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Prenatal Evolution of Chiari Ii Malformation After Intrauterine Fetal Mmc Repair. Patients Selection, Maternal, Fetal and Neonatal Results

KEYWORDS: fetal surgery, spina bifida, maternal complications, fetal complications

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ABSTRACT *The aim of our study was to analyze the Chiari II malformation and maternal complications, intrauterine fetal development and newborn outcomes after intrauterine myelomeningocele repairs (IUMR). 71 cases of IUMR performed on singleton pregnancies, aged 20,0-25,6 weeks of gestation. After IUMR hindbrain hernia (HH), hydrocephalus (HC), lower extremity movement (LM) as well as Fetus well being were evaluated by USG/MRI. Postnatal maternal morbidity, neonatological complications, need of ventriculo-peritonal shunt (VPS) placement up to 12 month were evaluated. After IUMR we noted: HH in 96,9% cases, Stationary HC in 50.7% fetuses. LM remained constant. Chorioamniotic separation in 21% of pregnancies, iPPROM 52.1%. Most pregnancies were delivered prematurely. The completely healed hysterotomy site was observed in 83%. Most neonates 37/70 scored 8-10 Apgar points at birth. Intracranial hemorrhage (IH) I°-II° up to 50%. Neonatal mortality 3 cases (4,2%).*

Proper IUMR qualification for fetuses with Chiari II results in decrease of neurological complications of MMC. We intend to monitor further development of our fetal patients.

INTRODUCTION

Fetal myelomeningocele (fMMC), is the most common and severe central nervous system (CNS) congenital malformation, belongs to a group of birth defects called neural tube defects (NTD). In most cases it results in a severe complication known as the Chiari II malformation (CM II) with HH and HC progression and central as well as peripheral nervous system impairment. Mortality among newborns and children with CM II is high [1,2]. In Poland, fMMC affects about 5-6/10 000 live births [3]. The idea of intrauterine treatment originates from animal model surgery and was later applied to the human fetus [4]. The first experiences with MMC intrauterine repairs were encouraging. However, some uncertainties required explanation [5]. The Management of Myelomeningocele Study (MOMS) was conducted in Philadelphia (Children's Hospital of Philadelphia), Nashville (Vanderbilt University) and San Francisco (University of California, San Francisco). Published by Adzick NS et al., the MOMS randomized trial results constitute uncontested proof of IUMR validity and can be defined as a milestone in the field of perinatology [2].

METHODS

Between 2005 and 2014, 71 IUMR in singleton pregnancies, aged 20-26 weeks of gestation, were performed at Gynecology Clinical Care Unit, Obstetrics and Oncological Gynecology in Bytom, Poland. Inclusion and exclusion criteria based on experiences of American medical researchers are listed in table 1 [6].

The patients were deemed eligible for surgery by a multidisciplinary team of perinatologists, pediatric surgeons, neonatologists, anesthesiologists, internists and psychologists. After IUMR most of the pregnant women stayed at our Center until the delivery ward (elective caesarean section). In 31-33 week of gestation fetal MRI was performed to assess the evolution of HC, level of HH, LM and fMMC recurrence. Finally, we aimed to show maternal, fetal and neonatal results including VPS up to 12 month.

Table 1. Inclusion and exclusion criteria for IUMR.

INCLUSION CRITERIA	EXCLUSION CRITERIA
Gestational age of 20-26 weeks	Kyphosis > 30°, oligohydramnios, placenta praevia, single umbilical artery, myomas, previous hysterotomies , classical cesarean section, uterine malformation, short cervix ≤ 20mm
Maternal age >18 years	Premature deliveries in anamnesis, cesarean section >1, multipara >3, eclampsia in previous pregnancy

Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

Singleton pregnancy	HBV, HCV, HIV, TORCH infection, pathological bacterial flora in cervical canal, upper respiratory tract infection
level of MMC location ≤L1, grade 1 or 2 hindbrain herniation , ≤17 mm maximum diameter of the posterior horns of the lateral ventricles, normal mobility of the lower extremities with/ without foot deformity (confirmed by USG and MRI)	Diabetes mellitus, arterial hypertension, BMI>35 kg/ m^2, thrombophilia, chronic uterine tract infections
Parental consent for IUMR	Contraindications to anesthesia- spinal deformities
Normal fetal karyotype	Conviction about high risk of IUMR
Absence of others congenital fetal defects,	Low family support
Normal hemodynamic integrity of the uterine-placental-fetal unit	Low economic status

Table 2. Maternal characteristics.

Characteristics of pregnant women	Study group n=71
Primiparas, n (%)	35 (49.2)
Maternal age, years (SD)	29 ±6.2
BMI, kg/m^2 (SD)	26.1 ±4.2
Female fetal sex, n (%)	40 (56.3)
Education, n (%)	
Tertiary education	18 (25.3)
Secondary education	22 (31.0)
Married/stable partner, n (%)	52 (73.2)
Addictions, n (%)	
Nicotinism	13 (8.3)
Alcoholism	0
Drugs	0
History of hysterotomy, n (%)	
Cesarean section	14 (9.7)
Myomectomy/others	0
Gravid uterus, n (%) Polyhydramnions	4 (5.6)
Cervical length >35mm, n (%)	30 (42.2)

RESULTS

The study group comprised 71 mothers whose children underwent IUMR. Table 2 and 3 demonstrate maternal and fetal characteristics at the time of qualification for the study, i.e. 20.0-25,6 weeks of gestation.

Table 4 presents maternal complications after IUMR. Spontaneous contractions of uterine muscle detected in cardiotocography before 37 weeks of gestation were the most common complication and occurred in 39 cases (55%).

The hysterotomy site after open fetal surgery was evaluated during cesarean section. A completely healed wound was observed in 59 cases (83%). Partial dehiscence in 1/3 length of the wound (defined as partial dehiscence I°) and partial dehiscence in 2/3 length of the wound (partial dehiscence II°) occurred in 8 cases (11,3%) and 1 case (1,4%), respectively. Complete dehiscence was found in 3 cases (4,3%). Fetal extrusion into the peritoneal cavity, resulting in a live birth, was reported in one case.

Table 3. Characteristic of the fetuses with MMC.

Characteristics of fetuses with MMC (USG/ MRI)	Study group n=71
Lateral ventricular width, n (%)	
< 10 mm	4 (5.6)
11-17 mm	67 (94.4)
> 18 mm	0
Agenesis of the corpus callosum, n (%)	15 (21.1)
Level of hindbrain herniation, n (%)	
0- none	2 (2.8)
1- small	4 (5.6)
2- mild	65 (91.5)
3- severe	0
Location of the upper MMC defect, n (%)	
L1-L5	67 (94.4)
<S1	4 (5.6)
Lower extremity disorders, n (%)	
Muscle dystrophy of lower extremities	4 (5.6)
Unilateral foot deformity	20 (28.1)
Bilateral foot deformity	38 (53.5)

Table 4. Maternal complications after IUMR.

Maternal complications n (%)	Study group n=71
Pulmonary edema without secondary intubation and ICU treatment	2 (2.8)
Preeclampsia/hypertension	2 (2.8)
Gestational diabetes	3 (4.2)
Blood transfusion	3 (4.2)
Peritonitis	1 (1.4)
Spontaneous contractions of the uterine muscle <37weeks of gestation	39 (55.0)

Fetal results and complications regarding fetal membranes, amniotic fluid and fetal well-being (biophysical profile evaluation) are listed in Table 5.

Table 5. Results and complications regarding fetal membranes, amniotic fluid and fetal well-being after IUMR.

Fetal membranes and amniotic fluid n=71		Fetal well-being n=71	
Chorioamniotic separation		Manning' s test < 8 points	9 (12.6)
Temporary < 21 days	9 (12.6)		
Permanent >21 days	6 (8.4)		
Idiopathic oligohydramnios AFI< 5, > 21 days	7 (9.8)	Doppler UA PI>1	9 (12.6)
iPPROM	37 (52.1)	Centralization of fetal circulation BSE CPP < 1,08	3 (4.2)
Chorioamnionitis	3 (4.2)	Non-reactive NST > 29 weeks of gestation	8 (11.2)
Premature placental abruption	3 (4.2)	Fetal bradycardia during IUMR	4 (5.6)

The MRI was repeated in 32 fetuses (31-33 weeks of gestation) as not all of the pregnant women were able to have their control examination in that particular time and most pregnancies were delivered prematurely. Partial and

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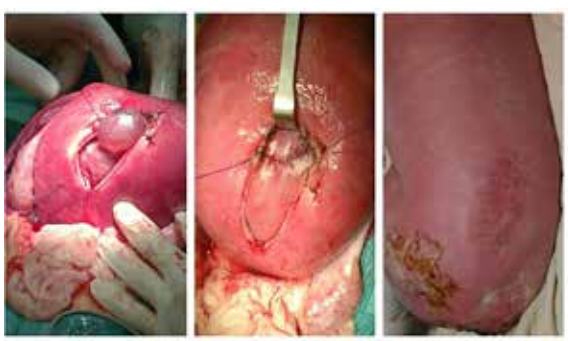
complete HH reduction was noted in 14 (43.7%) and 17 (53.2%) cases, respectively. One fetus demonstrated medium hindbrain hernia progression. Stationary hydrocephalus (assessed before delivery in ultrasonography scans) was observed in 36 cases out of 71 (53.2%).

One antenatal death (1.4%) occurred among 71 fetuses with prenatal fMMC closure. 29.5% pregnancies were delivered at ≤ 30 weeks of gestation, 25.3% between 31-33 weeks of gestation and 26.7% between 34-36 weeks of gestation. There were 13 (18.3%) term deliveries at ≥ 37 weeks of gestation. Mortality in perinatal period < 7 days amounted to 3 (4,2%).

Most neonates (37 out of 70) scored 8-10 Apgar points at birth. In 26 neonates the score was 4-7 and in 7 neonates the score was 0-3. Ventilation support due to respiratory distress syndrome (RDS) was used in 49 cases (31.4% nCPAP, 38.5% mechanical ventilation). Half of the newborns demonstrated intracranial hemorrhage (IH) I°-II° and 44.2% showed no signs of IH. Neonatal infection was observed in 45.7% of the neonates. Foot deformity was noted in 33 cases.



a b c

Figure 1: a) fMMC during IUMR b) Repaired fMMC c) fMMC closure site after delivery 36 weeks of gestation.

DISCUSSION

The main criterion for IUMR was the diagnosis of CM II according to the protocols of the two centers in USA [6,7] and our own modification of inclusion and exclusion criteria. The main differences concerned the level of fMMC location that in our study was ≤ L1 and the ventricular diameter did not exceed 17 mm. In fetuses with thoracic MMC ventricular diameter was more than 18 mm but they were excluded from the study because of concomitant kyphosis >30°. In all of the fetuses enrolled into the study fetal legs movements were observed during ultrasonography examination. We excluded the cases with single umbilical artery as they were associated with other abnormalities.

MRI for evaluation of the pelvic anatomy and placental morphology was first performed in 1983. Since that time, constant development has allowed for high-resolution imaging of the central nervous system anatomy. At present, MRI is an important diagnostic tool in decision making about IUMR [8]. Fetal MRI enables one to evaluate, more accurately than with ultrasound, fetal brain morphology, especially regarding the posterior fossa, spinal canal, spinal cord and meningocele contents [9]. Fetal MRI was performed in all of our 71 pregnant patients. We are of the opinion that MRI is a method of choice when open fetal surgery for MMC is considered. Although MRI is not exempt from misdiagnosis, it is difficult to question its supremacy as far as important diagnostic and prognostic details are concerned [10].

Our experiences, as well as of the randomized MOMS trail, Golombeck et al. report and historical reports indicated a low maternal risk associated with open fetal surgery and MMC closure [9,11]. However, the procedure of the open fetal surgery needs to be rediscussed in the aspects of maternal and fetal safety. The main problem we faced was chorioamniotic separation diagnosed in 21% of pregnancies after IUMR. The incidence of iPPROM in our study reached 52.1%. In the MOMS study, the figures were 26% for chorioamniotic separation and 46% for iPPROM. So far we have had no experiences with artificial skin for intrauterine coverage of the back lesion [12].

Placenta abruption was diagnosed in 4.2 % of cases. One was a stillbirth at 24 weeks of gestation. Fetal bradycardia was observed four times during IUMR. We verified the amniotic fluid amount and the umbilical cord collision, and if necessary additional uterine relaxation, increased oxygen therapy, fentanyl, atropine, and pancuronium were applied. About 55% of pregnancies were delivered before 34 weeks of gestation. In CHOP experiences reported by Johnson et al., it was 34 weeks and 4 days and 34.1 weeks in the MOMS trial [2,7]. The high percentage of preterm labour in our center is entailed with primary technical experiences. In open fetal surgery as well as in the endoscopic procedures, preterm labour and iPPROM seem to be the two main problems. The iPPROM activates prostaglandins synthesis in the decidual tissues and in the amniotic fluid [13]. Two fetuses without HH underwent surgery. The decision was made because the progression of hydrocephaly (AD from 11mm to 17 mm) was observed. MRI was repeated in 32 fetuses (31-33 weeks of gestation) to assess HH and lateral ventricular width evaluation. Grade 0 was assigned for normal posterior fossa, grade 1 for visible fourth ventricle and cistern magna without cerebellar displacement below the foramen magnum (tentorium could be vertically oriented, and tectal beaking could be present). Grade 2 was given for visible cisterna magna without displacement of the cerebellum below the foramen magnum, no visible fourth ventricle. Grade 3 was assigned when the displacement of cerebellum below the foramen magnum and obliteration of all posterior fossa Cerebral Spinal Fluid spaces were observed [14].

Partial (decrease of one degree or more) or complete (normal posterior fossa) hindbrain reduction was noted in 14 (43.7%) and 17 (53.2%) cases, respectively. One fetus demonstrated medium HH progression.

Our study demonstrates that HH is significantly reduced in fetuses treated prenatally. Postnatal MMC repair is more frequently associated with bladder and bowel dysfunction and loss of motor skills of lower extremities. Approximately 90% of untreated fMMC is associated with Chiari II malformation, with respiratory stridor, swallowing disorders and others accompanying grade 3 HH [4]. IUMR enables protection of the spinal cord and prevention of severe late results of HH. FMMC open fetal surgery counteracts later life consequences, decreases the need of VPS implantation and enhances the possibilities of better mental development [2]. Evaluation of the hysterotomy site during cesarean section revealed wound dehiscence in 6 cases (8.4%). We had one hysterotomy rupture with fetal extrusion. The MOMS trial reported variable degrees of dehiscence at hysterotomy site in 10% of the cases. A worthy goal is for

Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

the development of improved uterine opening and closure techniques to prevent iPPROM and hysterotomy site dehiscence.

Four perinatal deaths occurred, including 1 antenatal death caused by placenta abruption and 3 (delivered before <30 weeks of gestation) within 14 days after IUMR as an effect of the extreme prematurity.

Newborn birth weight <3 percentile and <10 percentile was 4.2% and 19.7% of the cases, respectively. Most neonates scored 8-10 Apgar points and more than half received support ventilation. The criteria of the IH degree were based on early experiences of Papile et al [15]. Higher percentage of neonatal infection results from iPPROM and long-term preservative treatment and postnatal procedures. However there were no newborn deaths due to neonatal infection.

In our study the need of VPS placement up to 12 months after delivery was <30% of cases. This observation remains consistent to our previous research in which we shown that 70% of neonates after IUMR does not need VPS vs. control group (postnatal repair) 80% [16].

CONCLUCION

Intrauterine repair serves as a treatment option for mothers whose children were prenatally diagnosed with MMC. Some of the results are not satisfactory, especially regarding neuromotor function [16]. Also, problems such as bowel and bladder continence and sexual function remain to be solved. Polish experiences in fMMC open fetal surgery so far have been most encouraging. Probably, some technical aspects of the operation could be refined. We intend to monitor further development of our fetal patients.

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