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Clinical Features and Outcomes of Perinatally Diagnosed Meconium Peritonitis

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Objective: Meconium peritonitis (MP) is defined as sterile chemical peritonitis, resulting from intrauterine bowel perforation. MP is rare but has high morbidity and mortality in neonates. We aimed to review the treatment and clinical course of MP, and to find out the possible relationship between perinatal parameters and outcomes.

Methods: All patients diagnosed with MP between February 2006 and October 2016 were investigated retrospectively. MP was diagnosed with prenatal ultrasonography and the types of MP were identified intraoperatively. Findings of prenatal ultrasonography, gestational age, gender, birth weight, delivery type, APGAR score, clinical symptoms, causes of MP, mortality and morbidity, and hospital stay were analysed.

Results: Thirteen patients were antenatally diagnosed with MP. Median gestational age was 37 weeks. All patients were diagnosed using prenatal ultrasonography. Calcification was found in 13 patients, bowel dilatation in 8, fetal ascites in 7, polyhydramnios in 6, and pseudocyst in 3. Five were females and 8 were males. Median birth weight was 2,930 g. Symptoms of abdominal distension were reported in 10 patients, bilious vomiting in 2, pneumoperitoneum in 2, and no symptoms and signs of MP in 1. One patient recovered with conservative management and the other 12 patients required surgery. All patients who underwent surgery had underlying pathologic causes; jejunoileal atresia, ileal perforation and transverse colonic perforation. Two cases of mortality occurred.

Conclusion: The mortality patients were haemodynamically unstable and had received preoperative pressor agents and ventilator care. More studies are needed to investigate the correlation between mortality and preoperative vital status.

Key Words: Fetal ultrasonography, Intrauterine bowel perforation, Meconium peritonitis, Prenatal sonography

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Introduction

Meconium peritonitis (MP) is defined as intrauterine bowel perforation caused by mesenteric ischemia, intestinal atresia, volvulus, intussusceptions, meconium plug syndrome, inguinal hernia, infection, Hirschspurng's disease, cystic fibrosis (CF) and others.[1-4] Incidence of MP is estimated at 1:30,000.[5,6] The survival rate of patients with MP has been increasing;[7-9] however, there is still a strong demand for surgical intervention in patients with MP. MP is rare but fatal; therefore, cooperation of the perinatal medical team, including obstetricians, neonatologists, and pediatric surgeons is essential. This study aimed to review the treatment and clinical course of MP, and to find out the possible relationship between perinatal parameters and outcomes over 10 years.

Methods

Thirteen patients were perinatally diagnosed with MP between February 2006 and October 2016 in our center. The patients' medical records were reviewed retrospectively. A total of 14 patients were prenatally diagnosed with MP or suspicious of MP by obstetricians, and referred to our services postnatally. One patient was excluded because the infant did not have postnatal symptoms and signs of MP, nor postnatal radiologic abnormalities; the infant's prenatal ultrasonography included fetal ascites, calcifications with meconium pseudocyst. Thirteen patients were confirmed as MP using postnatal imaging studies as well as symptoms and signs. We analysed the ultrasonographic findings of prenatal and postnatal periods, demographics, clinical features, and treatment of MP. The variables we investigated were age, gender, gestational age (GA), birth weight (BW), delivery type, Apgar score, clinical symptoms and signs, laboratory findings, radiologic and ultrasonographic findings, types of MP, possible causes of MP, operative methods and post-operative outcomes. The prenatal ultrasonographic images were reviewed by an expert obstetrician. Fetal intra-abdominal calcifications, fetal bowel dilatations, ascites, polyhydramnios, and meconium cyst were findings indicating MP. Prenatal ultrasonography findings were scored according to Zangheri's scoring system: grade 0, isolated calcification; grade 1, intra-abdominal calcifications and ascites or pseudocyst or bowel dilatation; grade 2, two associated findings, and grade 3, three associated findings.[10] The most important factors of indication for surgery were symptoms and signs as well as underlying anatomical causes. The types and possible causes of MP were confirmed intraoperatively. This study was approved by the ethics committee/institutional review board of Keimyung University Dongsan Medical Center. Statistical analysis was performed by SPSS software version 23.0 (IBM Inc., Armonk, NY, USA). Fisher's exact test and Mann-Whitney *U*-test were used to determine the statistical differences of post-operative outcomes. $P<0.05$ was considered as statistically significant.

Results

Among 13 patients who were perinatally diagnosed with MP, 8 were males and 5 were females. Median gestational age at birth was 37 weeks (range, 31^{+1}–39^{+3} weeks and days). Median birth weight was 2,930 g (range, 2,020–4,000 g). Ten patients were delivered with Caesarean section and 3 with normal spontaneous vaginal delivery. Median APGAR score in 1-minute and 5-minute was 7 (range, 1–8) and 8 (range, 5–9), respectively. Median gestational age of detecting fetal abnormality was 28 weeks (range, 24–35 weeks). All of the 13 patients underwent prenatal ultrasonography and were diagnosed with MP. Intra-abdominal calcification was the most common finding (n=13) followed by fetal bowel dilatation (n=8), ascites (n=7), polyhydramnios (n=6) and meconium cyst (n=3) (Table 1). Each patient's specific characteristics were described: gender, GA at prenatal diagnosis, GA at birth, birth weight, prenatal sonography scoring, types and causes of MP, operatie strategy and survival (Table 2).

Postnatal symptoms and signs included: abdominal distension (n=10), vomiting (n=2), pneumoperitoneum (n=2), white meconium (n=1) and no meconium passage (n=1). One of the

Table 1. Clinical Characteristics of Meconium Peritonitis Patients

Characteristic	N=13
Gender	
Male/female	8/5
Gestational age (wks and days)	37 (31^{+1}–39^{+3})
Body weight at birth (g)	2,930 (2,020–4,000)
Delivery type	
NSVD/C-sec	3/10
APGAR score	
1 min/5 min	7 (1–8)/8 (5–9)
GA of detecting fetal abnormality (wks)	28 (24–35)
Prenatal USG (prenatal diagnosis 13/13, 100%)*	
Intra-abdominal calcification	13
Fetal bowel dilatation	8
Ascites	7
Polyhydraminos	6
Meconium cyst	3

Values are presented as number or median (range).
Abbreviations: NSVD, normal spontaneous vaginal delivery; C-sec, Caesarean section; GA, gestational age; USG, ultrasonography.
*Overlapped with 2 or more findings.

Table 2. Characteristics of Patients with Perinatally Diagnosed MP

No.	Gender	GA at prenatal diagnosis	GA at birth (weeks and days)	Birth weight (g)	Prenatal Sonography Scoring*	Type	Cause of MP	Operative strategy	Survival
1	M	25	37^{+3}	3,360	3	C	Jejunal atresia	Enterostomy	Y
2	M	29	35^{+6}	4,000	3	C	Jejunal atresia	Segmental resection and anastomosis	Y
3	M	27	38^{+3}	3,260	1A	C	Ileal atresia	Segmental resection and anastomosis	Y
4	M	24	37^{+0}	2,930	1A	H			
5	M	24	37^{+2}	2,930	2	C	Ileal perforation	Enterostomy	Y
6	F	28	33^{+2}	2,310	3	C	Ileal atresia	Enterostomy	Y
7	F	32	38^{+4}	2,840	3	G	Ileal atresia	Enterostomy	Y
8	F	25	38^{+6}	3,960	1C	G	Jejunal atresia	Segmental resection and anastomosis	Y
9	M	32	38^{+0}	2,890	2	F†	Ileal atresia	Segmental resection and anastomosis	Y
10	M	28	31^{+1}	2,020	1A	G	Ileal perforation	Enterostomy	N
11	F	34	35^{+4}	2,410	2	F†	Ileal atresia	Enterostomy	Y
12	M	32	38^{+4}	2,690	2	G	Ileal atresia	Enterostomy	N
13	F	25	39^{+3}	3,630	3	C	Transverse colonic perforation	Primary closure	Y

Abbreviations: MP, meconium peritonitis; GA, gestation age; M, male; C, pseudocyst type; Y, yes; H, healed type; F, female; G, generalized peritonitis type; N, no.
*Zangheri's Scoring system of intra-abdominal calcifications for MP[10].
†Means fibroadhesive type.

Table 3. Postnatal Symptoms and Signs, and Postnatal Imaging Study Modalities and Specific Findings

Postnatal symptoms and signs	N=13
Symptoms and signs	12
Abdominal distension	10
Bilious vomiting	2
Pneumoperitoneum	2
White meconium	1
No meconium passage	1
No symptom	1
Postnatal imaging findings	
Plain abdominal radiography	13
Intraabdominal calcification	8
Mass with multiple calcification	2
Intestinal obstruction	3
Contrast enema	10
Microcolon	9
Abdominal ultrasonography	8
Pseudocyst	2
Obstruction/Bowel dilatation	2
Cystic mass	1
Calcification	1
Nonspecific	2
Computed tomography	1
Huge cyst	1

13 patients (patient 4 in Table 2) had none of the above symptoms and signs, so that the patient was diagnosed as healed type of MP. Postnatal imaging studies were also performed including plain abdominal radiography, contrast enema, abdominal ultrasonography, and computed tomography scan. Calcifications were the most common radiologic finding (n=10) (Table 3). Postnatal images and intraoperative findings with huge cyst (patient 1 in Table 2) were shown in Fig. 1.

Twelve patients out of 13 had surgery except for the healed type patient. One patient had emergency operation because of severe abdominal distension after birth (patient 5 in Table 2). All the other 11 patients had progressing symptoms, thus surgical treatments were decided. Types and possible causes of MP were confirmed intraoperatively. Types of MP were divided into pseudocyst (n=6), generalized type (n=4), fibroadhesive type (n=2) and healed type (n=1). Jejunoileal atresia was the most common cause of MP; ileal perforation (n=2) and transverse colonic perforation (n=1) were also the pathologic cause of MP. Enterostomy creation, segmental resection and anastomosis, and primary closure were performed for surgical treatment (Table 2).

Two cases of mortality (15.4%) and three of morbidity (23.1%) occurred; prematurity with respiratory distress syndrome and sepsis were the causes of mortality. Two patients

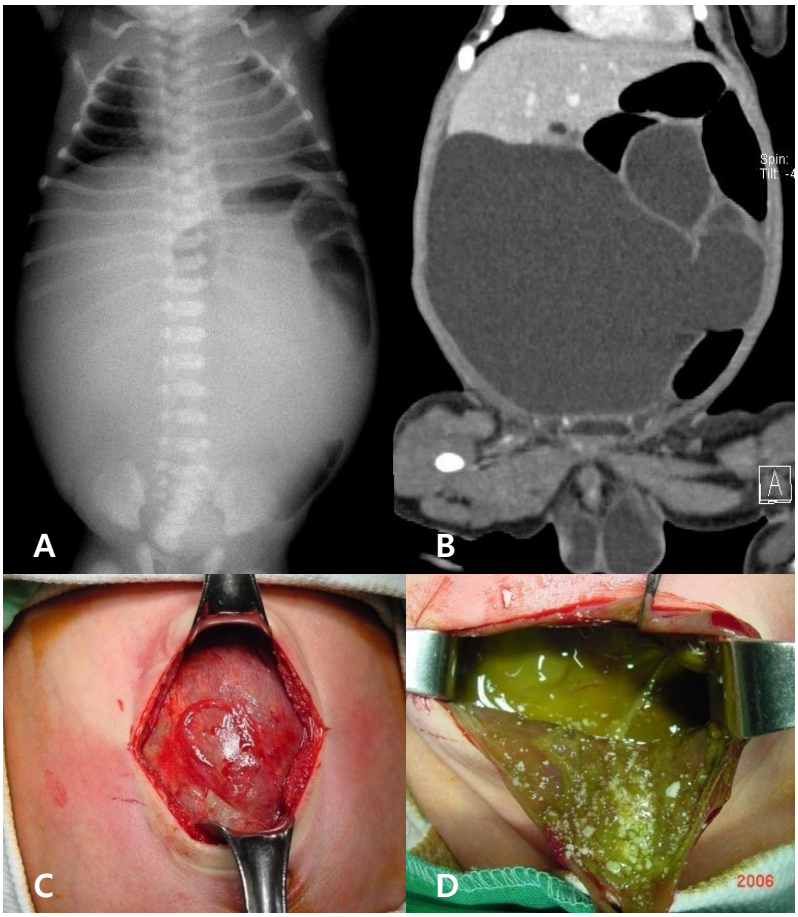

Fig. 1. Postnatal images and intraoperative findings (patient 1 in Table 2). (A) Postnatal plain X-ray; space occupying lesion in whole abdomen and bowels were positioned in left upper and lower quadrant. (B) Coronal image of computed tomography; fluid-containing cyst was seen and bowels were shifted to the left side. (C, D) Intraoperative findings; huge meconium cyst containing meconium and white calcification.

had additional surgery because of mechanical ileus caused by severe adhesion. Anastomosis leakage and stoma necrosis occurred sequentially in one patient. Medial hospital stay was 23 days (range, 1–76 days). Several variables were compared between the survival group and the mortality group. Only two variables were significant: preoperative hemodynamic instability and preoperative ventilator care (P=0.013) (Table 4).

Discussion

All patients with MP were diagnosed by prenatal ultrasonography at a median of 28 weeks of gestation (range, 24–35 weeks). Ping et al. reported high specificity of prenatal ultrasonography (100%) but low sensitivity (22.2%).[11] Tsai et al. reported that only 10% of MP was definitely confirmed by prenatal ultrasonography.[9] Recent studies suggested three-dimensional ultrasonography in conjunction with high definition mode as a complementary diagnostic tool to conventional two-dimensional ultrasonography.[12]

Prenatal ultrasonographic fetal intra-abdominal calcification can be found in any part of an abdominal organ and is related to a wide spectrum of etiologies. Scattered calcifications seen on the liver line strongly implies MP.[13,14] Calcifications can be detected after 18 weeks of gestation and appear approximately 8 days after intrauterine bowel perforation.[1] Zerhouni et al. reported that surgical intervention was not

Table 4. Comparison between Survival and Mortality Groups in Meconium Peritonitis Patients

	Survival (n=11)	Mortality (n=2)	*P*-value
GA (days)	36.8±1.87	34.5±4.95	0.641
BW (g)	3,159±589	2,355±473	0.103
Age at operation (day)	2.50±1.35	2.0±0.0	0.758
Preoperative pH	7.31±0.91	7.07±0.41	0.769
Preoperative base excess (mEq/L)	-5.70±3.10	-15.70±19.86	0.909
CRP (mg/dL)	0.90±2.32	0.23±2.96	0.758
WBC (/μL)	15,665±6,990	10,930±5,642	0.485
Preoperative hemodynamic instability	0	2	0.013 (<0.05)
Preoperative ventilator care	0	2	0.013 (<0.05)
Hospital stay (days)	39±25	8.5±7.7	0.154

Preoperative hemodynamic instability and preoperative ventilator care were compared by using Fisher's exact test and other variable were compared by Mann-whitney test for non-parametric test.
Abbreviations: GA, gestational age; BW, birth weight; CRP, C-reactive protein; WBC, white blood cell.

imperative for patients with intraabdominal calcification alone.[14] Associated findings of bowel dilatation or polyhydramnios were valuable predictors for postnatal surgery. Saleh et al. compared the prenatal ultrasonographic findings of a group that underwent neonatal surgery for MP to a group that did not.[15] Only bowel dilatation was the statistically significant variable associated with surgical intervention. Zangheri et al. insisted on the relation between prenatal ultrasonographic features and postnatal outcomes; however, there was no significant correlation in our study. Grade 0, isolated calcification, was associated with excellent outcomes and patients did not require operations.[10] Higher grades of MP were associated with higher rate of surgical interventions. Thus, attention might be needed when the score is high.

Twelve patients underwent surgical treatment and one patient was treated conservatively. The patient 4 (Table 2) had no symptoms or signs of MP though prenatal and postnatal radiographs presented multiple calcifications. The rate of surgically treated MP varied from 61% to 100%;[11,16] the demand for surgical treatment was still explicit.

Types and possible causes of MP were confirmed intraoperatively. Types of MP were divided into pseudocyst (n=6), generalized type (n=4), fibroadhesive type (n=2) and healed type (n=1). The original classification of MP types was based on ultrasonographic findings[17] and an alternative classification into simple MP and complex MP had been suggested.[1] Ileojejunal atresia was the most common possible cause of MP (75%) followed by ileal perforation (16.7%) and colonic perforation (8.3%) in our study. The possible causes of MP reported by several Asian centers were different. Intestinal atresia was the most common cause of MP; intestinal atresia in 14 (45%) and uncertain ileal perforation in 10 (32%) out of 31 MP patients in the report by Nam et al.[8]; intestinal atresia (47%) and volvulus (47%) out of 15 MP patients by Uchida at al.,[18] and intestinal atresia 18 (90%) and meconium ileus in 2 (10%) out of 20 MP patient by Kamata et al.[17] A report in Taiwan described bowel perforation (n=5) as the most common cause followed by bowel atresia (n=2) in 9 MP patients.[9] CF is also a known underlying cause of MP in Western countries, and screening for CF is indicated when specific gastrointestinal abnormalities are detected.[19] It is rare in Asian countries; thereby screening for CF was not performed in our study.[8,18]

Two cases of mortality (15.4%) occurred; one patient deceased of prematurity and respiratory distress syndrome and the other patient could not recover from septic shock and ongoing multi-organ failure. Recent studies reported good outcomes compared to decades ago.[8,9,20] Uchida et al. demonstrated that postnatal circulation deficiency and serum C-reactive protein (CRP) were predictive factors for morbidity and mortality.[18] In our study, all the two mortality cases were in an unstable haemodynamic status preoperatively and were treated with pressor agents and preoperative ventilator care was imperative (P=0.013). There were no statistically significant differences between the mortality and survival group with respect to GA, BW, age at operation, preoperative serum level of pH, and base excess, CRP, white blood cell count and hospital stay.

Although this study was limited by its small sample size, our study demonstrated the treatment and clinical course of MP and the possible relationship with perinatal parameters and outcomes.

In conclusion, careful postnatal attention and treatment are required when an infant is prenatally diagnosed with MP. It is likely to analogize the interrelation of preoperative hemodynamic stability to postoperative outcomes in spite of

small sample size. More studies are needed to investigate the correlation between preoperative vital status and mortality with enrollment of more patients. We cautiously suggest studies for long term follow up of MP patients over adolescent periods to inquire quality of life, complications, bowel movement, and malignancy.

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