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Case Report

A Free Terminal Ileal Perforation From Active Crohn Disease in Pregnancy: A Diagnostic Challenge

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The surgical management of the complications of Crohn disease is often challenging. These difficulties are compounded in pregnancy by competing interests of the mother and the baby. In this report, we describe the presentation and surgical management of a patient in her second trimester with active Crohn disease who required emergent surgical intervention. She had presented with the uncommon complication of a free perforation in the presence of active untreated disease.

Key words: Crohn disease – pregnancy – ileal perforation – peritonitis

Crohn disease is a chronic transmural inflammatory condition of the gastrointestinal tract that is frequently diagnosed in patients aged 15 to 30 years.[1] In fact, 50% of patients with inflammatory bowel disease are diagnosed before the age of 35.[5] The distribution of Crohn disease is bimodal, thus many women will be diagnosed in their reproductive years.[2] Literature reporting on pregnancy outcomes in Crohn patients show mixed results and is confounded by the heterogeneity of the population studied. It is clear, however, that active disease during pregnancy is associated with adverse perinatal outcomes.[3] In a recent single institution study, inflammatory bowel disease during pregnancy was associated with an increased incidence of small-for-gestational age births, spontaneous preterm birth, and preterm premature rupture of membranes.[1] In this study, however, only ulcerative colitis was significantly associated with an increased incidence of spontaneous preterm birth and preterm premature rupture of membranes.[1] The impact of pregnancy on the severity of Crohn disease is unclear. A recent study examining the incidence and types of surgical complications associated with Crohn disease in pregnancy from a national database demonstrated a higher incidence of both overall surgical disease and specifically anorectal sepsis and intestinal-genitourinary fistulas in this population.[9] Disease activity at conception appears to be an

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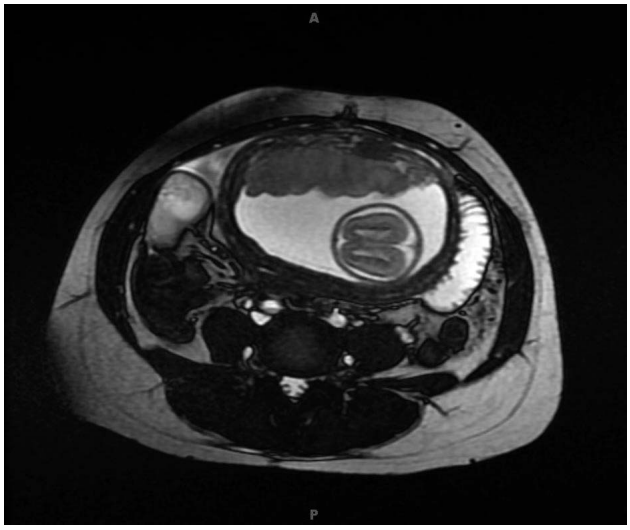

Fig. 1 Cross-sectional MR scan of abdomen demonstrating small bowel dilatation and localized right-lower quadrant fluid collection. An intrauterine fetus is noted.

important factor in determining severity of disease during the pregnancy.[5]

Complications of Crohn disease requiring surgical intervention during pregnancy are ideally best prevented. Nevertheless, in those patients who require surgery, decision making and management can be challenging.

We present a case of Crohn disease requiring emergent operative intervention for a free perforation secondary to active disease during her pregnancy that highlights the unique diagnostic difficulties in this population.

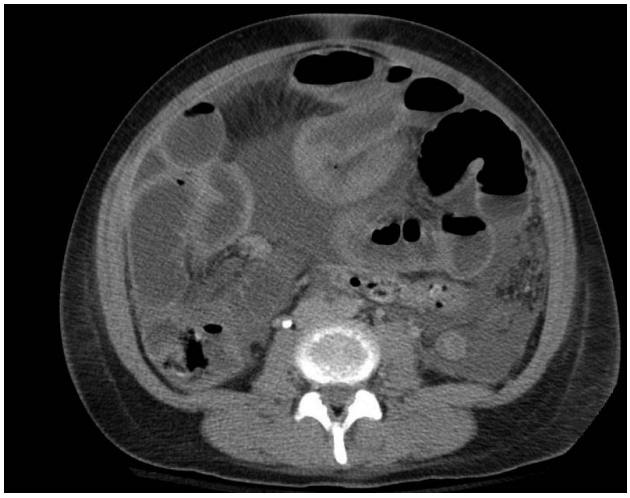

Fig. 2 Cross-sectional CT image, showing free abdominal fluid and locules of free air.

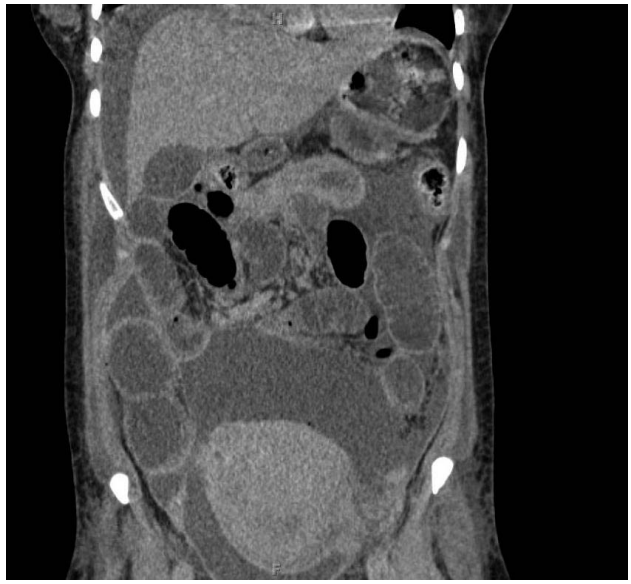

Fig. 3 Coronal CT image from the same series demonstrating a large amount of pelvic free fluid.

Case Report

A 29-year-old, gravida 1, para 0, with a history of Crohn disease, presented to the obstetrical emergency unit with abdominal pain and vomiting during the 19th week of her pregnancy. She was afebrile. Inflammatory markers were not elevated on presentation. Prior to her pregnancy, she had been on oral sulfasalazine, but was not compliant with either her medication or follow-up. She has had no prior surgery for her disease.

Her examination findings were nonspecific. Fetal monitoring was initiated and a magnetic resonance scan (MR) of her abdomen was ordered. A moderate amount of free fluid mainly localized to the right-lower quadrant and nonspecific small bowel dilatation were noted (Fig. 1).

Antibiotic therapy was instituted and the patient was observed. Forty-eight hours after admission, the patient developed preterm labor and delivered a nonviable fetus with a complete placenta. Within 12 hours of the miscarriage, she developed increasing abdominal distension with pain, tachycardia, and diaphoresis. An emergent computed tomography (CT) scan demonstrated markedly increased intra-abdominal fluid, and locules of free intraperitoneal air (Figs. 2 and 3). She underwent an emergent laparotomy during which a significant volume of enteric contamination and a full thickness terminal ileal perforation were noted. An ileocecectomy was performed and pathological evaluation confirmed

terminal ileal Crohn disease with a transmural perforation. Intestinal continuity was restored with a stapled side to side ileocolic anastomosis. The patient was admitted to the intensive care unit postoperatively and required aggressive fluid resuscitation, and cardiovascular and ventilatory support. On postoperative day 5, she developed suspicious drainage from the midline surgical wound. An abdominal pelvic CT scan that had been done on the day prior to the event had not demonstrated at discrete collection; some free fluid and nonspecific small bowel dilatation was noted. Concern about a possible anastomotic dehiscence or a contained abscess led to re-exploration with the surgical plan to take down the anastomosis and defunction the bowel with an end ileostomy, should there be evidence of an anastomotic leak. No discrete abscess was identified. The anastomosis was not visualized at this time as a dense inflammatory reaction had set it and mobilization of the bowel was not possible without a risk of significant injury. The abdominal cavity was widely drained and the patient returned to the intensive care unit. She was eventually discharged after a protracted hospital course.

Discussion

Large epidemiological studies reviewing outcomes in pregnant patients with inflammatory bowel disease (IBD) have documented higher rates of adverse fetal outcomes.[2] Among the independent predictors noted in a recent epidemiological study in the United States were a history of surgery for inflammatory bowel disease and nonwhite ethnicity.[3] In this same study, severity of disease and medical treatment were not associated with adverse outcomes. In a meta-analysis evaluating the effects of IBD on pregnancy, the authors noted that women with IBD were more likely to experience premature labor, low birth weight, and congenital abnormalities.[4] However, this tendency toward poorer perinatal outcomes has not been consistently demonstrated in individual studies. In a recent single institution study, the authors note that Crohn disease is associated with an increased risk of small for gestational age births, but that only ulcerative colitis was significantly associated with preterm birth and preterm rupture of membranes.[1] The authors suggest that this finding which is in contrast to older studies may be due to the use of clear definitions of case findings and a more extensive control of confounding factors. They also note that older studies may not accurately reflect recent trends in medication use between patients with Crohn disease and those with ulcerative colitis.[1] There is thus some variability between studies examining pregnancy outcomes in patients with Crohn disease and this is partly related to the heterogeneity of the populations studied, and the difficulty in accounting for confounding factors.

It is clear that patients with active disease during their pregnancy are at highest risk of adverse outcomes.[3] Interestingly, when interviewed, women with inflammatory bowel disease were more concerned about the perceived effect of medications on their unborn child than on the more serious adverse consequences of active Crohn disease on their pregnancy outcome.[2] The observation that this concern over teratogenicity of medications often leads to noncompliance has been noted in the literature and may have contributed to the clinical presentation in our case.

The influence of pregnancy on disease activity is variable. Approximately one-third of patients will experience a flare-up during their pregnancy while the remaining two-thirds will remain stable or experience some remission of their disease.[3] In a recent meta-analysis of pooled heterogeneous studies, it was noted that women who have active inflammatory bowel disease during the periconceptual period are more likely to experience active disease during their pregnancy.[5] The authors note, however, that in the studies reviewed almost half the patients with active Crohn disease at the time of conception did not remain active during the course of their pregnancy.[5] Thus recommendations on medications cannot be standardized to all patients. It appears though that preconceptual control of inflammation reduces the risk of a disease flare-up during the antenatal period. Active disease during the pregnancy is significantly more difficult to manage, is resource intensive and, as our case demonstrates, is associated with adverse fetal outcomes.

Multiple studies have reviewed the safety of various agents used in the treatment of Crohn disease. Aminosalicylates are associated with minimal side effects to the fetus.[2] However, mesalamine (Asacol; Warner Chilcott Deutschland GmbH, Weiterstadt, Germany) should be used with caution because of skeletal and reproductive tract abnormalities observed in animal studies from the coating agent dibutylphthalate.[2] The safety of mercaptopurine and its prodrug azathioprine has been demonstrated in multiple studies in transplantation and

rheumatology.[2] Biological agents cross the placenta mainly in the third trimester and should be avoided after 30 weeks.[2] Corticosteroids, with the exception of dexamethasone, are inactivated by placental enzymes and thus do not suppress the hypothalamic pituitary axis of the fetus.[2] The effects of maternal corticosteroids on fetal development, birth weight, and head circumference are conflicting; however, these drugs are rarely used as remission therapy.

Free perforation from Crohn disease is a rare event with an incidence quoted between 1 to 3%.[6] A free terminal ileal perforation during pregnancy is quite rare with only 2 prior reports identified in our review.[7,8] Our case illustrates the difficulty associated with making the diagnosis of a free intestinal perforation during the late second trimester due to the limitations of the clinical examination and suboptimal imaging. The history of noncompliance to medical therapy and antenatal follow-up further complicates the picture by suggesting the possibility of acute inflammatory disease as the cause for her initial presentation. Acute inflammatory Crohn disease is treated with intensive medical therapy. In the initial evaluation of our patient, this was felt to be the most likely diagnosis as there was no clear evidence either on physical examination or the initial MR study that there was an intestinal perforation present. Free perforation remains a serious complication of Crohn disease and is associated with significant morbidity despite intervention. In pregnancy, this unusual complication can be catastrophic and may, as in this case, lead to an adverse pregnancy outcome. Clinical examination findings and laboratory investigations can be misleading. Early imaging is mandatory in the evaluation of these patients. The choice of imaging modalities in pregnancy is complicated by the concern about fetal radiation exposure. This is probably best approached through a discussion with the patient about the perceived risks from fetal exposure to ionizing radiation during diagnostic studies and the danger from delayed recognition of a severe complication through the use of a suboptimal or poorly performed imaging study. Although MR avoids fetal exposure to ionizing radiation and is being increasingly used for the evaluation of acute intestinal or biliary tract disease in pregnancy, a recent review reports a learning curve for MR examinations for acute appendicitis and specifically delineating right-lower quadrant anatomy in late second and third trimesters.[10] The estimated average dose from a single abdominal and pelvic CT examination is 17–25 milligray (mGy). Fetuses at 16 to 25 weeks are at risk of developing mental retardation at exposures greater than 250 mGy.[10] Of more concern, however, is the unsettled controversy over increased risk of childhood cancer from exposure to ionizing radiation from abdominal and pelvic CT imaging. Studies in this regard have been equivocal with a recent population based study showing no difference in risk between exposed and unexposed groups.[10] In a statement released by the International Commission on Radiological Protection, the best quantitative estimate of risk is approximately 1 cancer per 500 fetuses exposed to 30 mGy of radiation.[11] Iodinated contrast does cross the placenta, but there is no know report of teratogenicity. It is currently a United States Food and Drug administration category B drug. Thus, although ultrasound and MR imaging should be considered first in the evaluation of the pregnant patient, the risks from ionizing radiation exposure associated with abdominal and pelvic CT imaging are low and may be outweighed by the potential harm from a delayed or missed diagnosis.[10] In a more recent review on recommendations for abdominal pelvic imaging in pregnancy, the authors conclude that CT imaging should not be delayed when deemed necessary because of concerns about fetal exposure to ionizing radiation.[11]

From the extensive peritoneal contamination noted at the laparotomy in our case, this perforation may have already been present at time the MR scan was obtained. This suggests that earlier surgical intervention in the 48 hours preceding the patient's miscarriage may have averted the ensuing complications. It is certainly possible that at this stage, the perforation could have been treated with a laparoscopic-assisted approach. In addition, earlier surgical treatment of the perforation may potentially have prevented the systemic sepsis syndrome that led to the patient's rapid clinical deterioration and subsequent intensive care unit admission. However, it is uncertain whether earlier intervention would have averted the miscarriage. The adverse pregnancy outcome is likely the result of a combination of factors—most importantly, the presence of active untreated disease during the antenatal period and the systemic inflammatory response associated with the free abdominal perforation.

Conclusion

Complications of Crohn disease during pregnancy are best prevented by an early discussion on medication and follow-up compliance. This discus-

sion should ideally take place in the pre- conceptual period. Communication between the various specialty services participating in the patient's care is important. Most medications used in the treatment of the disease are safe during pregnancy. In spite of this, public misconceptions to the contrary appear widespread. In those few patients who present with Crohn-related complications in the antepartum period, early and aggressive intervention is essential to ensure a good outcome for both the mother and fetus.

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