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TECHNIQUE

Percutaneous fetoscopic patch closure of human spina bifida aperta: advances in fetal surgical techniques may obviate the need for early postnatal neurosurgical intervention

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Abstract
Background A percutaneous minimally invasive fetoscopic approach was attempted for closure of a spina bifida aperta in two fetuses with L5 lesions. The goal was to obviate the need for postnatal neurosurgery to manage this condition.
Methods and Results The percutaneous fetoscopic procedures were performed by a two-layer approach at respectively 22 ± 2 and 22 ± 4 weeks of gestation. The fetuses were delivered respectively at 32 ± 6 and 32 + 3 weeks of gestation. Their neural cords were completely covered although in small areas skin closure was incomplete. Postnatally, complete skin closure occurred beneath an occlusive draping within 2 to 3 weeks such that neurosurgical intervention was not required. Both neonates showed reversal of hindbrain herniation, near-normal leg function, and satisfactory bladder and bowel function. For one of the two fetuses, ventriculoperitoneal shunt insertion was not required.
Conclusions Percutaneous minimally invasive fetoscopic patch closure of spina bifida aperta offers a substantially less maternal trauma than open fetal surgical repair and currently may even obviate the need for postnatal neurosurgical repair. With a little further improvement in surgical techniques and a better understanding of incorporating surgical patches into the fetus, complete skin closure seems possible in the near future.

Keywords Fetus · Spina bifida aperta · Myelomeningocele · Myeloschisis · Chiari malformation · Hydrocephalus · Fetal surgery · Fetal intervention · Fetoscopy · Amniotic insufflation

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After technical feasibility studies with inanimate models and sheep, we clinically introduced a percutaneous minimally invasive fetoscopic method that allowed simple patch coverage of spina bifida aperta in human fetuses using polytetrafluorethylen material [1, 2]. This simplified approach permitted temporary protection of the exposed neural tissue against the intraamniotic environment. Yet because the patch was fixed onto the healthy skin surrounding the spina bifida aperta, which itself remained untouched, definitive neurosurgical closure of the malformation was required in the postnatal period.

The purpose of this technical report is to present recent improvements in our percutaneous fetoscopic approach that for two fetuses with spina bifida obviated the need for postnatal neurosurgical repair.

Patients and methods

Selection criteria

To be eligible for percutaneous fetoscopic patch closure of spina bifida aperta, the fetuses had to be at 19 ± 0 to 25 ± 0 weeks of gestation, free of other organ abnormalities, and of normal caryotype. Further requirements were a lesion greater than S2 and/or hindbrain herniation accompanied by a lateral ventricular diameter less than 15 mm, as assessed by magnetic resonance imaging (MRI) or ultrasound.

Before the procedures, the pregnant women underwent physical and psychological evaluation as well as maternal electrocardiogram (ECG), echocardiography, fetal MRI, and transvaginal ultrasound for evaluation of the maternal uterine cervix. If no maternal exclusion criteria were detected, an interdisciplinary team obtained informed consent for the procedure. Both procedures were approved by the local committee of human research and performed in accordance with the ethical standards for human experimentation established by the Declaration of Helsinki.

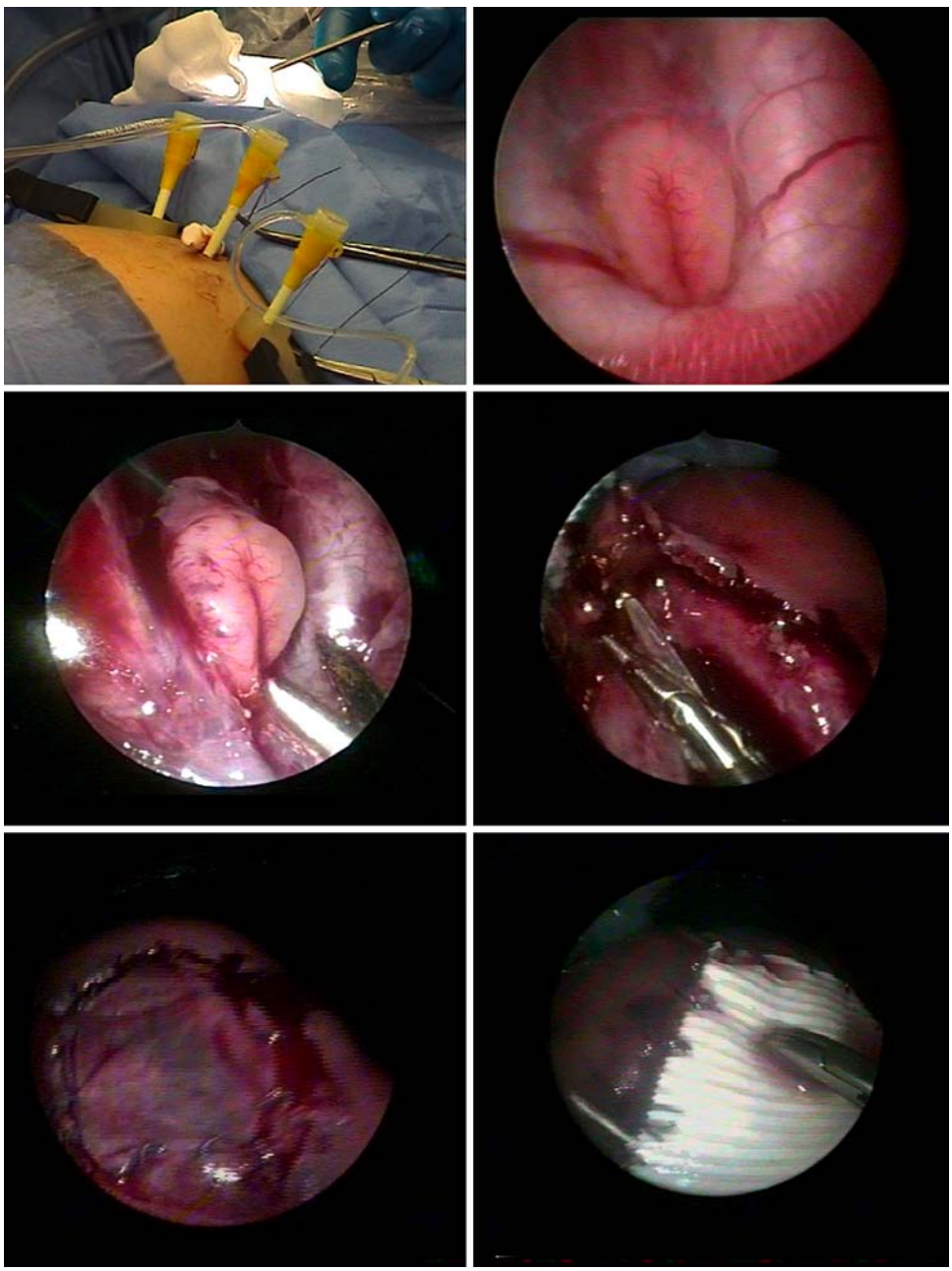

Fig. 1 Percutaneous fetoscopic patch closure of spina bifida aperta for a human fetus at 22 ± 4 weeks of gestation via three trocars with an outer diameter of 5 mm (case 2). *Top row*: *Left*: External view of the percutaneous setup. The three trocars had to be placed across the lower maternal abdomen because of an anteriorly situated placenta. *Right*: Fetoscopic visualization of the exposed neural tissue (L5 lesion) with a 3.3-mm, 30° fetoscope after amniotic insufflation. At this time of gestation, the width of the malformation from side to side covers about two-thirds of the fetal back. *Middle row*: *Left*: Fetoscopic view with a 2.9-mm, 70° fetoscope during dissection of the rostral placode end. *Right*: The skin is undermined before insertion of the absorbable patch. *Bottom row*: *Left*: Fetoscopic view after complete coverage of the neural tissue with a Durasis patch. After this maneuver, the skin is approximated above this patch as much as possible. *Bottom row*: *Right*: Finally, the surgically managed area is protected with an additional Gore-PTFE patch

Operative technique

The two fetoscopic procedures were performed respectively at 22 ± 2 and 22 ± 4 weeks of gestation with the patients under general maternofetal anesthesia using remifentanil and sevoflurane as well as perioperative tocolysis with indomethacin suppositories and temporary infusion of an oxytocin antagonist. Under maternal transabdominal ultrasound and fetoscopic monitoring, three trocars (external trocar diameter, 5 mm), were percutaneously inserted into the amniotic cavity in each case (Fig. 1).

Trocar insertion was followed by partial evacuation of amniotic fluid and carbon dioxide insufflation of the amniotic cavity for optimization of fetal visualization and manipulation. Using fetoscopic instruments, the fetal lumbosacral region was positioned beneath the three trocars. In both cases, a myelomeningocele with an upper lesion level of L5 was present that extended caudally over the sacrum.

The placode was circumcised, and the junctional zone tissue was removed within the vicinity of normal skin (Fig. 1). The spinal cord then was completely covered with a large 3.5 × 2-cm absorbable patch (Durasis; Cook, Mönchengladbach, Germany) sutured onto the paraspinal musculature. Finally, the skin was mobilized and reattached to cover the free edges of the patch.

These manipulations were followed by protection of the surgically managed region against the uterine milieu with an additional nonabsorbent polytetrafluoroethylene patch (Gore MVP, Flagstaff, AR, USA). After these efforts, the insufflation was halted, the gas evacuated, and the amniotic cavity refilled with warmed crystalline solution. Finally, the uterine and abdominal trocar insertion sites were closed, and mother and fetus recovered from the anesthesia.

Postoperative course

After each procedure, maternal recovery was uneventful. Tocolysis was continued until the first postoperative day. Uterine contractions were not observed in the two cases during the postoperative period. Oral intake and ambulation of the two women resumed the first day after surgery. Their pregnancies continued uneventfully except for oligohydramnios, which developed in the first days after the procedures and persisted until delivery.

Case 1

The fetus in this case was delivered by cesarean section at 32 ± 6 weeks of gestation because of premature uterine contractions (birth weight, 2,025 g). Besides a mild respiratory distress syndrome that required attention by continuous positive airway pressure, no other complications of preterm delivery were observed in the infant.

At delivery, the spinal cord was firmly covered by skin and patch material. The upper nonabsorbable patch had dehisced along three edges. The lower absorbable patch had become almost entirely overgrown or ingrown by skin except for a central area measuring about 2 × 1 cm. Postnatally, complete skin closure occurred beneath an occlusive draping (Varihesive; ConvaTec, Deeside, UK) within 3 weeks such that neurosurgical closure was not required.

Furthermore, MRI showed reversal of hindbrain herniation. Yet ventriculoperitoneal shunt insertion was required at 5 weeks of postnatal life because of progressive ventricular distension.

When the baby was discharged at 8 weeks, it exhibited normal leg movements and reflexes. The anal sphincter tone was normal, and no bladder taps were required. Yet at that time, small adherences of the neural cord to the skin were observed in the region of the operation.

At this writing, the child is 6 months old and doing well. One revision of the shunt has been required.

Case 2

The fetus in this case was delivered by cesarean section at 32 ± 3 weeks of gestation because of premature uterine contractions (birth weight, 2,010 g). Besides a type 3 respiratory distress syndrome and a pneumothorax that required ventilation over 4 days, no other complications from preterm delivery were observed in the infant.

At delivery, the neural tissue was completely covered by skin and patch material (Fig. 2). Removal of the upper patch showed that the lower absorbable patch had become almost entirely overgrown or ingrown by skin except for a central area measuring about 0.7 × 1.5 cm. Postnatally, complete skin closure occurred beneath an occlusive draping (Varihesive; ConvaTec within 3 weeks such that neurosurgical closure was not required. Furthermore, MRI showed reversal of hindbrain herniation.

When the baby was discharged at 4½ weeks of age, it exhibited near normal leg movements and reflexes. The anal sphincter tone was normal, and no bladder taps were required. Sensitivity and motor function were present in both feet including the toes. In contrast to case 1, no adherence of the neural cord to the skin was observed in the region of the operation.

At this writing, the child is 3 months old and doing well. To date, ventriculoperitoneal shunt insertion has not been required.

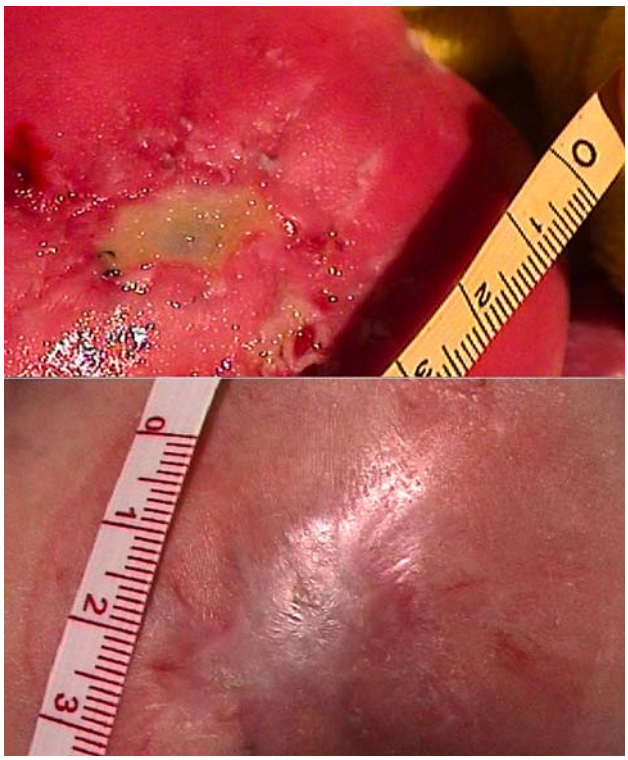

Fig. 2 Postnatal aspect of the surgically managed area after percutaneous fetoscopic patch closure of spina bifida aperta at 22 ± 4 weeks of gestation (case 2). No tethering of neural cord tissue to the surgically managed region is observed. *Top row*: Image taken after removal of the outer patch. Note that at 32 ± 3 weeks of gestation, the width of the malformation covers only one-tenth of the width of the fetal back. Despite the long interval between fetal surgery and delivery, still a 1.5 × 0.7-cm area of the absorbable patch is not fully covered by skin. As in the first case, the surgically managed area has been covered with a hydrocolloid film (Varihesive; ConvaTec, Deeside, UK) for more than 2 weeks. *Bottom row*: View of the surgically managed area after complete closure of the skin defect showing an excellent cosmetic result (mild erythema and reddish rim originate from removal of Varihesive just before the image is taken)

Discussion

Closure of spina bifida aperta during fetal life aims at protecting the exposed spinal cord from mechanical and chemical damage by the intraamniotic environment and at preventing the continued intraamniotic leakage of cerebrospinal fluid [3]. As a consequence, the procedure may help to maintain leg function and improve upon hindbrain herniation and hydrocephalus [4–8].

Over the past decade, open fetal surgery for spina bifida aperta has evolved to become the most common open fetal surgical procedure. This procedure currently is under investigation in the United States in a prospective randomized trial (MOMS study). In contrast, the development of fetoscopic surgery for spina bifida aperta has been slow because of the meticulous planning and attention to detail required to meet the many demands of this challenging procedure.

A first fetoscopic approach for spina bifida aperta patch coverage by direct trocar placement into the uterus after maternal laparotomy was developed and clinically introduced by Bruner and Tulipan in the mid–90s [9, 10]. Their attempt soon was abandoned because of technical difficulties and replaced by the open operative approach [11]. For similar reasons, fetoscopic closure of spina bifida also was given up by Harrison et al. [12].

Based on studies with sheep and inanimate models that primarily focused on the development of minimally invasive techniques for fetal cardiac intervention [13–16], we started with technical modifications and procedure training to rekindle the development of a fetoscopic approach to the management of fetal spina bifida aperta. Using an ovine model, we developed a simple percutaneous fetoscopic patch coverage approach that subsequently was introduced into the clinical arena some years ago [1, 2]. This allowed us slowly to acquaint ourselves with the issues of multiple management and safety as well as the technical challenges of using complex minimally invasive surgery for human fetuses.

Our approach involved designing and developing technical gadgets such as an instrument that could deliver patch material measuring up to 5 × 4 cm through a trocar lumen smaller than 4 mm. It also involved gathering a large body of clinical experience concerning maternal and fetal safety of maternofetal anesthesia and gas insufflation of the amniotic cavity over operating periods as long as 6 h. As a result of the latter efforts, we were able to develop an anesthetic protocol exclusively tailored to the requirements of general maternofetal anesthesia during minimally invasive fetal surgery that proved to be exceedingly safe for pregnant women and their fetuses undergoing surgery for spina bifida and other conditions [17].

Furthermore, extensive studies with sheep helped us to avoid dangerous pitfalls such as placental abruption after the clinical introduction of percutaneous partial amniotic carbon dioxide insufflation (PACI). In our opinion, PACI represents the most important strategy for improving visualization and controlling bleeding events during fetoscopic surgical procedures [18].

To our disappointment, in our early clinical experience, the period between surgery and delivery ranged only from 22 to 36 days (mean, 29 days), resulting in a mean gestational age at delivery of 29 ± 5 weeks [2]. We speculated that the earlier deliveries with the far less invasive percutaneous fetoscopic approach were not related to procedure length or PACI, but rather to the persistence of membranous leaks from insertion of the three trocars. These insertions favored chorioamniotic separation, amniotic

fluid–induced uterine inflammation, and ultimately, preterm premature rupture of membranes.

Based on this speculation and the observation that the membranous damage after our fetoscopic procedures was not amenable to simple closure by collagen plugs, we have taken major steps over the past 3 years to develop a new closure method. An early design was applied for the two cases described in this report, resulting in far longer periods between surgery and delivery (74 and 69 days, respectively). Upcoming cases now will need to show whether this promising development resulted from the novel closure method or from chance.

Safe general maternofetal anesthesia, control of PACI, and the improved method for uterine closure were the pillars that allowed us to advance our fetoscopic approach from simple patch coverage to a far more complex percutaneous fetoscopic surgical procedure encompassing tissue manipulations such as dissection, resection, skin mobilization, suturing, and control of homeostasis. As the two reported cases demonstrate, this more mature minimally invasive approach has reached an important landmark because the need for early postnatal neurosurgical attention has been obviated. Yet further improvements clearly are required, and the aim is to achieve secure complete skin closure until delivery and to prevent spinal cord adhesions that necessitate future untethering.

To achieve these tasks, we have turned our focus on the development of new instrumentation that, regardless of unfavorable trocar positions, will facilitate dissection of the minute fetal spinal cord, allow complete removal of the surrounding junctional zone tissue, and offer sufficient skin mobilization. Furthermore, we are pursuing a better understanding about the ingrowth of surgical patches into the fetus and about the origin of oligohydramnios after fetal surgery.

As soon as complete skin closure at delivery is reliably achieved for fetuses after percutaneous fetoscopic closure of spina bifida aperta, their normal vaginal delivery will become possible because the small trocar holes do not impair the integrity of the uterine wall. In contrast, the position and size of the uterine scar from the open operative approach to date require delivery by cesarean section of both the surgically treated fetus and any future sibling because of the risk for uterine dehiscence during normal delivery.

In conclusion, fetoscopic closure of spina bifida may now obviate the need to perform postnatal neurosurgery on affected fetuses.

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