

Brief Report

DERMOID INCLUSION CYSTS AND EARLY SPINAL CORD TETHERING AFTER FETAL SURGERY FOR MYELOMENINGOCELE

CATHERINE A. MAZZOLA, M.D., A. LELAND ALBRIGHT, M.D.,
LESLIE N. SUTTON, M.D., GERALD F. TUITE, M.D.,
RONALD L. HAMILTON, M.D., AND IAN F. POLLACK, M.D.

MYELOMENINGOCELE occurs in approximately 1 of every 2000 live births.¹ The prenatal incidence is higher, because many parents elect to terminate the pregnancy, once the diagnosis has been made.² Myelomeningocele often results in permanent impairment, including loss of sensorimotor function in the legs, hydrocephalus, incontinence of bladder and bowel, skeletal deformity, and type II Chiari malformation (cerebellar [vermis] and medullary herniation and inferior displacement below the level of the foramen magnum). Advances in ultrasonography and ultrafast fetal magnetic resonance imaging (MRI) have made it possible to diagnose myelomeningocele and other neural-tube defects early, but much remains to be learned about the optimal treatment of these disorders.

In recent years, in utero closure of myelomeningocele has been recommended to prevent damage to the spinal cord as a result of exposure to amniotic fluid through the open defect.³⁻⁵ Approximately 220 in utero closures have been performed to date at four institutions. Although improvement in motor function has not been confirmed in children treated in utero, there has been a documented improvement in cerebellar herniation.⁶ In addition, a comparison with historical controls suggests that children who have been treated in utero are less likely to require ventricular shunting for hydrocephalus, presumably because closure of the myelomeningocele sac provides a more normal pattern of spinal fluid circulation.^{7,8} The amelioration of these

sequelae may improve the quality of life for affected children.

However, these potential benefits must be weighed against the known postoperative complications of in utero repair, including induction of early labor, preterm delivery, infection, and death related to prematurity, as well as maternal morbidity. As more of these procedures are performed, other adverse sequelae may also become apparent. We describe three girls who had spinal cord tethering and large dermoid inclusion cysts in infancy. All three had undergone in utero closure of myelomeningocele at one institution.

CASE REPORTS

In Utero Closure

The preoperative evaluation and in utero treatment of the three patients have been described previously.⁶ After written informed consent had been obtained from each mother, fetal MRI was performed with a single turbo spin-echo sequence on a 1.5-T unit, at 19 to 23 weeks of gestation. Surgical repair of the neural-tube defect was performed at 22 to 24 weeks of gestation. In each case, after general anesthesia had been administered to the mother, a hysterotomy was performed, and the lumbar area of the fetal spine was exposed. Primary dural closure was attempted with the use of standard techniques, and attempts were made to close the skin around the open defect. In each case, it was not possible to close the dura and skin, so a graft of acellular human dermis was used to cover the defect (AlloDerm, LifeCell). Amniotic fluid was replaced with warmed, sterile, lactated Ringer's solution. Tocolysis was initiated and maintained postoperatively to prevent preterm labor.

The mothers underwent MRI studies every three weeks postoperatively, in order to monitor fetal neural-tube development. The infants were delivered by elective cesarean section after lung maturity had been confirmed by the ratio of lecithin to sphingomyelin in the amniotic fluid at 30 to 36 weeks of gestation. Uncontrollable premature labor, which has precipitated early delivery in a number of other cases, did not occur in the three cases reported here. At birth, the three infants appeared to have nearly normal motor function in the legs, and no bladder dysfunction was detected clinically. Voiding cystometrograms were normal.

Subsequent Evaluation and Treatment

The three girls were followed postoperatively by local pediatric neurosurgeons. Loss of neurologic function occurred at an average age of 10 months (range, 9 to 11). Two of the girls had loss of motor function in both legs. In one of the two, decreased spontaneous movement of both legs was noted by the family, and radiographs of the lumbosacral spine showed progressive scoliosis. In the other infant, who had only slight plantar flexor weakness at birth, the motor function of the right leg was diminished and there was tenderness on palpation in the lumbosacral area. The third child presented with progressive bladder dysfunction. Whereas she had had normal voiding with a good stream and a normal cystometrogram after birth, a cystometrogram obtained at six months of age showed poor bladder compliance, with passive leakage at high intravesicular pressures. All three infants underwent MRI studies of the spine, without the administration of contrast material. The MRI scan from one of the infants is shown in Figure 1. Dermoid cysts and spinal cord tethering were present in all three infants.

Because of the findings on clinical examination and neuroimaging studies, surgical exploration was recommended for the three infants. The previous skin closures were reopened and extended in a cephalad direction. The dura was exposed and opened. Dura was adherent to the dermoid cysts. The capsules of the cysts were opened and

From the Departments of Neurosurgery (C.A.M., A.L.A., I.F.P.) and Pathology (R.L.H.), University of Pittsburgh and Children's Hospital of Pittsburgh, Pittsburgh; the Department of Neurosurgery, University of Pennsylvania School of Medicine and Children's Hospital of Philadelphia, Philadelphia (L.N.S.); and the Department of Neurosurgery, University of South Florida and All Children's Hospital, St. Petersburg, Fla. (G.F.T.). Address reprint requests to Dr. Pollack at the Department of Neurosurgery, University of Pittsburgh, Children's Hospital, 3705 Fifth Ave., Suite 3705, 3rd Fl., Pittsburgh, PA 15213, or at ian.pollack@chp.edu.

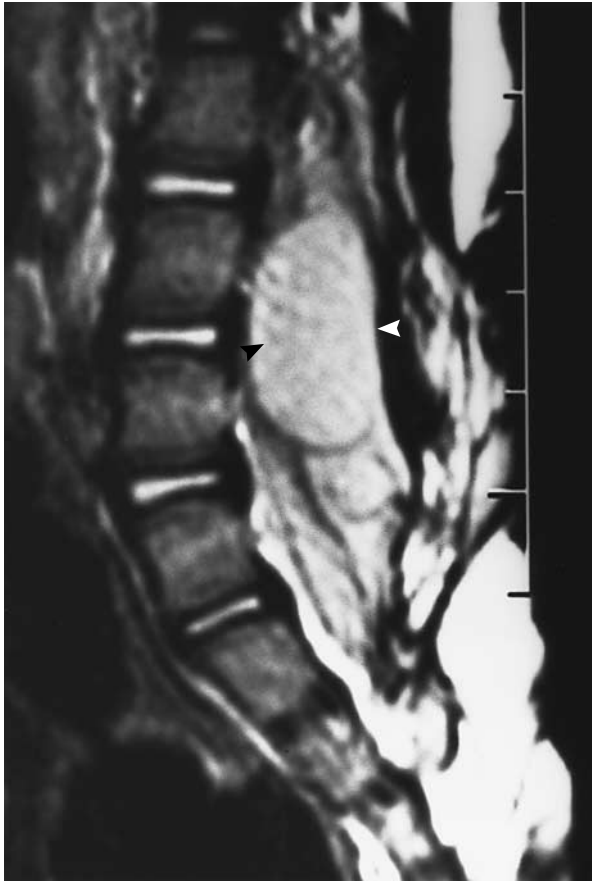


Figure 1. T₂-Weighted Sagittal MRI Scan Showing an Intradural Mass (Arrowheads) in an Infant Who Had Undergone in Utero Closure of Myelomeningocele.

Normal cerebrospinal fluid spaces are absent, and there is cystic compartmentalization of the lesion.

the contents evacuated to facilitate separation of the cyst walls from the surrounding neural structures. Fine hairs and white caseous material were present in all three cases. Care was taken to prevent the escape of the cyst contents into the cerebrospinal fluid. Microsurgical release of all intradural adhesions was performed to achieve circumferential untethering. Complete excisions of the cyst and capsule were performed in two infants, with primary closure of the dura. In the third infant, the entire cyst could not be resected because of dense adhesions on the dorsal end of the spinal cord; a dural graft was required to obtain a water-tight closure. On histopathological examination, all the lesions had the characteristic features of a dermoid cyst, with simple, squamous epithelium. There were hair follicles and cholesterol-containing debris in each cyst (Fig. 2).

Follow-up

Postoperatively, two of the children regained their previous neurologic function. In the third child, whose cyst could not be completely resected, motor function improved but did not return to the level observed immediately after birth. At the most recent follow-up visit, 7 to 14 months after the second surgery, none of the children had recurrent symptoms.

DISCUSSION

With improvements in the techniques of fetal surgery, their use to treat several congenital anomalies has been proposed on the basis of promising results in animal models.^{9,10} Theoretical advantages of in utero treatment over postnatal treatment include a greater potential for healing and regeneration in the fetus and the prevention of complications related to the primary developmental anomaly.¹¹ Currently, in utero surgery is used to treat fetal lung and airway lesions, diaphragmatic hernia, and some tumors.¹² In utero treatment is warranted in such cases because the developmental malformations are life-threatening to the fetus and because prenatal surgical correction is technically feasible. Although myelomeningocele is not directly life-threatening, in utero surgery has been proposed as a means of restoring or preserving neurologic function.

Although initial attempts at in utero repair of myelomeningocele, performed endoscopically, were unsuccessful, the feasibility of in utero repair performed through a hysterotomy at 28 to 30 weeks of gestation was subsequently demonstrated.⁵ More recent efforts have focused on earlier intervention, with surgical closure of open defects at a gestational age of 24 weeks or less.¹³ The rationale for performing closure as early as is technically feasible is based on studies in animals, which suggest that the neurologic deficits associated with myelomeningocele may result in part from chronic injury of neural tissue by exposure to amniotic fluid.¹⁴ Studies also suggest that in utero closure of myelomeningocele may improve hindbrain herniation and reduce the risk of hydrocephalus.^{3,6-8}

The potential benefits of in utero closure are apparent when one considers the results of postnatal closure, which is performed mainly to minimize the risk of infection rather than to improve neurologic function. Symptomatic hydrocephalus develops in 83 to 92 percent of children treated immediately after birth, and up to 20 percent have life-threatening symptoms of hindbrain herniation,¹⁵⁻¹⁸ which is the leading cause of death in infants with myelomeningocele.

Progressive neurologic deterioration as a result of spinal cord tethering or enlargement of an intradural dermoid inclusion cyst from the initial closure has also been reported in children operated on at birth for myelomeningocele. Although prospective data on the incidence of these complications are not available, retrospective studies have shown that symptomatic spinal cord tethering develops in 10 to 13 percent of children with myelomeningocele.^{16,19} In one of these studies, 100 of 1000 children in whom myelomeningocele was closed at birth (10 percent) had subsequent symptoms of a tethered spinal cord that required surgical repair.¹⁹ The symptoms included loss of motor function in the legs, change of gait, low back pain, scoliosis, and deformity of the feet. In 15 of the children

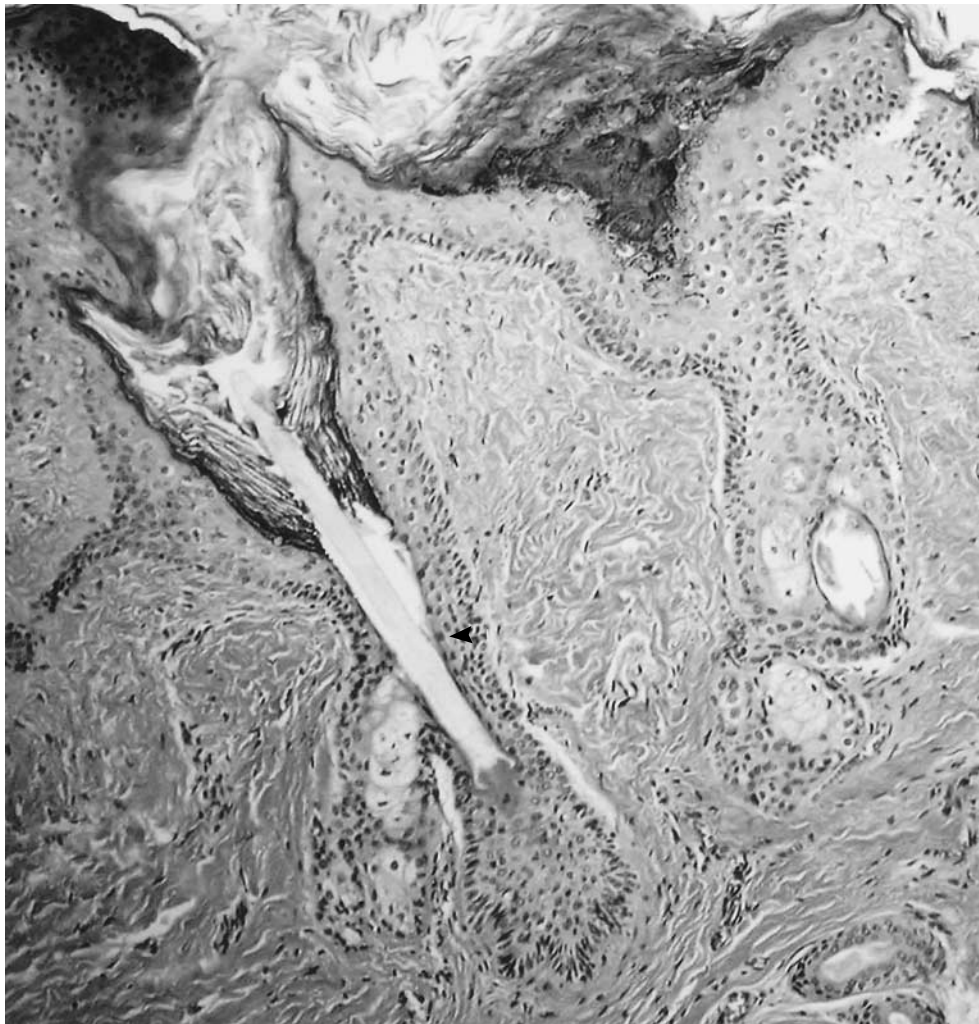


Figure 2. Photomicrograph of a Hair Follicle Containing Hair (Arrowhead) in Dermoid Tissue from One of the Infants ($\times 100$).

(1.5 percent of the total), a dermoid cyst was identified at the time of surgery.¹⁹ Since the symptoms related to the development of a dermoid cyst are indistinguishable from those related to a tethered spinal cord, whatever the cause, many dermoid cysts are identified only at the time of surgery to release a tethered spinal cord. The true incidence of dermoid cysts could well be higher, since imaging and surgical exploration are performed only in patients with symptoms and signs that are a cause for concern.

In each of the children we describe, spinal cord tethering was associated with a dermoid cyst. All three children underwent in utero repair of myelomeningocele at a single institution, where 49 closures have been performed in utero to date. Thus, the incidence

of symptomatic dermoid cysts after in utero repair of myelomeningocele at this one institution is 6.1 percent (3 cases in 49 procedures), and the overall incidence after in utero surgery is 1.4 percent (3 in 220). We are not aware of other reports of such occurrences, although we cannot exclude this possibility. It is also possible that other children who underwent in utero closure may present in the future with signs and symptoms of spinal cord tethering and dermoid cysts.

In all three cases we describe, symptoms developed at less than 1 year of age, whereas after neonatal surgery, the average reported age at presentation with the tethered cord syndrome was 6 years in one study and 11 years in another study.^{19,20} In the largest reported series, only 1 of 100 children presenting with

symptoms and signs of a tethered cord was as young as one year of age.¹⁹

The presence of a dermoid cyst and severe tethering in the three infants we describe may suggest that dermis was inadvertently enclosed within the reconstructed thecal sac. In addition, there may be a greater potential for the rapid growth of entrapped skin when these lesions are closed in utero rather than after birth. The use of acellular human dermis (AlloDerm) to cover the neural-tube defect and protect the distal spinal cord may also have contributed to the development of these large dermoid cysts. It is not known whether all the children who have undergone in utero closure are at risk for the premature development of dermoid cysts, or whether only those who required a dural graft are at risk. It is possible that duraplasty supports or permits the ingrowth of dermal or epidermal elements, which may confer a predisposition to the development of dermoid cysts. However, the exact cause of these inclusions is not known. The extent and complex nature of the dermoid lesions in these infants made complete resection difficult, increasing the risk that the cyst and tethering would recur. In addition, it remains possible that such infants have delayed functional deterioration. Had the symptoms in our three patients gone unnoticed, there would have been an even greater risk of irreversible deterioration.

These three cases of dermoid cysts with associated spinal cord tethering in children who were less than one year old and who had undergone in utero surgery for myelomeningocele may reflect a previously unrecognized risk associated with this procedure. These cases make it clear that children who have undergone in utero closure of myelomeningocele should be carefully observed for any signs of deterioration in motor or bladder function. In addition, refinements of fetal surgical techniques that reduce the risk of intradural inclusions merit evaluation. Long-term data on outcomes among children who undergo in utero closure, as compared with those who undergo surgery at birth, are needed to determine the risk-benefit ratio of this promising but still experimental technique.

REFERENCES

1. Copp AJ. Neural tube defects. *Trends Neurosci* 1993;16:381-3.
2. Lary JM, Edmonds LD. Prevalence of spina bifida at birth — United States, 1983–1990: a comparison of two surveillance systems. *MMWR CDC Surveill Summ* 1996;45(SS-2):15-26.
3. Adzick NS, Sutton LN, Crombleholme TM, Flake AW. Successful fetal surgery for spina bifida. *Lancet* 1998;352:1675-6.
4. Bruner JP, Richards WO, Tulipan NB, Arney TL. Endoscopic coverage of fetal myelomeningocele in utero. *Am J Obstet Gynecol* 1999;180:153-8.
5. Tulipan NB, Bruner JP. Myelomeningocele repair in utero: a report of three cases. *Pediatr Neurosurg* 1998;28:177-80.
6. Sutton LN, Adzick NS, Bilaniuk LT, Johnson MP, Crombleholme TM, Flake AW. Improvement in hindbrain herniation demonstrated by serial fetal magnetic resonance imaging following fetal surgery for myelomeningocele. *JAMA* 1999;282:1826-31.
7. Bruner JP, Tulipan N, Paschall RL, et al. Fetal surgery for myelomeningocele and the incidence of shunt-dependent hydrocephalus. *JAMA* 1999;282:1819-25.
8. Bruner JP, Walsh WF, Boehm FH, et al. Open fetal repair of myelomeningocele improves neurologic outcome in the neonate. *Am J Obstet Gynecol* 1999;180:Suppl:31S. abstract.
9. Farmer D, Peacock W, Danielpour M, et al. 0468 Repair of myelomeningocele in utero. I. Experimental pathophysiology, natural history, and initial UCSF clinical experience. *Am J Obstet Gynecol* 2001;184:S140. abstract.
10. Paek BW, Farmer DL, Wilkinson CC, et al. Hindbrain herniation develops in surgically created myelomeningocele but is absent after repair in fetal lambs. *Am J Obstet Gynecol* 2000;183:1119-23.
11. Adzick NS, Nance ML. Pediatric surgery. *N Engl J Med* 2000;342:1726-32.
12. Sutton LN, Sun P, Adzick NS. Fetal neurosurgery. *Neurosurgery* 2001;48:124-44.
13. Adzick NS, Sutton LN, Crombleholme TM, Flake AW. Fetal surgery for spina bifida. *Lancet* 1999;353:407.
14. Meuli M, Meuli-Simmen C, Hutchins GM, et al. In utero surgery rescues neurological function at birth in sheep with spina bifida. *Nat Med* 1995;1:342-7.
15. McLone DG, Dias L, Kaplan WE, Sommers MW. Concepts in the management of spina bifida. In: Marlin AE, ed. *Concepts in pediatric neurosurgery*. Vol. 5. Basel, Switzerland: Karger, 1985:97-106.
16. Steinbok P, Irvine B, Cochrane DD, Irwin BJ. Long-term outcome and complications of children born with myelomeningocele. *Childs Nerv Syst* 1992;8:92-6.
17. Lorber J. Systematic ventriculographic studies in infants born with meningomyelocele and encephalocele: the incidence and development of hydrocephalus. *Arch Dis Child* 1961;36:381-9.
18. Iskandar BJ, Oakes WJ. Chiari malformations. In: Alright AL, Pollack IF, Adelson PD, eds. *Principles and practice of pediatric neurosurgery*. New York: Thieme, 1999:165-87.
19. Herman JM, McLone DG, Storrs BB, Dauser RC. Analysis of 153 patients with myelomeningocele or spinal lipoma reoperated upon for a tethered cord. *Pediatr Neurosurg* 1993;19:243-9.
20. Scott RM, Wolpert SM, Bartoshesky LE, Zimble S, Klauber GT. Dermoid tumors occurring at the site of previous myelomeningocele repair. *J Neurosurg* 1986;65:779-83.

Copyright © 2002 Massachusetts Medical Society.