In utero Repair of Myelomeningocele with Bovine Pericardial Patch. Case Report

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Case Report

Keywords: In utero MMC repair, bovine pericardial patch, intrauterine surgery, fetal neurosurgery, Chiari type 2

Posted Date: April 27th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1549336/v1

Abstract

We present the first case of meningomyelocele (MMC) in utero repair with the bovine pericardial patch performed in Belarus. We followed the maternal and fetal inclusion and exclusion criteria used by the MOMS trial. Prenatal fetal magnetic resonance imaging (MRI) shows the anomaly of cerebellar tonsils, brain stem herniation and MMC at the level of L5-S1 vertebra. During the standard surgical hysterectomy, we performed exposure of the fetus and applied microsurgical repair of the MMC defect with the use of bovine pericardial patch. In our case, we demonstrated the use of bovine pericardial patch for MMC defect repair as optimal and safe material which resulted into skin epithelialization by the first month of life.

Introduction

Myelomeningocele (MMC) is the most common congenital non-fatal anomaly of the central nervous system. It is a failure of closure of the neural tube within the first 6 weeks of gestation [1, 9]. Epidemiologic studies of MMC normally include related congenital central nervous system defects under the general classification of neural tube defects (NTDs). It is estimated that within 300,000–400,000 infants worldwide are born with NTDs annually [15]. In order to reduce the prevalence of MMC, it is recommended for women of childbearing age to consume folic acid of minimum 400–800 mg daily [2, 10].

MMC is associated with a wide clinical spectrum, including motor deficiencies, orthopedic abnormalities, neurocognitive abnormalities, urinary, anal incontinence and sexual dysfunction, as well as sensitivity alteration below the affected lesion level. Hydrocephalus associated with MMC develops secondarily together with the Arnold-Chiari (AC) malformation type 2, defined by permanent herniation of the medulla oblongata and the cerebellum through the foramen magnum [8, 21]. According to the “two-hit” hypothesis, development of hydrocephalus is associated with fluid leakage that results into cerebellar tonsils and brainstem herniation. Neurological disorders are associated with incorrect formation of spinal cord at the level of a defect and the toxic effect of amniotic fluid on the spinal cord [1, 9].

The diagnosis of fetal MMC is frequently performed by ultrasonography or magnetic resonance imaging in routine prenatal scans after 16 weeks of gestation. Amniocentesis is performed to determine genetic syndromes and measure alpha-fetoprotein levels in order to find out a patient’s risk of having a fetus with open neural tube defects (ONTD) between 15 weeks and 21 weeks, 6 days gestation [13, 16].

Mostly, MMC repair surgery takes place in the neonatal period although intrauterine repair of MMC may reverse AC and limit hydrocephalus progression and alleviate the severity of the defect’s resulting sequel and further deterioration of nerve tissue in the spine [18]. Obstetric complications after repair MMC in uterus are rare. The most common medical complications are pulmonary edema occurring in 2,8% of the cases, gestational diabetes - in 3,7%, gestational hypertension/preeclampsia - in 3,7%, blood transfusions - in 3,2%. The rates of perinatal mortality vary from 1,8 to 6,0% depending on the experience in different

centers. Paulista Medical School performed a trial with 220 cases showing perinatal mortality rate of 1,8%; MOMS trial – 2,5% and the Children's Hospital of Philadelphia (CHOP) – 6% [4, 12, 14].

MOMS results have been widely described in the modern literature. MOMS trial was terminated earlier due to its efficacy in the prenatal period: at 187 patients of the originally planned 200 randomized ones. Decrease in the ventricular-peritoneal shunt rates 40% versus 82%. Radiographic findings at the 12-month follow-up were also more favorable in the prenatal surgery group, showing lesser degrees of hindbrain herniation, brainstem kinking, and syringomyelia observed relative to the postnatal group. Different outcomes were found between prenatal and postnatal MMC repair. Bayley Mental Development Index and motor level improvement at 30 months were better in the prenatal surgery group. Patients treated prenatally were more likely to have a level of function two or more levels better than it was expected according to anatomical level, despite having more severe lesions than their postnatally treated counterparts. Regarding the urological outcomes, no significant difference was found between the patients operated prenatally and postnatally, which, however, is still not enough to determine the impact on renal insufficiency [5, 10, 17].

The operative principle of MMC repair consists of consecutive separate closure of the neural placode, dura mater, lumbar fascia, subcutaneous layer, and skin. The neurosurgical technique for the closure of the neural placode and dura mater has remained unchanged over decades, but different soft tissue closure techniques are still being discussed in the literature [7]. Recent animal data suggest the potential for the use of materials to aid in closure of MMC defects and to isolate exposed neural tissue from amniotic fluid and surrounding tissues to prevent damage of spinal cord, tethering and its long-term sequelae. Materials utilized as scaffolds and/or defect coverings for in utero MMC defect repair in animal models include collagen- or gelatin-based scaffolds, small intestinal submucosa, and polymeric materials including silicone, high density poly ethylene, and polypropylene [19].

The use of bovine pericardial patch and fibrin sealant for the soft tissue postnatal closure of MMC was successful in eight infants by Bora Gürer et al [6]. Fetoscopic repair technique and the closure of MMC using a biocellulose patch (Bionext) over the placode were described in the literature earlier. The biocellulose patch induces the development of the neodura mater as a result of fetal wound healing [3, 11, 20].

The aim of this report is to describe this first successful experience in utero repair of MMC with bovine pericardial patch, as well as the treatment process.

Case Description

Patient prenatal course

The pregnant female patient (23 years old, primigravida) who underwent the prenatal MMC repair was of 26 weeks gestational age. We followed the maternal and fetal inclusion and exclusion criteria used by the MOMS trial. Prenatal fetal magnetic resonance imaging (MRI) showed the anomaly AC type 2, cerebellar

tonsils herniation 9.86 mm below the Chamberlain line, lateral ventriculomegaly 11 mm and MMC at the level of L5-S1 vertebra. According to US imaging, the size of MMC defect was 2x3cm (Fig.1).

Our main goal was to make hermetic closure of MMC in order stop cerebrospinal fluid (CSF) leak and limit the contact spinal cord with amniotic fluid. At the same time, we analyzed the size of the defect and we predicted the problem of closure of the defect using fetal tissue due to its size determined by fetal 3D US examination. Different types of patches were not available at that time, therefore, we prepared bovine pericardial patch («Biocard» by JLLC Ergon Est, Belarus) for this aim which was approved by the Ethics Committee of our Scientific Center**.** After explanation of the risk and complication of the bovine pericardial patch use, the patient's mother approved its use as well.

Subsequent progress of the pregnancy was followed thoroughly. After MMC repair, MRI showed no signs of cerebellar tonsils, hindbrain herniation and no MMC defect (Fig. 2).

Surgical course

The patient was on its 26 week of gestation. To avoid uterine contractions during the operation we used a loading dose of Atosiban with continuous IV infusion.

After combined spinal-epidural (sufentanil 10 mg and morphine 150 mg injected into the subarachnoid space + 0.5% ropivacaine 15 ml injected into the epidural space) + general anesthesia (sevoflurane, rocuronium), the abdominal wall was opened by means of a lower median laparotomy. We performed the longitudinal hysterectomy measuring around 8 cm. The fetal heart rate and placenta were monitored during the surgery by ultrasound (US).

The amniotic liquid was constantly irrigating bicarbonate buffer solution for continuous hemodialysis/hemofiltration with an osmolality of the finished solution of about 300 mOsm into the uterus to replenish the lost amniotic fluid during the entire fetal surgery. Care was taken to stabilize the fetus without excessive pressure in order to avoid diminished fetal cardiac function. The umbilical cord was placed to a safe position. The fetus was immobilized and the spinal lesion exposed through the uterine incision. An intramuscular injection of 1 ml Fentanyl was made in the left thigh of the fetus to ensure a higher degree of analgesia.

Microsurgical repair of the MMC was started by neurosurgeons at this point, the sac was mobilized circumferentially using gentle traction and a knife blade No. 15. All of the epithelialized skin was sharply excised from the placode using iris micro scissors, cutting into the arachnoid that surrounded the placode and releasing the connection to the sac circumferentially.

After releasing the placode along with the rostral spinal cord from the sac, non-running stitched forming a neural tube was closed, skin defect was tense. Therefore, we decided to close the defect with bovine pericardial patch suturing (Biocard Belarus) to skin with Poly Vinyli Dene Fluoride P.V.D.F. a Non-Absorbable 7.0 material. There were no signs of CSF leak after repair. Hemostasis during the operation was carried out by local use of absorbable hemostat and by the point bipolar coagulation (Fig. 3).

The uterine wall was then closed in two planes with PGA 2.0 thread. The total surgery time was 45 min, and the time of fetal exposure and fetal surgery was 20 min. The post-operative US showed the absence of placenta detachment, absence of hematoma. In the post-operative period, uterine contractions were inhibited with Atosiban 37.5 mg IV for 48 h.

Newborn delivery

Cesarean delivery took place at 33 weeks of gestation. It was performed under spinal block anesthesia after spontaneous onset of labor. The newborn female was preterm, adequate for gestational age, weight=2,150 g, Apgar 8/9, head circumference=34 cm, with the myelomeningocele corrected. The encephalic neonatal US on the first day of life showed RLV=14 mm and LLV=9 mm.

Post-operative course

The newborn clinical status was monitored. There were no clearly visible neurological deficits. The MMC repair bovine pericardial patch was without sign of inflammation or CSF leak. During delivery, there was not fetal and maternal complication (Fig. 4).

During the first month of close life monitoring required for the newborn, the newborn was in prone position most of the time. Saline was applied to the pericardial bovine patch every day and in the 3-week Zinc Oxide cream was applied around the patch.

Skin epithelialization under pericardial bovine patch ended in 4 weeks after delivery (Fig.5). No clinical sign of hydrocephalus during head US examination and clinical status was found.

Conclusion

An open fetal repair of MMC requires a wide and close monitoring of fetal and maternal status. The use of bovine pericardial patch for MMC defect repair was optimal and safe for our case, which resulted into skin epithelialization by the first month of life. Our first experience of in uterus repair surgery demonstrated a positive outcome in the treatment of Chiari type 2 and motor function on the limbs. We assume that this technique can be considered a viable option in cases where native tissue is not available to achieve closure for MMC repair.

Declarations

Acknowledgments We would like to express our gratitude to all the group of the doctors and medical staff of the State Institution Republican Scientific and Practical Center “Mother and Child” for their participation in our first experience.

Conflict of interests: None

Disclosure of funding: None

The consent for participation and publishing the clinical details of the patient was provided by the patient's mother.

Competing interest: The authors have no financial relationships related to this article to disclose.

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Figures

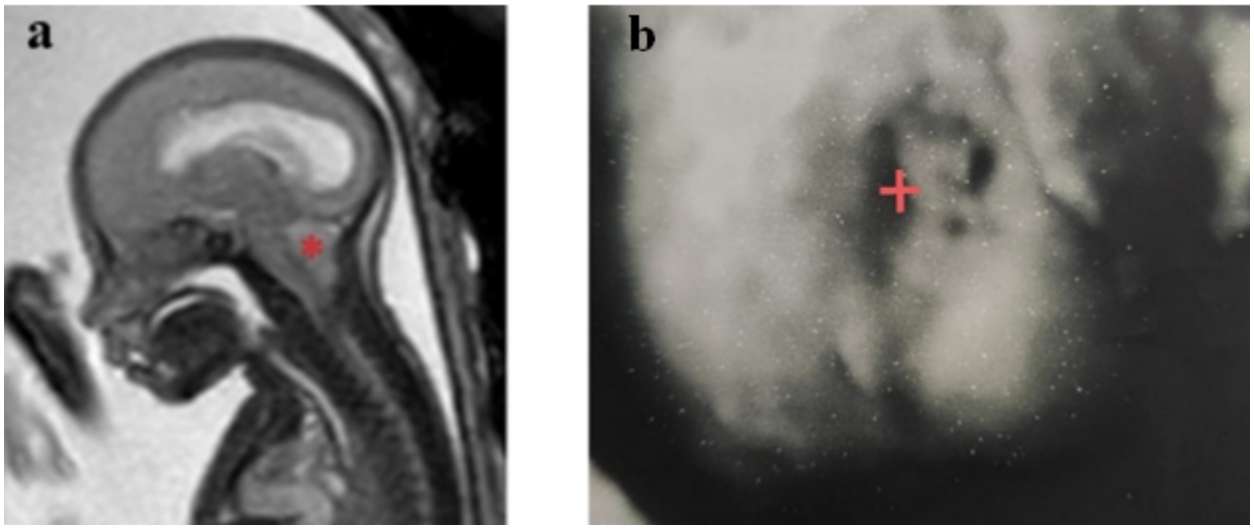

Figure 1

Pre in utero MMC repair MRI of fetus a, depicts sagittal views. (**a**, noted by the asterisk) Hindbrain herniation as seen in Chiari II is demonstrated. (**b**, noted by the plus sign) Fetal 3D ultrasound MMC at the level of L5-S1 vertebra

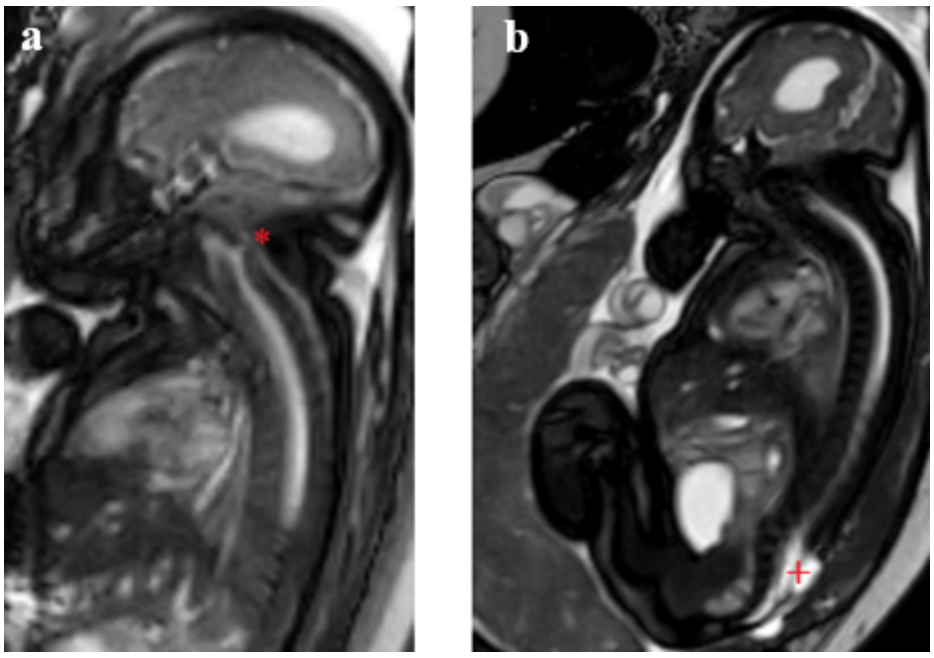

Figure 2

Post in utero MMC repair MRI of fetus. **a, b** Depicts sagittal views. (**a**, noted by the asterisk) Non-hindbrain herniation is demonstrated. (**b**, noted by the plus sign) MMC repair with bovine pericardial patch at the level of L5-S1 vertebra

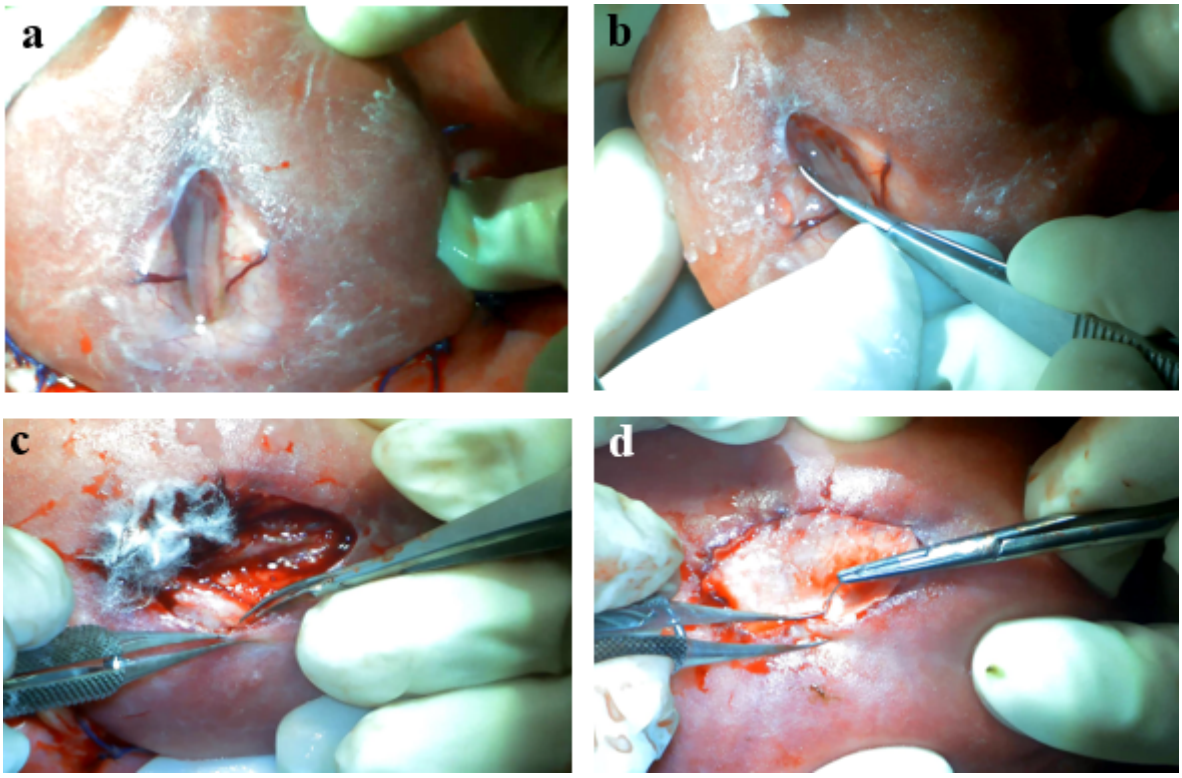

Figure 3

a Fetus with MMC in utero. (26 weeks). **b** Cutting into the arachnoid that surrounds the placode and releasing the connection. **c** Releasing the placode along with the rostral spinal cord that simultaneously hemostasis with absorbable hemostat. **d** Bovine pericardial patch suturing to skin with Poly Vinyli Dene Fluoride P.V.D.F. a Non-Absorbable 7.0 material

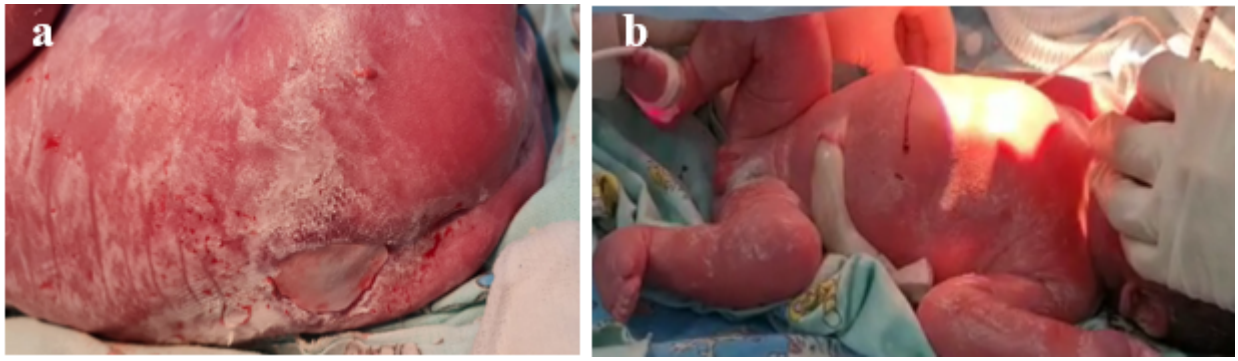

Figure 4

Neonate with myelomeningocele in utero repaired at delivery (35 weeks). **a** Detail of MMC closed with pericardial bovine patch. **b** Lower limbs active movements

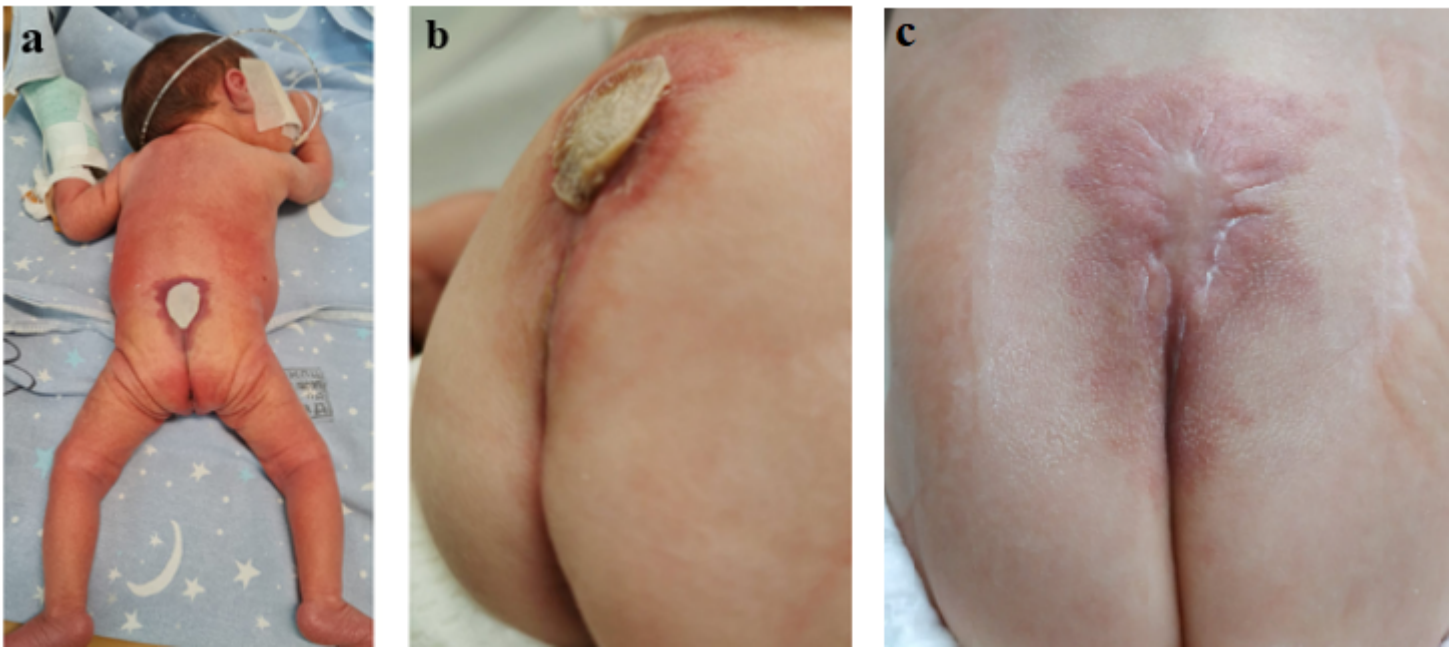

Figure 5

a Postoperative photomicrograph of an infant showing the bovine pericardial patch over the reconstructed neural placode and the dura mater after one week. **b** Photomicrograph showing the bovine pericardial patch in the 3 week. **c** Photomicrograph showing the end of the skin epithelialization and no bovine pericardial patch in the 4 week