Inflammatory Bowel Disease with an Onset during Pregnancy

H Akbar, H Fallatah

Citation

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Abstract

A 35-year-old Egyptian woman, was pregnant with twins and had gestational diabetes. She developed severe watery diarrhea at 32 week of gestation. This was thought to be due to infectious diarrhea, but she did not respond completely to the treatment with antibiotics. After extensive work up we diagnosed her for the first time to have the inflammatory bowel disease (IBD) Crohn's disease. She responded completely to the treatment with prednisolone and mesalamine and she had favorable pregnancy outcome.

INTRODUCTION

Inflammatory bowel disease (IBD) is common in females during the reproductive age and the pregnancy outcome is usually not affected by the disease nor will the pregnancy affect the disease progression or severity. The medications used to treat IBD are usually safe during pregnancy and they generally do not require dose adjustment more than non pregnant females. However in some pregnancies, IBD may be associated with complications including premature delivery, therapeutic or spontaneous abortions, congenital anomalies and impaired fetal weight.(1) On the other hand medications used to maintain IBD or to control the disease activity are also known to have negative impact on pregnancy like stillbirth. (2,3) since the outcome of pregnancy in IBD patients in remission is similar to the general population, IBD patient's planning pregnancy must have the disease controlled before conception.(4,5)

CASE REPORT

A 35 year old Egyptian woman G6P5 + 0 were pregnant at 32 week of gestation with twins. She had gestational diabetes for 4 month. She had diarrhea for 3 month. The stool was of large volume greenish watery in consistence about 13-15 motions daily. That was associated with intermittent low grade fever and attacks of moderate diffuse colicky abdominal pain. During the 3 months, she received multiple courses of antibiotics including quinolones, metronidazole and cephalosporins. She had transient improvement while on antibiotics and the frequency of bowel motion reduced to 4 to 5 times daily. She did not have history of IBD or chronic diarrheal illness before. There was no history of contact with febrile patient and no report of similar cases in her family or contacts. Her medications included insulin for gestational diabetes, and iron and calcium supplements .

On physical examination, she was febrile temp 38,5C□, BP 110/70 mmHg, pulse 80 beat/minute regular and of normal volume. The chest and cardiovascular examinations were normal. The abdomen was distended with fundal height at 35 week. She had diffused mild abdominal tenderness mainly in the flanks. The two fetal heart sounds were normal.

Complete blood count (CBC) showed white blood cells (WBC) of 5.4K/ul, hemoglobin(Hb) 9.7g/dl low (normal 12-15) and platelets (plat) 171k/ul normal. Electrolytes and renal function tests showed: sodium (Na) 137mmol/L normal, potassium (Ka) 3.9 normal, urea (BUN) 1.6 mmol/L low but expected for pregnant woman (normal 2.5-6.4), and creatinine 34 umol/L (normal 53-115).

Blood sugar results while on insulin were 5.1 mmol/L fasting and 5.9 mmol/L random. Both are normal. Hemoglobin A1C (HbA1C) was 5.1% (Reference range 4.8-6%). Stool analysis was negative for blood and parasites and eggs. Stool culture was positive for E. coli. Clostridium difficile toxin-A was negative in stool. Thyroid function tests (TFT) revealed Thyroid stimulating hormone (TSH) 6.32 ulU/L (normal 0.27-4.2), free T4 (FT4) 13.36 pmol/L (normal 12-22) and free T3 (FT3) 3.17 pmol/L (normal 2.8-7).

She had testing for autoimmune profile and the result showed: Antinuclear antibody (ANA) 1:320 (moderately positive), Double stranded DNA antibody107 iu/ml (normal 0-200), cytoplasmic and perinuclear antineutrophil cytoplasmic antibody (P_ANCA and C-ANCA) were negative. The liver enzymes were elevated: Aspartate Aminotransferase (AST) 181U/L (normal 15-37), alanine aminotransfersase (ALT) 379U/L (normal 30-65), alkaline phosphatase (ALP) was normal 109U/L, Total Bilirubin (TBIL) was normal 9umol/L and Albumin (Alb) 23g/L (normal 34-50). Hepatitis serology was positive for HCV Ab but hepatitis C virus Polymerase chain reaction (PCR) was negative for detection. Obstetric ultrasound was normal for gestational age.

She was given one week course of ceftriaxone. Repeated stool culture was negative but she continued to have watery bowel motions 15-20 daily. She was started on intravenous fluid infusion to avoid dehydration. She was also given trials of loperamide, cholestyramine and subcutaneous injections of octreotide but the diarrhea did not improve. Blood sugar was well controlled on triple dose of subcutaneous insulin. Upper gastrointestinal endoscopy (OGD) was performed and it was normal. Duodenal mucosal biopsy showed no evidence of celiac disease. Colonoscopy showed skip lesions pattern of loss of normal mucosal vascular pattern friability and multiple aphthus ulcers. The colonic biopsy was consistent with inflammatory bowel disease. It showed chronic inflammatory cells infiltrate cryptitis and no evidence of vasculitis. Solofalk (mesalamine) 500mg TID was started for 2 days but no response. Then intravenous Hydrocortisone 100mg TID was added. Over three days the frequency of bowel motions improved from 15-20/day to 5-8/day. However over one week of treatment she had dramatic weight gain of 20 kg and massive edema. The BP was normal and the test for 24 hour urine protein was 0.4.g. IV fluid was stopped and she received a course of parenteral then oral frusemide and the edema improved.

Her medication was changed to 30 mg prednisolone orally and gradually reduced to 7.5 mg. The frequency of bowel motions was 1-2/day and the liver enzymes improved to normal. Five weeks after the diagnosis of IBD she had cesarean section delivery of her 6th baby girl 2.72 kg and her first baby boy 2.63 kg. Our final diagnosis was IBD, most likely Crohn's disease due to the colonoscopic appearance. The postpartum period was unremarkable and she was followed in the outpatient department. Azathioprine(AZA) 50 mg daily was started and prednisolone was gradually stopped. On her latest follow up she remained asymptomatic maintained on AZA 50mg daily and solofalk 500mg TID.

DISCUSSION

The above presentation of inflammatory bowel disease is unusual. Most of the patients with pregnancy associated IBD are diagnosed before pregnancy and the target in these patients are to keep the disease in remission[1, 4]. During our search we did not come across a case of Crohn's (CD) disease with an onset during pregnancy. Only few cases of ulcerative colitis (UC) were diagnosed during pregnancy [6]. The presence of low grade fever and positive stool culture raises the possibility of infectious diarrhea. However the long duration and unresponsiveness to antibiotic make that unlikely. Pseudomembranous colitis (PMC) after the initial courses of antibiotic was also considered but the colonoscopic, histopathological and laboratory test for toxins made PMC unlikely diagnosis. OGD and colonoscopy are known to be safe during pregnancy with minimal fetal risk[7,8]. Adult onset celiac disease can also present with watery diarrhea but the duodenal mucosa in the OGD was normal with normal small intestinal biopsy. Positive ANA raised vasculitis as another possibility but the P-ANCA and the C-ANCA were negative and the colonic biopsy did not show evidence of vasculitis. Functional symptoms from Irritable Bowel Syndrome (IBS) can be aggravated by pregnancy but though the patient is of type a nervous personality, she did not report past symptoms of IBS. The severity of diarrhea together with unresponsiveness to trial anti-diarrheal medication made IBS unlikely to be the cause of this patient diarrhea. She had low albumin level and low hemoglobin level. This could be explained by the chronicity of diarrhea but may be part of physiological changes related to pregnancy. The amounts and frequency of diarrhea of 12-15 times daily were expected to compromise the physiological weight gain due to pregnancy but this was probably masked by the weight gain due to associated gestational diabetes and twin pregnancy. Presence of secretory diarrhea, skip pattern on colonoscopic examination and the poor response to Mesalamine support the diagnosis of CD more than UC. Small bowel examination by enteroclysis and abdominal Computed Tomograph (CT) were delayed until after delivery. The patient had remarkable improvement on systemic steroids but on the other hand she had poor control of the blood sugar and massive fluid retention with 20 kg weight gain over one week. Preeclampsia was excluded and she responded to fluid restriction, frusemide and gradual reduction of steroid. The patient symptoms were controlled on oral prednisolone and mesalamine until she had elective

cesarean section delivery five weeks after diagnosis. Previous reports on the use of immunomodulators during breast feeding were discouraging but more recently the data showed no significant risk on the infants[9]. After delivery she was maintained on AZA 50 mg daily and mesalamine 500 TID she chose not to breast fed her infants.

CONCLUSION

Though IBD are commonly associated with pregnancy, new onset disease during pregnancy is very rare. The use of the diagnostic modalities like radiological investigations may be limited during pregnancy. The final diagnosis need to be confirmed by histological examination. The response to treatment is similar to non pregnant patients. Close monitoring of the treatment and early diagnosis and management of exacerbation during pregnancy is important to avoid complications.

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Author Information

Hisham O Akbar, MBCh B, FRCPC
Associate Professor Consultant Gastroenterologist & Hepatologist, King Abdul Aziz University Hospital Jeddah Saudi Arabia

Hind I Fallatah, MBCh B, Arab Board and Saudi Board of Internal Medicine, MACP-ASIM
Consultant Gastroenterologist & Hepatologist Assistant Professor, King Abdul Aziz University Hospital Jeddah Saudi Arabia