Original Article

Meconium peritonitis: Prenatal diagnosis of a rare entity and postnatal management

Keiichi Uchida*, Yuhki Koike, Kohei Matsushita, Yuka Nagano, Kiyoshi Hashimoto, Kohei Otake, Mikihiro Inoue, Masato Kusunoki

Department of Gastrointestinal and Pediatric Surgery, Mie University Graduate School of Medicine, Mie, Japan

Summary   The aims of this study were to review our therapy and outcome for meconium peritonitis (MP) patients, and to clarify predictors of postoperative morbidity and mortality. We retrospectively reviewed a total 15 patients with MP who received surgical intervention at our institute from December 1990 to November 2012. Diagnosis of MP was confirmed by operative findings. We analyzed the relationship between outcome and patients' factors including patients' characteristics, prenatal diagnosis, type of MP, general condition, and surgical procedure. There was no relationship between outcome and the following factors: gender, gestational age, body weight at birth, delivery type, Apgar score, prenatal diagnosis, types and causes of MP, and surgical procedure. However, the preoperative presence of circulation deficiency and serum CRP values were statistically significant predictors of outcome in our MP patients. Prenatal diagnosis is essential for the first step of perinatal therapy for MP. Surgical strategy should be selected according to the information of prenatal diagnosis. Early surgical procedures to reduce systemic and abdominal inflammation just after birth may improve the outcome of severe MP cases.

Keywords: Meconium peritonitis, prenatal diagnosis, surgery

1. Introduction

Meconium peritonitis (MP) is an aseptic chemical peritonitis, which results from perforation of the gut in utero (*1*). Possible causes and pathogenesis of MP include ischemia in the mesentery, volvulus, intestinal atresia, meconium plugs, internal hernia, Hirschsprung's disease, colon atresia, torsion of a fallopian tube cyst, and cystic fibrosis (*1-7*). It can have a wide range of presentations and is classified into 3 types as follows: generalized, cystic, and fibroadhesive types (*1*). Fifty years ago, the mortality rate of MP was reported as approximately 70% (*8*). Recently, the survival rate for MP increased to over 90% (*9*). This improvement is the result of an advance in fetal diagnostic techniques and

proper management including surgical procedures and intensive care after birth (*2,10,11*).

All cases of MP have the same etiology; perforation of the intestine in utero and intraperitoneal inflammation by subsequent spillage of meconium. The differences among disease types depend on the timing of gut perforation during pregnancy. Meconium is clearly a strong pro-inflammatory mediator as evidenced by in vitro stimulation and clinical disease (*12-14*). In animal models, procoagulant activity and tumor necrosis factor-α (TNF-α) production by macrophages are significantly increased in response to meconium stimulation (*15*).

Several studies have evaluated the predicting factors for patients' outcome, such as the accuracy or sonographic features of prenatal diagnosis, type of MP at operation, and the patient's general condition (*2,10,16-18*). Generally, preoperative systemic inflammatory status and poor preoperative condition increase postoperative morbidity and mortality in adult patients (*19*). However, there has been no clarification on the relationship between US findings and systemic inflammatory status in the fetus or neonate with MP. In this study, we reviewed the therapy and outcome

*Address correspondence to:
Dr. Keiichi Uchida, Department of Gastrointestinal and Pediatric Surgery, Mie Universty Graduate School of Medicine
2-174 Edobashi, Tsu, Mie 514-8507, Japan.
E-mail: ucchie@clin.medic.mie-u.ac.jp

for MP at our institute, and analyzed the prenatal US examination, postnatal patient's condition, and surgical outcome.

2. Patients and Methods

We retrospectively reviewed a total 15 patients with MP who received surgical intervention at the neonatal pediatric surgical unit of the Perinatal and Maternal Care Center in Mie University Hospital, Mie, Japan. Diagnosis of MP was confirmed by operative findings. MP was divided into 3 types as follows: generalized (G type), cystic (C type), and fibroadhesive type (F type) (*1*). We reviewed clinical course of our patients with MP, and analyzed predictors of outcome. Eleven of 15 patients received prenatal US examination by gynecologists. Typical findings such as dilated bowel, fetal ascites, pseudocyst and polyhydramnios just before delivery were evaluated in this study. Polyhydramnios is defined as an amniotic fluid index > 24 cm.

After birth, patients were transferred to the neonatal intensive care unit in the PMCC and evaluated by neonatologists and pediatric surgeons. Some patients received intensive care including cardio-pulmonary support. Our surgical strategy for MP is a two- or three-stage approach with abdominal drainage or temporary enterostomy and elective reconstruction of intestinal continuity (stoma closure) according to the cases. The two-stage approach consists of enterostomy and elective stoma closure. The three-stage approach consists of the abdominal drainage procedure, enterostomy and elective stoma closure. Abdominal drainage was performed using a Penrose drain or catheterization under regional or general anesthesia. Recently, the first choice for cystic type MP was abdominal decompression by catheterization closed drainage.

All patients were investigated after obtaining the parent's or guardian's informed consent to participate in this study. This study was approved by the Mie University Graduate School of Medicine Ethics Review Board.

All statistical analyses were performed using StatView software (version 5; Abacus Concepts, Berkeley, CA, USA). The results were expressed as median or means ± standard deviation (S.D.). The Mann-Whitney *U* test and Chi-square test were used for comparisons among unpaired groups. *P* values of less than 0.05 were considered statistically significant.

3. Results

The patients' characteristics are shown in Table 1. The 15 patients consisted of 9 males and 6 female babies. Four of 15 patients without prenatal diagnosis were referred to our institute if abdominal distension, bilious vomiting, or pneumoperitoneum was noted after birth. In 11 of 15 patients, prenatal diagnosis using

Table 1. Patients' Characteristics

Patients	15
Gender (M:F)	9:6
Gestational age* (weeks and days)	36 (31w3d-39w5d)
Body weight at birth* (g)	2992 (1770-3600)
Delivery type (NVD: CS)	9:6
Apgar score at 1 min*	6 (2-10)
Admission day after birth*	1 (1-3)
Operation day after birth*	1 (1-3)
Prenatal diagnosis (yes: no)	11:4
Polyhydramnios	11 (26-35w)
Bowel dilatation	8 (26-35w)
Ascites	5 (31-33w)
Pseudocyst	2 (35w)
Type of MP; G/C/F	3/4/8
Cause of MP; V/IA/CA	7/7/1
Follow up period* (months)	76 (4-264)

* Median; NVD, normal vaginal delivery; CS, caesarian section; MP, meconium peritonitis; G, generalized; C, cystic; F, fibroadhesive; V, volvulus; IA, intestinal atresia; CA, colon atresia.

ultrasonography (US) was made from 26 to 35 weeks of gestational age. Polyhydramnios was detected in 11 patients, bowel dilatation in 8 patients, ascites in 5 patients, and pseudocyst in 2 patients. MP consisted of 3 G types, 4 C types, and 8 F types. Causes of MP consisted of intestinal atresia in 7 patients, volvulus in 7 patients, and colon atresia in 1 patient. No associated anomaly was found in this series. None of the patients had cystic fibrosis because of the hereditary characteristics of Japanese. The median follow up period was 76 months (range, from 4 to 264 months).

At the first surgical procedure, enterostomy was performed in 9 patients, drainage by laparotomy or catheter in 3 patients, and enterostomy after decompression in 3 patients according to postnatal US or intraoperative findings. After the 1st procedure, 5 morbidities (33.3%) occurred including wound infection in 1 patient, intestinal fistula in 1 patient, abdominal abscess in 1 patient, cerebral hemorrhage due to disseminated intravascular coagulation (DIC) in 1 patient, and sepsis in 1 patient. After the 2nd procedure, 13 patients had intact survival, 1 patient had cerebral palsy, and 1 patient died due to multiple organ failure (MOF).

In order to clarify prognostic factors, we examined the relationship between prognosis and several factors. We divided 15 patients into 2 groups according to the occurrence of morbidity after the 1st procedure; Group A without morbidity or Group B with morbidity (Table 2). There were no differences in types and causes of MP between Groups A and B. Surgical procedures had no relationship with patients' morbidities after the 1st procedure. In the preoperative condition, there were no differences between the groups for gender, gestational age, body weight at birth, delivery type, Apgar score, and prenatal diagnosis. However, there was a significant difference between the groups for preoperative presence of circulation deficiency and serum CRP values (Group

Table 2. Patients characteristics with or without morbidities

Items	Group A (*n* = 10) (without morbidity)	Group B (*n* = 5) (with morbidity)	*P* value
Gender (M:F)	5:5	4:01	*n.s.*
Gestational age (weeks)	36.3 ± 1.6	35.7 ± 2.8	*n.s*
Body weight at birth (g)	3025 ± 292	2746 ± 593	*n.s*
Delivery type (NVD: CS)	6:4	3:2	*n.s*
Apgar score at 1 min	6.4 ± 2.2	6.3 ± 3.8	*n.s*
Admission day after birth	1.1 ± 0.3	1.6 ± 0.9	*n.s*
Operation day after birth	1.3 ± 0.7	1.6 ± 0.9	*n.s*
Prenatal diagnosis (yes: no)	8:2	3:2	*n.s*
Preoperative condition			
Circulation failure (yes: no)	0:10	3[†]:2	0.006
Base excess of BGA	-6.7 ± 2.9	-5.4 ± 1.8	*n.s*
CRP values (mg/dL)	0.95 ± 1.0	6.7 ± 5.9	0.027
Ascites culture (positive: negative)	0:10	1[‡]:4	*n.s*
Type of MP; G/C/F	2/3/5	1/1/3	*n.s*
Cause of MP;V/IA/CA	5/5/0	2/2/1	*n.s*
Surgical procedure (E/EAD/D)	6/2/2	3/1/1	*n.s*
Follow up period* (months)	92 (13-233)	76 (12-264)	*n.s*

* Median. The Mann-Whitney *U* test and Chi square test were used for analysis. [†] hypotension 2 and persistent pulmonary hypertension 1, [‡] *E. coli* and *K. oxytoca*. NVD, normal vaginal delivery; CS, caesarean section; MP, meconium peritonitis; G, generalized; C, cystic; F, fibroadhesive; V, volvulus; IA, intestinal atresia; CA, colon atresia; BGA, blood gas analysis; CRP, C-reactive protein; E, enterostomy; EAD, enterostomy after decompression; D, drainage.
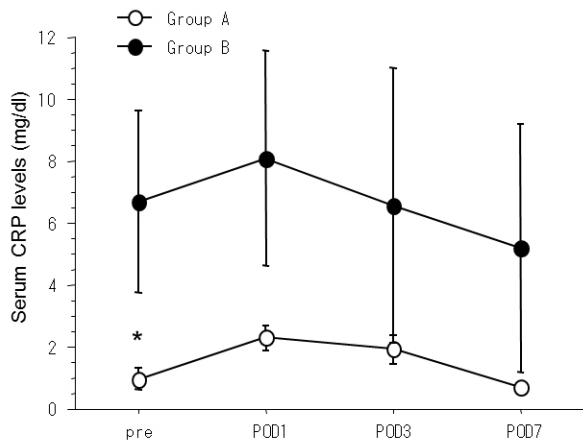

Figure 1. Serial changes in perioperative serum CRP values in Groups A and B after the 1st surgical procedure at our institute. Preoperative serum CRP values were significantly different between groups A and B (*p* = 0.0272).

A, *p* = 0.0062 and Group B, *p* = 0.0272, respectively). Figure 1 shows serial changes in perioperative serum CRP values. General inflammation in Group A patients was more severe than Group B patients during the perioperative period. Preoperative serum CRP values were significantly different between Groups A and B (*p* = 0.0272).

We present here an important case with Giant cystic type MP caused by intestinal volvulus had persistent pulmonary hypertension and systemic inflammatory syndrome preoperatively in Group B (Figure 2). After elective caesarean section (CS) because of non-reassuring fetal status with circulation deficiency, we immediately performed abdominal decompression by closed drainage catheterization (240 mL bilious discharge). After the patient's general condition was stabilized by intensive care with nitric oxide inhalation and Prostaglandin E1 administration, tube enterostomy was created under general anesthesia several hours later. After 2 weeks later, she received stoma closure operation with easy adhesiolysis and postoperative course was uneventful without wound infection and she is presently in good health.

4. Discussion

Possible causes and pathogenesis of MP include ischemia in the mesentery, volvulus, intestinal atresia, meconium plugs, internal hernia, Hirschsprung's disease, colon atresia, torsion of a fallopian tube cyst, cystic fibrosis and others (*1-7*). In this study, the most common causes of MP were intestinal atresia (47%) and volvulus (47%). This finding differs from other reports from Asian countries. Nam *et al*. (*9*) reported 31 MP patients who had intestinal atresia in 14 patients (45%), volvulus in 2 patients (6%), and uncertain ileal perforation in 10 patients (32%). Kamata *et al*. (*20*) reported 20 MP patients who had intestinal atresia in 18 patients (90%) and meconium ileus in 2 patients (10%). In our study, we also didn't find any cases of cystic fibrosis because of their rarity in Asian countries. MP can have a wide range of disease causes and clinical presentations. It is important to understand that patients in each clinical study for MP may have a different background compared with other studies elsewhere.

In our study, prenatal diagnosis was made in 73% of patients. The US findings with suspected MP were polyhydramnios (100%), bowel dilatation (53%), ascites (33%), and pseudocyst (13%). Several studies have assessed the accuracy of prenatal US examination
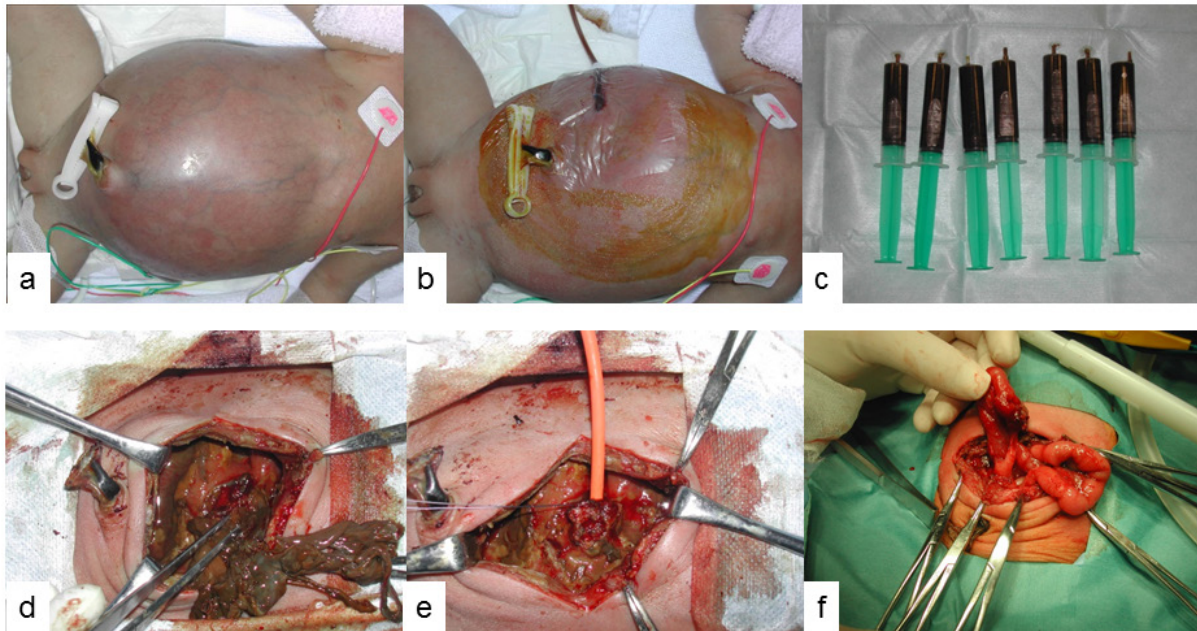
Figure 2. We present here an important case with Giant cystic type MP caused by intestinal volvulus had persistent pulmonary hypertension and systemic inflammatory syndrome preoperatively. After elective caesarean section (CS) because of non-reassuring fetal status with circulation deficiency, we immediately performed abdominal decompression by closed drainage catheterization **(a, b, c)**. After the patient's general condition was stabilized by intensive care with nitric oxide inhalation and Prostaglandin E1 administration, tube enterostomy was performed under general anesthesia several hours later **(d, e)**. After 2 weeks later, she received stoma closure operation with easy adhesiolysis **(f)** and postoperative course was uneventful without wound infection.

for diagnosing meconium peritonitis and predicting patients' outcomes (*2,16,18*). Previous reports have also demonstrated the relationship between the type of MP and patients' outcome (*9,11,20,21*). The present study did not show a significant relationship between prenatal diagnosis or types of MP and patients' outcome. A few case reports have recommended early surgical management including abdominal decompression to babies with suspected C type MP (*1,12,22*). We also recommend the surgical strategy combined with cyst drainage decompression followed by enterostomy just after birth and elective surgery at a later date for C type MP. The postnatal surgical procedure is dependent on the patients' clinical presentation and general condition.

Our surgical strategy is a two-stage approach with temporary enterostomy or drainage and delayed reconstruction of intestinal continuity. Nam *et al*. (*9*) reported that primary resection and anastomosis of the involved intestinal segment was carried out in 70% of MP patients they experienced, with an excellent morbidity rate of 2.4%. The present study demonstrated that there is no relation between surgical procedure and outcome. However, the first surgical approach after birth should be selected for complete drainage and prevention of bacterial infection.

Meconium is a complex mixture of bile salts, cell debris, and proteins. Spillage of these constituents has been shown to activate immune cells including macrophages (*23,24*). Macrophages infiltrate into the peritoneum and participate in a range of cellular

functions, including phagocytosis, release of chemical mediators, and antibody-dependent cell-mediated cytotoxicity (*25*). Experimental animal studies have demonstrated that TNF-α production by macrophages is significantly increased in response to meconium stimulation (*15*). Exaggerated production of chemical mediators including TNF-α enhances fibrin deposition and severe intra-abdominal adhesion, resulting in short bowel syndrome due to massive bowel resection or poly-surgery. Moreover, if sealing of the perforation does not take place, huge abdominal cyst formation and progressive pro-inflammatory cytokine reaction with ascites collection may cause fetal cardiac insufficiency, non-reassuring fetal status, preterm labor, and a poor general condition of the infant after birth.

In this study, we demonstrated that postnatal circulation deficiency and serum CRP values are predicting factors for morbidities and mortalities of MP patients. Shyu *et al*. (*18*) also demonstrated that persistent ascites and postnatal persistent pulmonary hypertension of newborns significantly correlate with neonatal mortality. The present study also demonstrated that fetuses with a severe systemic inflammatory status were likely to receive Caesarean section due to non-reassuring fetal status or require intensive care due to cardio-pulmonary insufficiency after birth. Moreover, they had a high morbidity rate after postnatal clinical course compared with fetuses with no inflammatory status. In order to improve the critical condition of patients, surgical intervention in utero such as fetal paracentesis

may be beneficial by reducing intraabdominal pressure and removing inflammatory debris and cytokines (*26,27*).

In conclusion, prenatal diagnosis is essential for the first step of perinatal therapy for MP. Timing of delivery and fetal intervention according to fetal conditions should be discussed with gynecologists, neonatologists, and neonatal pediatric surgeons in perinatal and maternal care centers. The surgical strategy should be selected according to the information of prenatal diagnosis. Proper surgical procedures for reducing systemic and abdominal inflammation after birth may improve the outcome of severe MP cases.

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