Management of pregnancy in patients with exstrophy-epispadias sequence: a case series and literature review

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Abstract

Exstrophy-epispadias sequence is an uncommon diagnosis in which surgical reconstruction has increased quality of life for these patients. As they are entering the reproductive phase of their life, consideration must be made for management of their pregnancies in the context of their genitourinary reconstruction. There have been few case reports of patients with cloacal exstrophy conceiving; therefore, information to guide management of their pregnancies is limited. Here we describe a patient with Omphalocele-Exstrophy-Imperforate Anus-Spinal defects (OEIS) and a patient with a history of bladder exstrophy both with spontaneous pregnancy managed by a multidisciplinary approach and primary cesarean delivery.

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Introduction

Exstrophy-epispadias sequence (EES) encompasses a wide range of anterior wall defects including OEIS and bladder exstrophy. OEIS complex, also known as cloacal exstrophy, was first described in 1978 and is a rare constellation of anomalies involving the urogenital, gastrointestinal, and skeletal system and has an estimated incidence of 1 of 200,000 to 400,000 live births.[1] Classic bladder exstrophy is more common than OEIS complex and has an estimated incidence of 1 of 50,000 live births.[2] Advances in genitourinary reconstruction have allowed exstrophy

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patients restoration of sexual function and improved fertility. However, EES remains a challenge in regard to basic gender reconstruction, urinary function, and reproductive health.[3-5] The most common recommendation for these patients during pregnancy is delivery by cesarean section due to the potential for trauma sustained during vaginal delivery or emergent cesarean that could result in injury to previous urologic reconstruction subsequently resulting in new or worsened bowel and bladder function and/or uterine prolapse.[4,5] Pregnancy in a patient with a history of EES is rare. Therefore, standard management plans are not established for care during pregnancy or delivery. The American Urological Association (AUA) has made recommendations for an urologic ultrasound at 16 weeks with continued re-evaluation for hydronephrosis, but no other recommendations were made for antepartum monitoring or delivery management.[6] Due to advances in surgical reconstruction, patients with EES will have a better functional quality of life which will likely result in more women desiring pregnancy. Obstetricians need to be aware of special considerations to preserve the patient's quality of life. Here, we describe the antenatal and intrapartum management of two women with OEIS and bladder exstrophy who both delivered term infants by primary cesarean section.

Case 1

A Gravida 0 26-year-old woman with OEIS presented for preconceptional consultation and desired removal of her etonogestrel implant. Her history was notable for omphalocele, bladder extrophy, imperforate anus, and pubic symphysis separation discovered at birth. On day of life two, she underwent omphalocele excision, bladder closure, which was continuous with the lower margin of the omphalocele, and suprapubic catheter placement. A patent urethra drained into the cloaca. She was also noted to have an absent left kidney and ureter, as well as malrotation of the intestine. She underwent colostomy placement to the left abdominal wall, appendectomy, and primary abdominal wall closure.

At four years of age, she underwent posterior sagittal anoplasty using an abdominal perineal approach. During the procedure, she was found to have two ovaries bilaterally and a small uterus attached to each ovary with fimbria confirming a uterine didelphys. The cloaca was found to have four openings, one for the rectum, two for the vagina, and one for the urethra. Six months later, she underwent genitoplasty with Z-flap reconstruction and herniorrhaphy. Subsequently, she underwent colostomy takedown with primary end-to-end anastomosis. At ten years of age, she underwent an anterior abdominal reconstruction with creation of an umbilicus, genital reconstruction (medialization of the clitoris) and scar removal. At twenty-two years of age, she underwent right and left periacetabular osteotomy for pain secondary to her bilateral hip dysplasia and pubic symphysis separation.

Approximately six months after preconception counseling and four months following etonogestrel implant removal, the patient spontaneously conceived. An ultrasound at 7 weeks confirmed a pregnancy within her right

uterine horn. She received counseling by our Prenatal Genetic Counselor at 12 weeks and she underwent integrated serum screening. She was counseled regarding her increased risks of preterm delivery, preterm rupture of membranes, breech presentation, and potential need for cesarean delivery. Fetal anatomy and cervical length were normal at 20 weeks. Her pregnancy was complicated by multiple urine cultures indicative of Escherichia coli colonization. A Urology consult at 13 weeks was obtained to discuss recurrent urinary tract infections (UTIs) and delivery options given her surgical history. She subsequently was placed on prophylactic antibiotics (trimethoprim/sulfamethoxazole based on sensitivities) until delivery.

Cesarean delivery was recommended at 39 weeks gestation due to her history of extensive genitourinary reconstruction and a perineal body < 1 cm. She was counseled regarding the risks associated with both vaginal and cesarean deliveries. A pelvic MRI was obtained prior to cesarean delivery to assist with surgical planning. The dome of the bladder was found to be more anterior and superior than normal anatomic position and approximately 8 cm inferior to the umbilicus as demonstrated in Image 1. Additionally, the bladder tracked superiorly to the left anterior iliac spine as seen in Image 2. MRI was also significant for a rectum and anus more anteriorly and vertically oriented than expected as well as diastases of the pubic symphysis. Given these findings, Urology assisted with abdominal entry during cesarean section due to the potential for surgical complications.

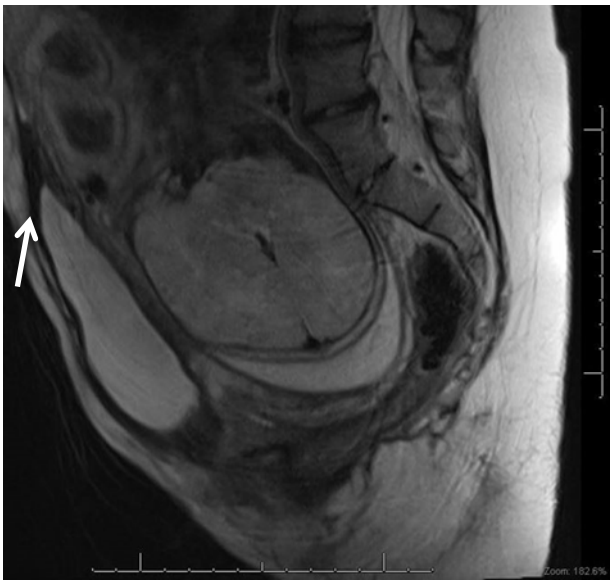

Image 1: Sagittal view MRI of pelvis without contrast at 38 6/7 weeks from Case 1 demonstrating the bladder near the anterior abdominal wall and tethered high toward the umbilicus (arrow).

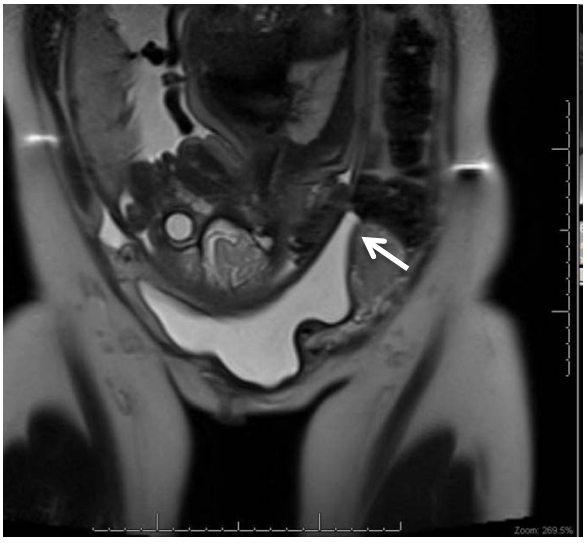

Image 2: Coronal image from Case 1 demonstrating the bladder edge extending superiorly to the left iliac spine (white arrow).

The patient's delivery was uncomplicated despite her extensive history. Spinal anesthesia was performed without difficulty. Her abdomen was entered via a vertical midline incision inferiorly at 6 cm below the umbilicus. The incision was extended superiorly due to risk of bladder injury. The bladder was adherent halfway to the umbilicus and was free from the uterus. A low transverse uterine incision was made in the right uterus and a viable male infant weighing 3185 gm with Apgars of 9 and 9 was delivered from vertex position. The patient's postoperative course was uncomplicated and she and her male infant were discharged to home on the third postoperative day. Both mother and infant were doing well at her 6 week postpartum visit and denied any incontinence or further UTIs.

Case 2

A Gravida 1 Para 0 26-year-old woman with a history of bladder exstrophy presented early in pregnancy for prenatal care. She underwent primary repair of the defect shortly after birth. She then underwent ureteral reimplantation surgery at three years old and reconstructive surgery at ten years old, which included a monsplasty, clitoroplasty, and umbilicoplasty. She had a history of recurrent UTIs and pyelonephritis as a child that resolved after her bilateral ureteral reimplantation. Her last UTI was three years prior to pregnancy. Before her pregnancy, she reported mixed incontinence, mostly occurring during intercourse. Her incontinence caused her to change her undergarments at least twice daily. She was seen and evaluated by Urology. Her incontinence was refractory to Kegels, pelvic floor physical therapy, and oxybutynin. Urodynamics were completed two months prior to conception and revealed stress incontinence with reduced bladder capacity and low filling pressures but no reflux. On ultrasound, she had two normal kidneys with her right kidney being slightly larger than the left (right kidney 11.4 x 5.9 x 4.3 cm versus left kidney 9.0 x 3.7 x 3.2 cm).

She was not seen for a pre-pregnancy consult. Her first obstetric visit at 9 4/7 weeks revealed an intrauterine pregnancy consistent with her last menstrual period. A pelvic exam revealed a shortened introitus, post-surgical changes around her mons/labia, and elongated anterior cervix. A Urogynecology consult at 12 4/7 weeks gestation was obtained due to ongoing urinary incontinence and recommendations for delivery planning. She underwent integrated serum screening, which was normal. She was counseled at her initial obstetric visit on her increased risk of preterm delivery, preterm rupture of membranes, breech presentation, and potential need for cesarean delivery. Fetal anatomy and cervical length were normal on ultrasound at 20 weeks. Serial growth ultrasounds were performed, which were normal. Overall, her pregnancy was uncomplicated and significant only for worsening stress incontinence and urinary frequency. She did not develop any UTIs during pregnancy.

After discussion with Urogynecology and Urology, cesarean delivery was recommended at 39 weeks due to her history of extensive genitourinary reconstruction. She was counseled regarding the risks associated with both

vaginal and cesarean delivery. A pelvic MRI was obtained at 23 5/7 weeks gestation to evaluate for uterine anomalies due to concern for a dilated sac area of the uterus posterior to the cervix and to assist with surgical planning for cesarean delivery. The MRI showed a normal position of the uterine fundus and body with thickening of the urinary bladder as seen in Image 3. At the time of delivery, the fetus was in transverse, back down lie.

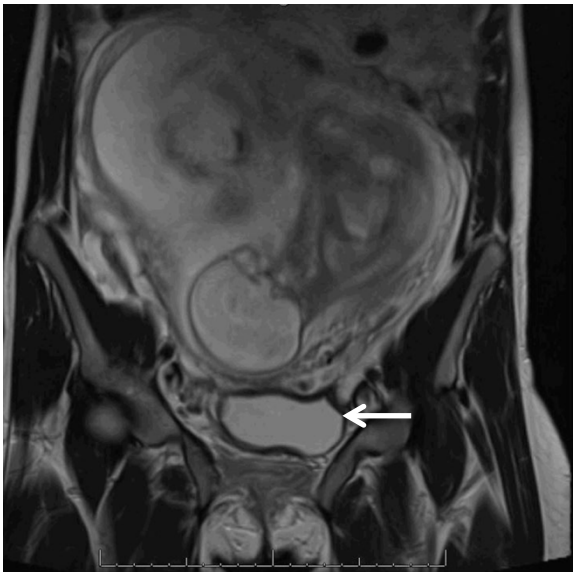

Image 3: Coronal view from MRI of pelvis without contrast at 24 6/7 weeks from Case 2 demonstrating a normal uterus and thickened bladder edge (white arrow).

The patient's cesarean delivery at 38 6/7 weeks gestation was uncomplicated. Spinal anesthesia was performed under ultrasound guidance. A paramedian incision was extended vertically without disruption of the bladder inferiorly. The bladder was found to be adherent to the anterior abdominal wall about 5 cm below the umbilicus. Additionally, the uterus with normal fallopian tubes and ovaries bilaterally was found intact and free from the bladder. A classical cesarean section was performed and a viable female infant weighing 2485 gm with Apgars of 8 and 9 was delivered from vertex. Urogynecology assisted with abdominal entry. Urology was not present during the delivery, although was available for immediate consultation. The patient's postoperative course was uncomplicated. She and her infant were discharged to home on the third postoperative day. Both mother and infant were doing well at her 6 week postpartum visit in which she was reported to have stable, non-worsening incontinence as compared to pre-pregnancy incontinence.

Discussion

Due to the complex past surgical history and female anatomy following reconstruction, it is our recommendation that pregnant patients with EES be managed at a tertiary care center where a multidisciplinary team approach can be implemented to ensure the patient maintains her established quality of life and genitourinary function after delivery. Given that these patients have a spectrum of defects with co-morbidities, each patient will need individualized evaluation and delivery planning will depend on their surgical history and baseline genitourinary function in addition to the usual obstetric considerations.

Urology, Urogynecology, General Surgery, and Plastic Surgery consultations should be considered due to the possible lack of adequate fascia for closure and extensive surgical history involving the anterior abdominal

wall, bladder and colon. Urology and/or Urogynecology should be consulted early in pregnancy to assist with patient evaluation and counseling. General Surgery and/or Plastic Surgery could be consulted later in pregnancy for assistance with surgical planning of abdominal entry. Although both urology and urogynecology helped with entry with case 1 and 2 respectively, it is important to consider potential urologic injury, including ureteral, needing repair. Additionally, an Anesthesiology consult towards the end of pregnancy should be considered, especially if the patient has a history of spinal defects (as in patients with OEIS) that may affect spinal anesthesia. An MRI should be considered late in pregnancy for surgical planning (around 30-34 weeks) if the patient has previously undergone significant urologic surgery and for anesthesia planning if the patient has significant spinal deformities. A vertical midline incision is recommended due to reconstruction history and possible bladder adhesion to the anterior abdominal wall. A paramedian incision may also be considered if the patient has a midline ostomy or had bladder reconstruction such as an augmentation cystoplasty. The patient should be counseled on the possible need for a classical uterine incision and the implications this has for future pregnancies. However, as in Case 1, a low transverse hysterotomy may be considered after abdominal entry and adequate exploration of the reconstructed anatomy. It is also important to note that cesarean section does not guarantee the patient will be free from complication. She is still at risk for surgical complications, postpartum uterine prolapse, fecal incontinence and urinary incontinence.[5] Although primary cesarean section will usually be indicated, vaginal delivery may be considered depending on the extent of the original genitourinary reconstruction, estimated fetal weight and gestational age at onset of labor. Of note, up to 57% of individuals with EES are noted to have breech presentation at delivery.[7] It is important to consider normal obstetric indications for cesarean delivery if a patient is already laboring, including breech presentation as above. However, urgent cesarean delivery should be considered in a patient if previously cesarean delivery has been considered to outweigh risks of injury during a vaginal delivery. However, one should consider difficulty of abdominal entry and potential for injury if needing timely abdominal entry. Consulting departments should be aware of the patient if there is a potential for immediate delivery if the patient is laboring.

In the literature, there are only a few case reports of patients with cloacal exstrophy becoming pregnant and therefore guidelines for management of patients with EES in pregnancy are limited. Many individuals with bladder and cloacal exstrophy have complications associated with decreased quality of life including uterine prolapse (up to 29.5%), urinary incontinence (up to 65%), recurrent UTI, and fecal incontinence.[4] Less than 10% of women with cloacal and bladder exstrophy have been reported to have pregnancies, and these pregnancies have been complicated by new onset or worsening of recurrent UTI, uterine prolapse, and urinary incontinence.[4,8] Matthews et al. described a case of

pregnancy in a patient with a history of cloacal exstrophy repaired initially by urinary diversion. The pregnancy was complicated by perforation of Koch's pouch during cesarean section, postpartum uterine prolapse, fecal incontinence, and urinary incontinence from the urinary diversion.[5] Many of these individuals also struggle with infertility due to uterine and vaginal anomalies. Unilateral renal agenesis, hydronephrosis, spinal dysraphism, and spinal/pelvic abnormalities, including widened pubic diastasis, have also been described.[3] Another study demonstrated that 56% of individuals with 46XX cloacal exstrophy lost one or both of their uteri via hysterectomy due to uterine prolapse and/or abnormal uterine location.[9]

An important consideration as demonstrated by these cases is that women with EES, while at risk for infertility, can have normal fertility. Evaluation for uterine and renal anomalies should occur when caring for patients in this population group. They have a higher prevalence of uterine, renal, and urogenital anomalies. One consideration in Case 1 will be the anatomical location of future pregnancies given that she does not have a right kidney. If a future pregnancy is in the left horn, any left hydroureter or urinary stasis will increase her risk of pyelonephritis given she already is predisposed to recurrent UTI. This will be important given the risks associated with pyelonephritis, which include preterm labor, preterm birth and acute respiratory distress syndrome.[10] For these reasons, prophylactic antibiotic use during pregnancy should be considered as in Case 1. It also can be considered to evaluate kidney function throughout pregnancy and potential need a diversion or percutaneous nephrostomy if decreasing kidney filtration or increased hydroureteronephrosis. This is a possible risk for this population due to potential abnormal ureter insertion or uterine anomalies.

Regarding the genetic heritability of EES, the underlying etiology of this condition is not well understood. Based on current knowledge, most individuals represent sporadic cases, and the recurrence risk in siblings of an affected individual is thought to be low (<1%).[1] Additionally, because so few affected individuals reproduce, there is limited data regarding the recurrence risk in offspring. No distinct genetic or environmental association has been identified, although an association with an unbalanced translation of chromosome 9 and the Y chromosome, HOX genes, and rare familial associations have been reported.[3] For the few previously described familial cases, the inheritance pattern has been most consistent with autosomal dominant inheritance with reduced penetrance and/or variable expressivity. As such, the risk to have a child affected with EES could be as high as 50%. Because there is not a known genetic etiology for EES, patients cannot be offered definitive prenatal diagnosis however a Level II ultrasound at a tertiary care center should be performed. Patients should also be offered the option of integrated screening and alpha fetal protein (AFP) level in the second trimester. We recommend a preconceptional genetics consultation, an early second trimester

ultrasound evaluation of the developing fetus, and a third trimester growth ultrasound (around 32 weeks) with a maternal-fetal medicine specialist.

In summary, medical and surgical advancements are making reproduction and pregnancy a more likely possibility for women with EES. A multi-disciplinary team approach and individualization of care plans are important for women with EES in order to help preserve their genitourinary reconstruction during pregnancy, preserve quality of life and ensure a safe pregnancy and delivery.

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