancies, the most commonly identified etiology is infection. Appendicitis is a well-known cause of peritonitis and systemic illness, complicating approximately 1/1700 pregnancies.

Case: A healthy 26 year old primagravida female at 24 weeks gestation presented with PPROM. She was managed expectantly and delivered at 26 weeks gestation due to suspected chorioamnionitis, manifested by abdominal pain and tenderness. Postpartum the patient complained of mild abdominal pain and nausea that was deemed appropriate for her post-operative state, and she was discharged home on post-operative day 3. The following day she presented to our emergency department with worsening abdominal pain. Imaging was suggestive of appendicitis, and the patient subsequently underwent surgery. Intra-operative findings were significant for an inflamed appendix matted to the posterior surface of the uterus and diffuse erythema of the uterine serosa. Final pathology reports confirmed acute appendicitis, chorioamnionitis and funisitis.

Conclusion: It is possible that an underlying appendicitis lead to intrauterine infection and subsequent preterm delivery in our patient.

INTRODUCTION

Preterm birth complicates 11% of all pregnancies, and 3% of all pregnancies are effected by preterm premature rupture of membranes (PPROM)¹. In cases of PPROM, the most commonly identified etiology is infection.^{1,2,3} Here we will discuss a case of a healthy 26-year-old primagravida female, with an antenatal period complicated by PPROM occurring at 24 weeks' gestation, with delivery at 26 weeks secondary to suspected chorioamnionitis. In the immediate post-operative period, the patient was re-admitted to the hospital and underwent surgery for acute appendicitis; leading to the question of which came first, the chorioamnionitis or the appendicitis?

Teaching Point:

Inflammation, from any organ system, can lead to the pathological cascade causing PPROM subsequent preterm delivery

CASE

26-year-old G3P0020 African American female at 24 6/7 weeks' gestation by first trimester sonogram presented to the labor and delivery unit of a small community hospital with complaint of leakage of fluid. PPROM was confirmed and the patient was trans-

ferred to our facility for further management. She was admitted to the antepartum service for expectant management. Following ACOG recommendations the patient received antenatal corticosteroid for fetal lung maturity, magnesium sulfate for neuroprotection and a 7-day course of antibiotics for latency. She was monitored closely with serial abdominal exams and daily lab work trending white blood cell count. Fetal monitoring consisted of continuous tocometry and external fetal monitoring. On hospital day 7, the patient developed a mild leukocytosis of 14,000. At this time, she complained of abdominal pain, but on physical exam, the abdomen was soft with no fundal tenderness, rebound or guarding. She remained afebrile with reassuring fetal heart rate tracing and was monitored closely.

On hospital day 10, at 26w1d gestation, the patient developed worsening abdominal pain. On exam, she displayed obvious abdominal tenderness. In conjunction with maternal fetal medicine, the decision was made to proceed to delivery for suspected chorioamnionitis. She underwent a primary classical cesarean section with a double layer uterine closure under spinal anesthesia. Intra-operative findings were significant for: 1) viable female infant with APGARs of 3 and 8, weighing 1lb 10oz (775g); 2) no amniotic fluid 3) friable placenta, noted to be unhealthy in appearance 4) diffuse irritation and erythema of the uterine serosa. Placenta cultures were obtained at time of delivery. The patients post-operative course was significant for mild leukocytosis of 13,000 and abdominal discomfort which was deemed appropriate for procedure. On post-operative day 3 the patient was discharged home.

CORRESPONDENCE:

Jennifer Gibbs, DO | jennifer.mceachron@gmail.com

The following day, the patient presented to the emergency room with complaint of lower abdominal pain, worsening since hospital discharge. On arrival to the ED, she was afebrile with WBC 14,000. Pfannenstiel skin incision was healing well without obvious evidence of infection. On exam the patient was noted to have tenderness in the right and left lower quadrant and a CT scan was significant for a dilated appendix and multiple appendicoliths. The patient was evaluated by general surgery, and the decision was made to proceed with surgical management. She subsequently underwent a laparoscopic appendectomy. Intraoperative findings were significant for inflamed appendix, markedly adherent to the posterior uterus, with diffuse erythema of the uterine serosa and surrounding peritoneum. Additionally there were multiple adhesions from the uterus to nearby structures including the bowel and anterior abdominal wall. Post-operatively she recovered well and was discharged home on post-operative day.¹

DISCUSSION

Preterm premature rupture of membranes (PPROM) complicates 3% of all pregnancies and is defined as rupture of membranes before 37 weeks' gestation. Management of PPRM is based on the gestational age. Delivery is recommended when PPRM occurs in late preterm gestations (34 0/7 – 36 6/7 weeks). Regarding PPRM in patients ranging from fetal viability to 33 6/7 weeks, such as our patient, expectant management is warranted to prolong the latency period. Latency is defined as time of rupture to time of delivery. This expectant management includes: antenatal corticosteroids, GBS prophylaxis, antibiotics and in those patients less than 32 0/7, magnesium sulfate for neuroprotection. As discussed previously, our patient was managed according to ACOG guidelines.^{1,2,3}

During expectant management, patients must be monitored closely for the development of chorioamnionitis, defined as acute inflammation of the placental membranes. In the face of rupture of membranes, the most reliable indicator is fever, defined as >38°C. Patients must be monitored closely for fever, uterine tenderness, maternal or fetal tachycardia and malodorous vaginal discharge. Fetal and neonatal morbidity is increased significantly in the case of chorioamnionitis. Those affected have higher incidence of RDS, IVH, sepsis and periventricular leukomalacia. Additionally, PPRM with intrauterine inflammation has been associated with an increased risk of neurodevelopmental impairment.^{3,4} The development of chorioamnionitis is an indication for prompt delivery to minimize fetal morbidity. Other indications for delivery include, but are not limited to, non-reassuring fetal status and placental abruption.

The most commonly identified risk factor for PPRM is infection.¹ Reviews of several large studies demonstrated bacteria within amniotic fluid in one-third of cases. The placental membranes are composed of an outer layer, the chorion, and the inner amnion. The amnion provides almost all of the tensile strength to the membranes, composed primarily of collagen types I and III. For this reason, collagen break down has been linked to rupture of membranes. Matrix metalloproteinases (MMP) are a family of enzymes involved in collagen break down. Studies of the amnion-chorion have demonstrated that MMP expression is increased with the inflammatory mediators IL-1, IL-6, TNF alpha. Similarly, other recent studies have demonstrated that bacteria endotoxin directly elicits

release of fetal fibronectin (FFN) from the amnion. FFN activates a signaling cascade that leads to the synthesis of prostaglandins and increased activity of MMP.^{2,3}

There are multiple pathways in which bacteria and inflammatory mediators gain access to the uterine cavity. The most commonly recognized pathway is ascending infection from the vagina, through the cervix, to the uterine cavity. This is based on the fact the most commonly identified organisms in chorioamnionitis are also found in the vagina. Other potential pathways of spread include hematogenous dissemination. As in the case of bacteremia, organisms gain access via the placenta. Organisms from the abdominal cavity may enter the fallopian tubes and seed the uterus via retrograde spread. Systemic illness and local inflammation has also been linked to preterm delivery, including pneumonia, urinary tract infections and pyelonephritis.⁴ Additionally, well documented evidence exists for the association of periodontal disease and increased risk of preterm birth. The association is not clear, but evidence suggests a variation in the inflammatory response in the oral cavity alters genital tract flora and systemic inflammatory mediators.^{2,3} This further illustrates that infectious source remote from the genital tract is able to initiate cascade of events ultimately culminating in preterm delivery.

The life time risk of developing appendicitis is 6.7% for females. The pathophysiology of appendicitis is incompletely understood, but thought to be due to luminal obstruction, secondary to fecaliths or hypertrophy of lymphoid tissue. This closed-loop obstruction leads to multiplication of the resident bacteria, leading to distension and inflammation that eventually spreads to the serosal surface. The initial distension of the appendix is responsible for the dull umbilical/epigastric pain and associated nausea. As the inflammation progresses to involve the serosa, the surrounding peritoneum becomes inflamed, producing the characteristic migration of pain to the right lower quadrant. Additional signs and symptoms of appendicitis include fever and leukocytosis.⁵ Acute appendicitis involves approximately 1/1700 pregnancies.⁶ In a large study conducted over a nine-year period involving 66,993 patients, the most common presentation of appendicitis in pregnancy mirrored that of the non-pregnant population. Despite the theory of appendiceal displacement by the gravid uterus, these investigators found that the most common location of pain regardless of trimester was found to be right lower quadrant, with associated nausea, fever, and leukocytosis.⁶

Can intra-abdominal infections cause chorioamnionitis and PPRM? At 20 weeks' gestation, the average fundal height of the uterus is at the level of the umbilicus. Even at this early gestational age, the uterus spans well outside of the pelvis and lies in contact with other intraabdominal structures, most notably the bowel. As previously discussed, the connection between inflammatory mediators and rupture of membranes has been well documented. Based on knowledge of the inflammatory process and pathology involved in the development of chorioamnionitis, the presence of acute appendicitis and the associated local inflammatory response, could have spread to involve the nearby gravid uterus. Inflammation of the uterine serosa, eventually spreading to involve the myometrium, endometrium and placental membranes is one theory. Our patient's pathology was significant for confirmation of acute appendicitis, chorioamnionitis and funisitis. Interestingly, cultures from the maternal and fetal placenta surfaces did not show bacterial growth, indicating acute inflammation without clear bacterial infection.

Would suspecting appendicitis have altered the management of our patient? As discussed previously, in the event of intra-amniotic infection, delivery is indicated to decrease neonatal mortality, regardless of the source of the initial infection. The symptoms of chorioamnionitis are markedly similar to many other intra-abdominal infections. Fever, abdominal pain, and tachycardia are generalized symptoms that apply to many disease states. The traditional teaching has been this: PPROM plus fever and/or abdominal pain, equals chorioamnionitis. Although multiple studies have demonstrated the safety of laparoscopic appendectomy in pregnancy,⁷ none have examined non-obstetric surgical interventions in the face of PPROM. We cannot definitely say whether an underlying early appendicitis was the sentinel event leading to PPROM, or the later development of chorioamnionitis. This case serves to remind us that inflammation, from any organ system, can lead to the pathological cascade causing PPROM, chorioamnionitis and subsequent preterm delivery. Suspicion of chorioamnionitis should prompt delivery for fetal benefit, but the differential diagnosis of potential other disease processes should remain for appropriate maternal management.

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