

Case Report

Inflammatory bowel disease in pregnancy: a report of 7 cases and review of the literature

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Received July 13, 2016; Accepted September 2, 2016; Epub March 15, 2017; Published March 30, 2017

Abstract: *Objective:* To explore the clinical manifestations of inflammatory bowel disease (IBD) in pregnancy. *Methods:* The clinical manifestations, therapy and turnover of 7 cases with IBD in pregnancy admitted in our hospital from 2000 to 2014 were analyzed, and related literature was reviewed. *Results:* Two cases were primary onset at early pregnancy, and 5 cases were of chronic recurrence. One patient showed acute onset at a gestational age of 14 weeks, and subject to induced labor at 19th week of pregnancy, followed by surgical treatment due to digestive tract bleeding. The other 6 cases showed a good outcome after close follow-up and standard treatment. Three patients received colonoscopy with satisfactory tolerance, and no adverse reaction was noticed. One patient received infliximab regularly during pregnancy until lactation, and no recurrence was observed. One patient did not receive vaginal delivery because of a surgical history of anal fistula. One patient had to receive induced labor in the second trimester. The delivery modes of the other 5 cases were in accordance with obstetric indications. *Conclusion:* Appropriate management of IBD before and during pregnancy in a timely and effective manner is crucial for the pregnancy of IBD patients.

Keywords: Pregnancy, breastfeeding, inflammatory bowel disease, therapy

Introduction

Inflammatory bowel disease (IBD), mainly includes ulcerative colitis (UC) and Crohn's disease (CD), affects women in their reproductive years [1-3]. Besides, a higher incidence of IBD is reported in patients after conception [1, 4], which may result in increased incidence of congenital anomalies, prematurity, caesarean section and low birth weight [5-8]. Thus, the effects of disease complications, disease activity and medications on pregnancy and fertility are of key concern to IBD patients [9].

In the past, women with IBD may choose to avoid pregnancy or discontinue medications due to their concerns [4, 10]. However, studies indicated the advantages of maintaining remission before and during pregnancy outweighs the risks of disease flares and related side-effects on the pregnancy outcome [9]. In addition, most of the drugs for the treatment of IBD are safe during pregnancy, and progression in the medical treatment allowed more women

with IBD to enter symptomatic remission [4]. Traces of drugs were detected in breast milk of women received drug therapy, but no major complications for neonates or fetus have been found [4]. Thus, analyzing the clinical manifestations, therapy and outcome of IBD patients during pregnancy is very important for the prognosis.

In our study, the clinical manifestations, therapy and outcome of 7 cases with IBD in pregnancy admitted in our hospital from 2000 to 2014 were analyzed, and related literatures were reviewed. Our study showed that appropriate management of IBD before and during pregnancy in a timely and effective manner is crucial for the pregnancy of IBD patients.

Materials and methods

Patients

The clinical data of 7 cases (age of onset: 24-31 yrs, averaged age: 27.9 yrs) with IBD in preg-

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Table 1. General conditions and clinical data of 7 cases in pregnancy

Case	Age	Diagnosis	Clinical stage	Affected site (s)	Clinical manifestation	Time of final diagnosis	Course of disease
1	34	UC	Chronic recurrent Whole colon Moderate active stage	Whole colon	Diarrhea Bloody purulent stool Fever	Progestation	10 years
2	30	CD	Chronic recurrent Ileocolon Moderate active stage	Whole colon Terminal ileum	Diarrhea Abdominal pain Bloody purulent stool Fever	Progestation	4 years
3	30	UC	Primary onset Whole colon Severe active stage	Whole colon Rectum	Bloody purulent stool Fever	14th week of pregnancy	1 month
4	32	UC	Primary onset Left hemicolon Moderate active stage	Sigmoid colon Rectum	Diarrhea Abdominal pain Bloody purulent stool Fever	9th week of pregnancy	2 month
5	37	CD	Chronic recurrent Ileocolon Moderate active stage	Whole colon Rectum Ileum	Diarrhea Abdominal pain Crissum polyrrhea Difficult defecation	Progestation	11 years
6	29	UC	Chronic recurrent Left hemicolon Moderate active stage	Left hemicolon	Diarrhea Abdominal pain Bloody purulent stool Hematochezia	Progestation	2 years
7	32	UC	Chronic recurrent Left hemicolon Light active stage	Sigmoid colon Rectum	Diarrhea Bloody purulent stool Fever	Progestation	1 year

nancy admitted in Peking Union Medical College Hospital from January 2000 to December 2014 were obtained, and related literature was reviewed. The case history, clinical symptoms, laboratory examination, results of colonoscopy and biopsy, therapy, pregnancy outcome and follow up were recorded for each patient. Written informed consent was obtained from each patient. This study was approved by the Ethical Committee of Peking Union Medical College Hospital.

Methods

The general conditions, clinical manifestations, therapy, pregnancy outcome and prognosis of 7 cases were analyzed, and related literature was reviewed. The diagnosis of IBD was carried out according to the previous description [11]. The severity of IBD was categorized according to the endoscope score. The activity of UC was evaluated according to the Mayo endoscopic subscore system [12]: 0 score, normal or no active lesions; 1 score, mild conditions (e.g. slight erythema, decrease of vascular lake); 2

score, moderate conditions (e.g. obvious erythema, lack of vascular lake, erosion); and 3 score, severe conditions (spontaneous bleeding and formation of ulcer). Also, UC activity was evaluated according to the Truelove-Witts score system in clinical practice. The patient conditions were divided into three groups according to the frequency of diarrhea, presence of bloody stool, body temperature, pulse, hemoglobin and erythrocyte sedimentation rate. The CD activity index (CDAI) was evaluated according to the previous description. The conditions were divided into five categories, including response period (<150 score), active period (≥ 150 score), mild severity (150-219 score), moderate severity (225-450 score), and severe conditions (<450 score).

Results

General conditions and clinical data

The course of disease ranged from 1 month to 11 years (**Table 1**). Among these patients, 2 cases were primary onset at early pregnancy,

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Table 2. Nutritional state of 7 cases with IBD in pregnancy

Case	Body mass index before pregnancy (BMI>18.5)	Hemoglobin (>110 g/L)	Seralbumin (35-55 g/L)	Serum iron (70-150 µg/dl)	Total iron binding capacity (200-400 µg/dl)	Transferin saturation (25-35%)	Ferritin (14-336 ng/ml)	Folacin (>3 pg/ml)	Vitamin B12 (180-914 ng/ml)
1	18.3	66~101	29~32	62	209	30	80	10	898
2	20.1	78~108	31~35	65	215	32	94	17	765
3	19.5	44~89	26~31	58	178	37	119	26	259
4	23.5	93~105	29~35	60	194	35	248	22	710
5	18.4	87~112	30~39	51	169	28	235	19	332
6	21.2	89~108	30~34	54	188	31	228	21	376
7	19.8	54~79	24~28	28	190	14	44	7	296

among which one patient showed acute onset at a gestational age of 14 weeks, while the other showed onset a gestational age of 9 weeks. The other 5 cases were of chronic recurrence with a frequency of 1 to 5 times. The main clinical manifestations of the 7 cases were diarrhea, abdominal pain, bloody stool and fever. The enteroscopy findings were as follows: patients with UC showed diffuse inflammation in mucous membrane, multiple ulcer, erosion and pseudopolyp; patients with CD showed noncontinuous changes or segmental changes, inflammation, slabstone like hyperplasia, and microtubule ulceration. The pathological findings of patients with UC were featured by inflammation in mucous layer and submucosa, and crypt abscess, while patients with CD showed segmental inflammation, and non-caseous necrosis granuloma.

Nutritional state in pregnancy

Among these patients, body mass index (BMI) before pregnancy in 2 cases were <18.5, another 5 cases had normal BMI. All the 7 cases had hypoproteinemia and iron deficiency anemia during pregnancy, of which 2 showed severe anemia, 4 with moderate anemia, and 1 with light anemia. All the 7 cases had no folacin and vitamin B₁₂ deficiency (**Table 2**).

Morbid state before pregnancy and therapy of IBD during pregnancy

Among the 7 cases, 5 were of chronic recurrence, and disease assessment was performed prior to conception. Pregnancy was prepared once the conditions were relieved. One patient terminated the medication upon pregnancy, and relapse was reported by the patient at a gestational age of 19 weeks featured by diarrhea, bloody purulent stool and hyperpyrexia.

The conditions were severe according to the Truelove-Witts score. This patient received enteroscopy at a gestational age of 23 weeks, and the Mayoscore was 3. Hormone and biological therapy were refused by the patient. On this occasion, oral administration of mesalazine and enema therapy were used, and the disease was effectively controlled. The patient determined the medication during the lactation, and the disease relapsed 2 months after delivery, the disease was relieved after received sufficient hormone and mesalazine. The disease of the other 4 cases were controlled after close follow-up and standard treatment. Among the 4 patients, one received infliximab regularly during pregnancy until lactation, and no recurrence was observed (**Table 3**).

Among these patients, 2 cases were primary onset at early pregnancy. One patient showed acute onset at a gestational age of 14 weeks featured by bloody purulent stool and fever. This patient received enteroscopy a gestational age of 18 weeks, and was finally diagnosed with UC. She chose to receive induced-labor at a gestational age of 19 weeks. Afterwards, the patient showed progression of the disease, manifested as digestive tract bleeding and hemorrhagic shock. For the treatment, colonic branch embolization, fistula of ileum and pan-colectomy under laparoscope were given. Enteroscopy findings in the recent 2 months indicated: inflammatory exudate, mucosal erosion, and crypt abscess. The Mayo score was 2. She received mesalazine and methylprednisolone and was advised to prepare for pregnancy after disease remission. The other patient showed onset a gestational age of 9 weeks, and was diagnosed with UC through enteroscopy performed at a gestational age of 19 weeks. The patient showed complete response

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Table 3. Morbid state before pregnancy, medical treatment and surgical treatment for patients with IBD during pregnancy

Case	Disease assessment before pregnancy	Receiving operation or not before pregnancy	Morbid state during pregnancy	Medical treatment during pregnancy	Effect of medical treatment	Receiving operation or not during pregnancy	Postpartum recurrence or not	Recent treatment	Recent disease control
1	Remission	Not	Controlled	Blood transfusion, mesalazine, methylprednisolone, sulfasalazine	Satisfaction	Not	Not	Mesalazine Hormone	Remission
2	Remission	Anal fistulectomy	Controlled	Mesalazine	Satisfaction	Not	Not	Mesalazine	Remission
3	Primary onset at 14th week of pregnancy	Not	Lower gastrointestinal hemorrhage, hemorrhagic shock	Received enteroscopy at 18th week of pregnancy, UC was final diagnosed, received mesalazine and sufficient hormone after induced labor	Poor	Selective embolization of the colon, Laparoscopic ileum stoma, total colon resection under laparoscope		Mesalazine Enema, oral hormone	Active
4	Primary onset at 9th week of pregnancy	Not	Active	Received enteroscopy at 19th week of pregnancy, UC was final diagnosed, received mesalazine and sulfasalazine	Satisfaction	Not	Not	Mesalazine	Remission
5	Remission	Not	Remission	Received infliximab regularly	Satisfaction	Not	Not	Infliximab	Remission
6	Remission	Not	Remission	Mesalazine	Satisfaction	Not	Not	Mesalazine	Remission
7	Remission	Not	Self drug discontinuance after gravidity, and the disease progressed	Received enteroscopy at 23 h week of pregnancy, moderate active was assessed, received blood transfusion, anti-infection. Hormone and biological preparation was advised, the patients refused, they received mesalazine	Effective	Not	Self drug discontinuance, recurrence in lactation	Mesalazine Hormone	Remission

Table 4. Treatment, pregnancy outcome and prognosis for patients with IBD during pregnancy

Case	Adverse reaction during pregnancy	Treatment	Mode of delivery	Body weight of neonatus (g)	Body length of neonatus (cm)	Apgar score of neonatus	Lactation	Growth and development of neonatus
1	Severe anemia, hypoproteinemia, aura late abortion, threatened premature labor	Blood transfusion, iron supplement, nutritional support, fetal heart monitoring, promoting fetal lung maturation	Cesarean section	2110 (SGA)	45	1' 10 5' 10	Artificial feeding	Normal
2	Moderate anemia, hypoproteinemia	Iron supplement, nutritional support, maternal and child care	Cesarean section	2640	48	1' 10 5' 10	Artificial feeding	Normal
3	Primary UC, metaphase induced labor, hypoproteinemia	—	—	—	—	—	—	—
4	Primary UC, mild anemia, hypoproteinemia	Iron supplement, nutritional support, maternal and child care	Vaginal delivery	3050	50	1' 10 5' 10	Breastfeeding for 10 months	Normal
5	Moderate anemia, hypoproteinemia	Iron supplement, nutritional support, maternal and child care	Cesarean section	3200	50	1' 10 5' 10	Artificial feeding	Normal
6	Moderate anemia, hypoproteinemia	Iron supplement, nutritional support, maternal and child care	Cesarean section	3100	49	1' 10 5' 10	Artificial feeding	Normal
7	Severe anemia, hypoproteinemia	Blood transfusion, iron supplement, nutritional support, maternal and child care	Vaginal delivery	3980	51	1' 10 5' 10	Breastfeeding for 2 months, stopping breastfeeding due to recurrence	Normal

Note: FGR: fetal growth restriction; SGA: small for gestation age infant.

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after medication of mesalazine and sulfasalazine, and no recurrence was observed after delivery. Among the 7 cases, 3 received colonoscopy with satisfactory tolerance, and no adverse reaction was noticed.

Treatment, pregnancy outcome and prognosis

All the 7 cases had hypoproteinemia, among which 2 received blood transfusion during pregnancy due to severe anemia. The other 5 cases had mild or moderate anemia, and iron supplement and nutritional support were given accordingly. One patient received oxygen inhalation, inhibition of uterine contraction, and promoting fetal lung maturation due to advanced threatened abortion a gestational age of 26 weeks, and threatened premature labor a gestational age of 33 weeks. One patient chose cesarean delivery because of a surgical history of anal fistula. The delivery modes of the other 5 cases were in accordance with obstetric indications. One newborn was small for gestational age (SGA), and the other 5 were showed normal body weight and height. The growth and development of 6 cases were normal after one year follow up. Two patients chose breast-feeding, and four chose artificial feeding due to the fear of drug effects (**Table 4**).

Discussion

Genetic or environmental factors (such as diet, smoking and life style) play an important role in the pathogenesis of IBD [13-16]. Compared with northern Europe, USA and other Westernized countries, the incidence of IBD are much lower in Asia [17, 18]. However, its incidence have increased in some Asian countries in recent years [13]. In China, more and more IBD cases have been reported in the recent years, and the increased incidence might be due to the environmental and/or genetic factors [14, 19]. The activity of IBD could affect pregnancy outcome, the pregnancy outcome could also lead to the recurrence and aggravation of IBD [4]. Thus, treatment and diagnosis of IBD patients during pregnancy is very important.

Colonoscopy play a central role in the diagnosis and therapy of IBD [20]. While safety of colonoscopy during pregnancy remained controversial [21]. About 20,000 females annually experience safe colonoscopy during pregnancy worldwide [21]. Generally, colonoscopy are con-

sidered to be safe during pregnancy with no evidence of adverse outcome, however, it should be reserved for strong indications and should be done in the second trimester whenever possible [22, 23]. To avoid vena cava compression, pregnant patients should be placed in left lateral position before, during and after colonoscopy [22]. In our study, three patients received colonoscopy at a gestational age of 18, 19 and 23 weeks respectively, with satisfactory tolerance, and no adverse reaction was noticed.

Pregnancy might affect the natural course of IBD, and the primary onset at pregnancy is usually severe and life-threatening [22, 24]. Abramson *et al.* reported that in 5 primary onset UC cases during pregnancy, in which 4 died of outbreak of disease after delivery or abortion [24]. In our study, 2 cases were primary onset at early pregnancy. One patient received enteroscopy at a gestational age of 18 weeks, and was diagnosed with severe UC. Then, the patient subjected to induced labor at a gestational age of 19 weeks, followed by pan-colectomy due to digestive tract bleeding and hemorrhagic shock. In contrast, the other patient with UC received mesalazine and sulfasalazine showed complete response after treatment, and no recurrence was observed. The difference of outcome in the two patients may be related to the the deterioration of UC by induced labor.

Breastfeeding has many beneficial effects on child health, and it is recommended as the primary nutrition form for infants [25]. Studies showed that breastfeeding could not increase the risk of IBD flare and may even has a protective effect against disease relapse in the postpartum period [26, 27]. Kane *et al.* reported an increased rate of disease flare in women who breastfed, which was attributed to discontinuation of medication [28]. In our study, one patient were self drug discontinuance after gravidity, and the disease relapsed at 19th week of pregnancy. The disease in the other 4 cases were controlled after close follow-up and standard treatment.

Women with IBD could increase the risk of adverse pregnancy outcome, which depended on the disease severity [22]. In our study, one newborn was SGA, and the remaining 5 were of normal gestational age. The growth and development of 6 cases were normal after one year

follow up. Our results may be related with the small cases.

The treatment of IBD during pregnancy includes nutritional support, medication and surgery [22]. Acute flares during pregnancy has a high risk of adverse outcome, and appropriate treatment should be performed in those patients. Most drugs used for the treatment of IBD is low risk during pregnancy, while thalidomide and methotrexate are contraindicated. Nutritional deficiencies such as vitamin B₁₂, folate, vitamin D and iron should be evaluated and treated as required. Surgery is required in approximately 70-80% of patients with CD and 30-40% of patients with UC [29-31]. Surgery is relatively safe but there is some limitations such as spontaneous abortion when operation in the first trimester and preterm labor in the third trimester [30]. Surgical procedures included hemicolectomy, proctocolectomy, ileostomy, and segmental resection. To our best knowledge, the choice of surgery is depend on the age, nutrition and disease conditions, complications, as well as the length of mesoileum and blood vessel distribution. Currently, the ileostomy is generally preferred after primary anastomosis, to decrease the risk of postoperative complications [22].

The mode of delivery should primarily be dictated by obstetric indications, but it should be combined with the colorectal surgeon to avoid the post partum sphincter impairment [22, 32, 33]. Most patients with IBD can deliver vaginally, but caesarean section should be performed if the obstetric risk is increased for other reasons [22, 34]. Indications for caesarean section are in patients with active perineal disease or in cases after ileal pouch anal anastomosis (IPAA) [35-37], which could avoid the risk of anal sphincter injury or worsening of perianal disease [38]. In our study, one patient selected caesarean section because of the risk of anal sphincter damage. The delivery modes of the other 5 cases were in accordance with obstetric indications.

In conclusion, the activity of IBD could affect pregnancy outcome, the pregnancy outcome could also lead to the recurrence and progression of IBD. Colonoscopy are considered to be safe during pregnancy with no evidence of adverse events. Most patients with IBD can deliver vaginally, but caesarean section should

be performed in patients with active perineal disease or in cases after IPAA.

Acknowledgements

This study was supported by the National Natural Scientific Foundation (No. 81270717, and No. 81490743).

Disclosure of conflict of interest

None.

Authors' contribution

Xu Y wrote the manuscript; Tian B, Ma L, and Qian J did the data collection; Song Y, Zhou X and Qi Q did the data analysis; Liu J revised the manuscript.

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