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Maternal-fetal surgery for myelomeningocele: Neurodevelopmental outcomes at 2 years of age

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Objective: This study was undertaken to examine short-term neurodevelopmental outcomes in children with myelomeningocele (MMC) who underwent in utero neurosurgical closure.
Study design: Between 1998 and 2002, 51 fetuses underwent in utero MMC closure at our Center. Thirty (63%) of these children have returned for neurodevelopmental testing at 2 years of age using the Bayley Scales of Infant Development and Preschool Language Scales.
Results: Overall shunt rate was 43% in this group. Neurodevelopmental testing found 67% with cognitive language and personal-social skills in the normal range, 20% with mild delays, and 13% with significant delays. Children with shunted hydrocephalus scored lower than those with unshunted ventriculomegaly.
Conclusion: Children who have undergone fetal MMC closure have characteristic neurodevelopmental deficits that do not appear worsened by fetal surgery, and developmental outcomes may be improved by decreasing the need for ventriculoperitoneal shunting.

The care and treatment of infants and children with myelomeningocele (MMC) continues to challenge health care providers and parents because of the multifaceted problems including hydrocephalus, the need for shunting, motor and cognitive impairments, urologic and bowel disorders, and social and emotional challenges. Hydrocephalus, shunting, and shunt malfunction are a primary focus of clinical follow-up. Infants will have an 80% to 85% risk of having hydrocephalus develop that necessitates placement of a cerebral spinal fluid shunt.[1] Hydrocephalus may not be apparent at birth but shunting is usually required within the first week of life after lesion closure. Rintoul et al[2] showed that lesion level significantly affected the incidence of shunting from a single center retrospective review of 297 patients with MMC with an overall shunt rate of

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Table I Selection criteria for fetal MMC closure

- Less than 26 wks' gestational age.
- Confirmed normal karyotype.
- Absence of associated congenital anomalies.
- Maximum lateral ventricular diameter of <17 mm.
- Grade III (severe) Chiari II malformation.
- Normal leg movement and absence of talipes deformity.

81% (100% thoracic, 88% lumbar, and 68% of sacral lesions).

Preliminary data from 2 centers suggested fetal MMC closure might favorably influence the outcome of this disease.[3-5] In each study, the incidence of shunting was reported to be lower after in utero surgical closure, due in part to reversal of cerebellar herniation that is a component of the Arnold-Chiari II malformation.[4,5]

Children with MMC are at increased risk for cognitive impairments including nonverbal skills, arithmetic achievement, and visual-motor integration that become more evident with increasing age.[6] Both shunt status and anatomic lesion level has been shown to affect cognitive functioning.[7] The relationship between the degree of cognitive impairment and uncomplicated shunted hydrocephalus have been variable suggesting that the presence of hydrocephalus has a profound effect on cognitive function,[8] whereas others found similar cognitive performance between unshunted and shunted patients when neither had a history of ventriculitis.[9] The relationship between shunt complications and cognitive outcome remain undefined, with studies suggesting an inverse relationship between number of shunt complications and intellectual deficits,[6,10] whereas others found no such correlation.[11]

Midgestation in utero closure of fetal MMC is presently under investigation in a prospective, randomized National Institute of Health (NIH)-sponsored clinical trial. However, such surgery has potentially serious maternal and fetal risks and exposes the fetus to combination anesthetic agents, alterations in amniotic fluid volume that may alter intraoperative placental blood flow, chronic exposure to tocolytic agents, and necessitates preterm delivery. There are no data reported on neurodevelopmental and cognitive outcomes in children who have undergone in utero MMC closure. We therefore followed a select population of fetuses that underwent midgestation in utero MMC closure before the NIH-sponsored clinical trial and examined neurodevelopmental outcome.

Material and methods

From 1998 to 2002, 51 fetuses with prenatally diagnosed MMC underwent in utero fetal neurosurgical closure and have subsequently delivered. Fetal surgery selection criteria (Table I) and pregnancy outcome data have been previously described.[5] This research was approved by The Children's Hospital of Philadelphia Institutional Review Board (no. 2000-2081, no. 2002-2354).

Infants were delivered by cesarean section and received neonatal care at our institution. Chart review was used to collect prenatal and neonatal information. Prenatal data included gestational age at surgery, preoperative ventricular size, and anatomic lesion level. Neonatal data included birth weight, gestational age at delivery, 1- and 5-minute APGAR score, and complications during newborn hospitalization. Newborn neurologic findings included postnatal magnetic resonance imaging (MRI) and sonographic determination of ventricular sizes at time of birth, and abnormalities of the corpus callosum and posterior fossa. Ventriculomegaly was classified as mild (10.1-15 mm), moderate (15.1-20 mm), moderate severe (20.1-25 mm), and severe (>25 mm).

Families were asked to return for follow-up at 1, 2, and 3 years of adjusted age. Each visit included evaluations by a pediatrician, physical therapist, psychologist, radiologist, neurosurgeon, and urologist. Data from their 2-year follow-up visit forms the basis of this study.

The children were assessed with the use of the Bayley Scales of Infant Development (BSID 2nd ed) and the Preschool Language Scales-III (PLS) for cognitive development. The BSID is a well-standardized assessment measure for children from birth to 3.5 years of age. It yields 2 scores: the Mental Developmental Index (MDI) assesses the child's current level of cognitive, language, personal-social skills, and the Psycho-Motor Index (PDI) assesses the child's fine and gross motor skills. The PLS is a standardized assessment of speech and language, and consists of PLS-EXP (expressive) that evaluates use of expressive language and PLS-REC (receptive) that assesses comprehension of language. The BSID and PLS yield scores with a mean of 100 and a standard deviation of 15.

Postnatal MRI and ultrasound studies were reviewed for brain abnormalities. Newborn and outpatient clinic charts were reviewed and parents contacted to determine which children had undergone shunt placement, age at placement, and incidence of shunt revision(s) or central nervous system (CNS) infection(s). Strict neurosurgical criteria for ventriculoperitoneal (V-P) shunt placement have been previously described.[5] The 2-sided t test, median test, and 1-way analysis of variance (ANOVA) test were used for statistical comparisons, and $P < .05$ was considered clinically significant.

Results

Fifty-one fetuses met selection criteria and underwent in utero neurosurgical closure. There were 3 neonatal deaths caused by complications of severe prematurity after preterm delivery. Details of the previously reported outcomes are listed in Table II. Of the 48 survivors, all