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Case Report

Neonatal bladder exstrophy: a case report and literature review of long-term outcomes

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Abstract: Bladder exstrophy (BE) is a rare, complex, congenital malformation predominantly observed in men. We report a case of a female infant with BE who underwent complete primary repair of BE (CPRE). After 5 weeks of appropriate medical care and nursing, the infant was discharged successfully without urinary retention, hematuria, fever, or abdominal distention. After discharge, the child was followed up via telephone. At 1.5 months post-op, the child showed no signs of urinary incontinence, hydronephrosis, or reflux. However, ultrasonography revealed an unfilled bladder. By the third month, the child voided volitionally through the urethra every 3 h. At 6 months of age, renal ultrasonography revealed an unfilled bladder. Children may undergo augmentation cystoplasty at 2 or 3 years of age. During telephone follow-ups, the parents expressed concerns regarding their child's sexual function and fertility in adulthood. Patient follow-up will be continued to determine long-term health outcomes.

Keywords: Bladder exstrophy, complete primary repair of bladder exstrophy, adulthood, long-term quality of life, continence, sexual outcome, fertility

Introduction

Bladder exstrophy (BE) is a rare, complex congenital malformation involving both the urinary and genital tracts. BE is part of the BE-epispadias complex (BEEC) diagnosis. It is primarily characterized by the exposure of the bladder mucosa and is often accompanied by defects in the lower abdominal wall, epispadias, and pubic symphysis separation [1]. Surgery is the primary treatment for patients with BE, and the main goal of exstrophy management is bladder closure. Several methods can be used for closing the bladder, including modern staged repair of BE (MSRE) and complete primary repair of exstrophy (CPRE). Additionally, most patients require extensive surgery to achieve urinary continence or genital reconstruction after primary surgery [2]. With the advancements in medical and surgical reconstruction, the survival rate of patients with BE has increased significantly. However, with this increased survival rate, concerns regarding the long-term quality of life of these patients have increased. From adolescence to adulthood, urinary incontinence and renal function are the key factors influencing quality of life. In adulthood, goals, such as sexual function, genital appearance, fertility, and pregnancy, are the primary concerns. The current research suggests that adults with BE achieve satisfactory continence following multiple surgical interventions. Despite some problems with sexual functioning, most patients with BE enter relationships and attain sexual satisfaction. Pregnancy carries a risk, and some women require assisted reproductive technology (ART); however, better pregnancy outcomes can be achieved through multidisciplinary care.

Case history

A female infant, one of two twins with a birth weight of 2,800 g, was delivered by Cesarean section (CS) at 36+5 weeks of gestation at a local hospital. The mother was 34 years old and had one previous miscarriage, and this pregnancy was achieved by in vitro fertilization.

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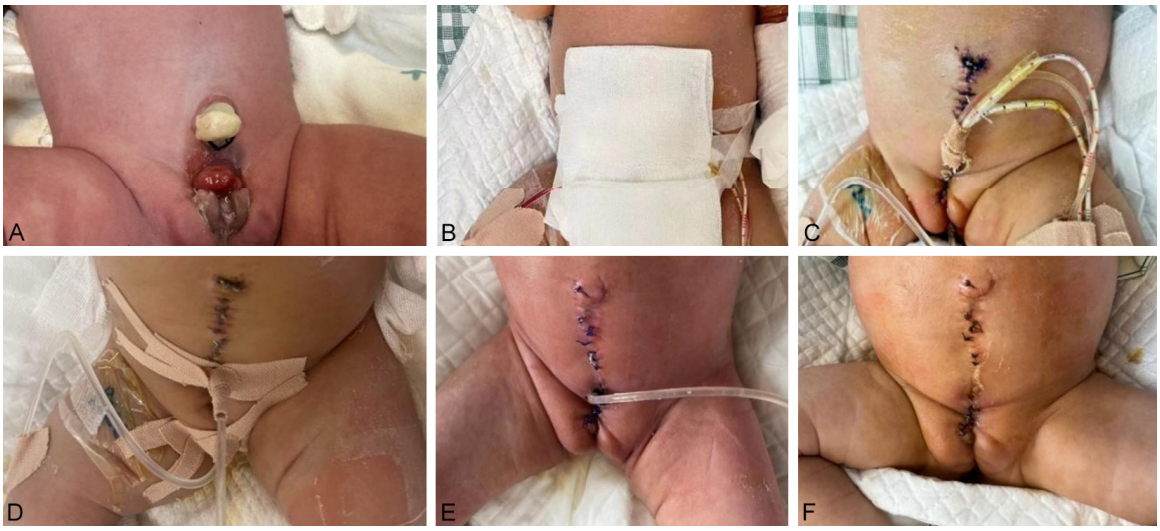

Figure 1. A. A female infant with classic bladder exstrophy. B-E. After surgery, two ureteral drains, a single-lumen ureteral catheter, and a cystostomy tube were placed. F. After approximately 5 weeks of treatment, the infant was discharged from the hospital successfully.

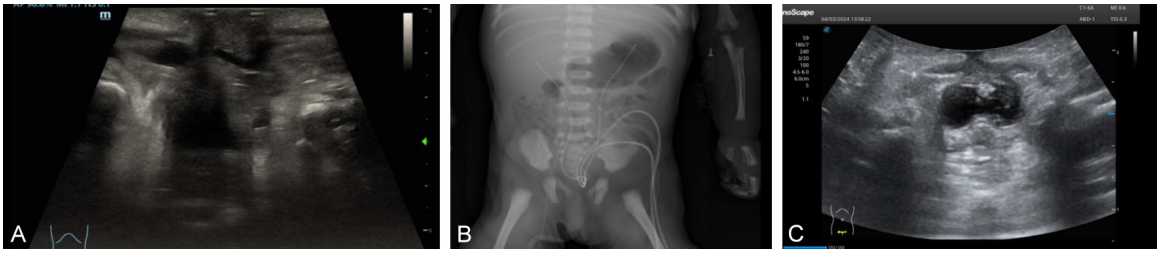

Figure 2. A. Renal ultrasound shows normal kidney morphology and size, and the bladder is not visualized. B. The ultrasound shows two ureteral drains; a single-lumen ureteral catheter and a cystostomy tube were placed postoperatively. C. At 1.5 months, the ultrasound revealed an unfilled bladder and no signs of ureteral dilation.

During pregnancy, the mother underwent regular prenatal checkups at a local hospital. The mother had no underlying diseases, pregnancy-related comorbidities, history of smoking, use of specific medications, or exposure to chemicals. No family history of disease or genetic predispositions was noted. Immediately after birth (15 February 2024), the infant was transferred to the neonatal intensive care unit (NICU) of our hospital because of a perineal malformation. The lower abdominal wall below the umbilicus was defective, and the bladder protruded from the defect. In addition, the perineum was malformed, with urine flowing from the malformed area (**Figure 1A**). Renal ultrasonography showed normal kidney morphology and size, with no significant dilation of the bilateral ureters; however, the bladder was not visualized (**Figure 2A**). No abnormalities were observed in other parts of the body. Based on clinical presentation and imaging findings, the infant was diagnosed with complete BE.

The infant underwent CPRE on the third day of life. A series of reconstructive procedures were performed, including BE repair, bladder neck reconstruction (BNR), urethral episiotomy repair, pubic symphysis closure, perineal plasty, repair of the abdominal wall defect, and umbilicoplasty. After surgery, two ureteral drains, a single-lumen catheter inserted through the bladder neck, and a cystostomy tube were placed (**Figures 1B**, **1C** and **2B**). Postoperatively, the infant received multiple consecutive transfusions of fresh frozen plasma and albumin owing to coagulation abnormalities and hypoproteinemia. Preoperatively, cefoperazone-sulbactam and sodium ampicillin were administered as infection prophylaxis. Postoperatively, fever and worsening infection led

to a change in the antibiotics to meropenem and ampicillin. During hospitalization, cardiac ultrasonography revealed a patent ductus arteriosus, and two courses of ibuprofen were administered to close the ductus arteriosus. Other medications included furosemide, torasemide, and dexamethasone for diuresis as well as anti-inflammatory drugs. The bilateral ureteral drains were removed on postoperative day 16 (**Figure 1D**), urinary catheter on day 25 (**Figure 1E**), and cystostomy tube on day 31 (**Figure 1F**). After 5 weeks of treatment, the infant was successfully discharged from the NICU without urinary retention, hematuria, fever, or abdominal distention (Supplementary Table 1).

We conducted regular follow-ups with the infant's parents by telephone after their discharge from the hospital. After 1.5 months, renal ultrasonography revealed an unfilled bladder (**Figure 2C**); however, the infant exhibited normal voiding function, with no signs of hydronephrosis, ureteral dilation, or vesicoureteral reflux. By 3 months of age, the infant voided voluntarily through the urethra every 3 h. At 6 months of age, renal ultrasonography revealed an unfilled bladder. Children may undergo augmentation cystoplasty (AC) at 2 or 3 years of age. During telephone follow-ups, the parents expressed concerns regarding their child's sexual function and fertility in adulthood. We will continue patient follow-up to determine long-term health outcomes.

Discussion

BEEC is a rare congenital genitourinary malformation that includes urethral episiotomy, BE, and cloacal exstrophy (CE), with CE being the most severe type [3]. BEEC can affect the abdominal wall, pelvis, urinary tract, genital system, and occasionally the intestinal system. Classic bladder exstrophy (CBE) is characterized by a defect of the lower abdominal wall with evagination of the bladder plate [4, 5]. Patients with BE undergo a series of surgeries between infancy and adult [6]. The primary goals of surgery are to manage urinary continence, preserve renal function, and repair the cosmetic and functional aspects of the genitalia. Currently, the primary surgical approaches used are MSRE and CPRE [7]. MSRE is performed in stages, involving bladder closure (within 72 h), exstrophy repair (6-16 months), and BNR (5-9 years) [8]. Meanwhile, CPRE is a widely adopted approach that provides complete primary repair in a single-stage surgery. Compared to MSRE, CPRE minimizes the number of surgical steps and provides a more physiological environment for the bladder. Furthermore, the initial reconstruction of the urethra and penis is beneficial for increasing outlet resistance and enhancing bladder cycling/expansion, thereby achieving urinary continence [9].

With advancements in medical care and surgical reconstruction, which have improved the survival rate of children with BE, the long-term quality of life of these patients has become increasingly important. Multiple surgeries and their subsequent complications significantly affect the quality of life and mental health of both children and adults, with continence being the most prominent complication. During childhood, the primary goal is to preserve renal function and manage urinary incontinence. Patients with BE require multiple reconstructive surgeries to achieve continence [10]. Continence procedures include BNR, BNR with AC or continental catheterizable stoma, and bladder neck closure (BNC) with continental catheterizable stoma [11]. Many studies have reported marked discrepancies in continence rates. Urinary incontinence is difficult to define. Broadly, it is defined as the ability to store urine and actively empty the bladder when appropriate. The definitions of continence and follow-up duration vary widely among studies [12, 13]. As reported in many studies, dry interval (DI) ≥3 h with voiding is an appropriate definition of continence after BE repair [14, 15]. Although the rate of volitional voiding post-primary BE closure was initially low, the continence rate will achieve excellent results after additional continence procedures [11, 16-19].

A large study has reported the continence outcomes for 432 (306 men and 126 women) patients with CBE at the median age of 14.8 years (range, 3.3-36.1). Only 23% of patients are able to void volitionally through the urethra without a catheter or urinary diversion (DI ≥3 h). Continence rate varies widely depending on the surgical procedure. Among the patients who underwent BNR alone, the continence rate was 64%. The continence rate was 93% in the patients who underwent BNC with a continent catheterizable stoma [18]. At the median fol-

low-up age of 5.7 years, 33/40 (83%) of BE patients with CPRE voided, and only 5/40 (13%) were continent with volitional voiding for >2 h; of these, 3 of 5 patients voided for >3 h (8%) [17]. Although the continence rate post-primary BE closure (CPRE or MSRE) was initially low (12.5%), it increased to 93.8% after continence procedures, such as BNR and/or AC at the median follow-up time of 18±5 years [16]. Of the patients, 16.2% (23/142) with BE gained DI ≥3 h after CPRE alone at the mean age of 12.1±5.2 years, whereas the remaining patients required complementary post-CPRE continence procedures, such as clean intermittent catheterization (CIC), BNR, or BNC to achieve continence [20]. In addition, patients with BE show signs of upper urinary tract dysfunction in adulthood. When patients were followed for renal function in adulthood at the median age of 30.1 years (range, 18-57), 7 of 16 patients (44%) had stage II or higher chronic kidney disease, 31% (5/16) had hydronephrosis, 44% (7/16) had bladder calculi, and 56% (9/16) had a history of pyelonephritis [21]. A urodynamic study has reported that most children with BE who underwent CPRE produced sustained detrusor contractions, although 40% were still incapable of voiding and required a catheter to empty the bladder [22].

In adulthood, patients aspire to live a normal life and face challenges in establishing relationships, sexuality, sexual function, and fertility. Most patients can have good long-term sexual outcomes after undergoing additional genital reconstruction surgeries. Age, education, and regional economic status may influence sexual outcomes in patients with BE. Patients with BE who have received higher education and live in developed areas are better able to cope with the disease and with life, and therefore, have higher confidence in sexual activity. Zhu et al. [23] investigated the long-term outcomes in a Dutch cohort of 17 adult BEEC patients with a median age of 36 years (range, 19-73 years). Nearly two-thirds of the participants had received a master's and/or bachelor's degree. Of the patients, 71% were in a committed relationship, and 82.4% were sexually active. The patients demonstrated minimal or no differences in sexual function and quality of life compared to the general population. In another USA cohort of 113 male patients with BE (median age, 32 years), 74 patients (65%) had at least received a university education. Seventy patients (62%) reported currently being in a relationship. Ninty-six patients (85%) had been sexually active during their lifetime, and 76 (70%) had high confidence in their ability to obtain and maintain erection [24]. A study investigated the long-term sexual outcomes of 29 adolescent and post-pubertal patients with BECC in Belgium (25 men, 4 women, and 3 with CE) with a median age of 21 years (range, 20-27 years). The study indicated that 96% of the men reported engaging in sexual activities. Of the men, 79% reported sexual satisfaction and 63% had normal ejaculation [25]. Another study evaluated sexual function and quality of life in male adults with BEEC (median age, 26 years; 84% with CBE) in Germany, 17/19 (89%) reported erections, 17 (89%) reported orgasms, and 13 (68%) reported ejaculations [26].

In developed regions, although most patients with BE have good sexual outcomes after multiple surgeries, both male and female patients with BE exhibit low fertility intentions, with half as much reluctance to conceive a child. Patients with BE experience varying degrees of fertility impairment during adulthood. Male patients with BE may experience weak or dribbling ejaculation, retrograde ejaculation, or ejaculation, which may affect sperm quality [25, 27]. In addition, some men with BE who want to conceive successfully need ART [24, 27, 28]. Female patients with BE may encounter complications, such as recurrent urinary tract infections, pyelonephritis, miscarriages, and preterm labor [29, 30]. Good antenatal care, involvement of a multidisciplinary team (maternal-fetal medicine specialists, urologists, and anesthetists), and planned delivery modes can reduce the risk of complications in pregnant women with BE and ensure good newborn outcomes [31, 32]. A 32-year-old naturally conceived primigravida had a history of congenital BE that was surgically treated. The patient had a neobladder with urethrostomy in the lower right abdomen and underwent CIC twice daily. At 36 weeks and 5 days of gestation, a healthy infant weighing 2.6 kg was successfully delivered by CS with the participation of a multidisciplinary team [31].

Overall, the results of the present study suggest that adults with BE could achieve satisfactory continence after multiple surgical interventions. Despite some problems with sexual functioning, most patients with BE enter relation-

ships and attain sexual satisfaction. Pregnancy carries risks; some women require ART, and better pregnancy outcomes can be achieved through multidisciplinary care. However, most studies have been conducted in developed countries, such as Europe and North America, and data from developing countries are lacking. In developed countries, owing to better economic conditions and higher healthcare standards, most patients with BE are able to attain higher education, engage in social work, and achieve a better quality of life than the general population. By contrast, in developing countries, different economic and healthcare levels may negatively impact the quality of life, with increased concerns, anxiety, and depression related to the disease. In addition, many studies have included patients with BE of different ages, overlapping adolescence and adulthood, and even older patients. Although this expands the sample size, it also increases the heterogeneity of the studies.

Conclusion

BE is a congenital defect primarily affecting the urinary and genital tracts. Children with BE often undergo multiple complex surgeries to achieve continence and satisfactory quality of life. The child in our study underwent CPRE within 72 h of birth. The continence outcome was satisfactory, and at the 6-month follow-up, the child voided volitionally through the urethra every 3 h. Children may undergo AC at 2 or 3 years of age. Long-term outcomes for the child should be a concern. Establishing a multicenter cohort and multidisciplinary team is essential in order to provide lifelong follow-up for patients with BEEC.

Disclosure of conflict of interest

None.

Abbreviations

BE, bladder exstrophy; CBE, classic bladder exstrophy; BEEC, bladder exstrophy-epispadias complex; CE, cloacal exstrophy; CPRE, complete primary repair of exstrophy; MSRE, modern staged repair of bladder exstrophy; ART, assisted reproductive technology; NICU, neonatal intensive care unit; BNR, bladder neck reconstruction; AC, augmentation cystoplasty; BNC, bladder neck closure; DI, dry interval; CIC, clean intermittent catheterization; CS, Cesarean section.

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Supplementary Table 1. The clinical events and main treatment during hospitalization

Date	Clinical Event	Auxiliary Examination	Treatment
Day 1 (Feb 15, 2024)	Birth with bladder exstrophy (lower abdominal wall defect, bladder protrusion, perineal malformation). Observed urine leakage (**Figure 1A**).	Renal ultrasound showed normal kidney morphology and size, with no significant dilation of the bilateral ureters; however, the bladder was not visualized (**Figure 2A**).	Preoperative: (1) Transfusions of fibrinogen and albumin. (2) Antibiotics (cefoperazone-sulbactam and sodium ampicillin) for prophylaxis.
Day 3 (Feb 18)	Surgery (bladder/abdominal reconstruction). Postoperative: (1) Bilateral ureteral drains, a single-lumen catheter inserted through the bladder neck, and a cystostomy tube were placed (**Figures 1B**, **1C**, **2B**). (2) Swelling of both lower limbs, and fever. (3) Coagulation abnormalities (DIC). (4) Hypoproteinemia. (5) Worsening infection.	(1) Coagulation function (DIC): Antithrombin III 33%, fibrinogen degradation product (FDP) 6.5 μg/mL, activated partial thromboplastin time (APTT) 59.1 sec, D-dimer 2.8 mg/L FEU. (2) Biochemical monitoring: Albumin 27.9 g/L, total protein 41.7 g/L, prealbumin 50 mg/L. (3) Routine blood examination: C-reactive protein (CRP) 18.4 mg/L; Platelets (PLT) 66 × 10^9/L.	Postoperative: (1) Transfusions of fresh frozen plasma and vitamin K1 (for DIC correction). (2) Transfusion of albumin. (3) Antibiotics escalated (meropenem and ampicillin). (4) Supportive care: - Invasive mechanical ventilation - Invasive arterial blood pressure monitoring - Intravenous hyperalimentation - Calcium gluconate - Norepinephrine - Furosemide - Fentanyl (analgesia) - Midazolam (sedation).
Days 4-8 (Feb 19)	(1) Persistent coagulation abnormalities and hypoproteinemia. (2) Progressive edema. (3) Vitamin D deficiency (Day 5).	(1) DIC markers (Antithrombin III 35-43%, FDP 6.5-25.9 μg/mL). (2) PLT recovery (66 × 10^9/L to 152 × 10^9/L). (3) Serum vitamin D (4.6 ng/ml).	(1) Daily transfusions of fresh frozen plasma and albumin. (2) Diuretics adjusted: Increased furosemide and added torasemide (day 7). (3) Intramuscular injection of vitamin D_2 (day 5).
Day 10 (Feb 25)	Anemia and coagulation abnormalities.	(1) Routine blood examination: Hemoglobin (HGB) 88 g/L. (2) DIC: Antithrombin III 37%, FDP 10.9 μg/mL, D-dimer 5.56 mg/L FEU.	Blood transfusion.
Day 11 (Feb 26)	Patent ductus arteriosus (PDA).	Cardiac ultrasound revealed a patent ductus arteriosus with a 3.8 mm wide left-to-right shunt at the level of the great vessel.	Two courses of ibuprofen administered to close the ductus arteriosus.
Day 15 (Mar 1)	DIC stabilizing and infection controlled.	(1) DIC: APTT 44.8 sec. (2) Routine blood examination: HGB 134 g/L, PLT 223 × 10^9/L, CRP < 0.5 mg/L.	(1) Discontinued calcium gluconate injection and norepinephrine (day 13). (2) Discontinued invasive arterial blood-pressure monitoring.
Day 16 (Mar 2)			Removed bilateral ureteral drains (**Figure 1D**).
Day 18 (Mar 4)	PDA persistent.	Repeat cardiac ultrasound showed patent ductus arteriosus (1/3).	A second course of ibuprofen was added.
Day 21 (Mar 7)	Physical examination showed significant improvement in edema.		(1) Reduced furosemide dose. (2) Discontinued torasemide and ibuprofen.
Day 25 (Mar 11)	PDA closed.	Repeat echocardiography showed closure of the PDA.	(1) Removed urinary catheter (**Figure 1E**). (2) Discontinued: Vitamin K1, antibiotics (meropenem & ampicillin), metoprolol, fentanyl. (3) Switched to non-invasive ventilator (NIV) assisted ventilation.
Day 27 (Mar 13)	Physical examination revealed no edema.		Discontinued furosemide.
Day 28 (Mar 14)	Difficulty in deoxygenation.		Dexamethasone added for anti-inflammatory treatment.
Day 31 (Mar 17)	No oxygen requirement.		(1) Discontinued non-invasive ventilator (NIV) assisted ventilation. (2) Removed cystostomy tube (**Figure 1F**).
Day 34 (Mar 20)	Discharge.	Reexamination serum vitamin D: 16.1 ng/ml.	Discontinued dexamethasone and intravenous nutritional support.