Italian Journal of
Gynæcology & Obstetrics
December 2019 - Vol. 31 - N. 4 - Quarterly - ISSN 2385 - 0868

Management of pregnancy and birth in a patient with a history of surgically treated bladder exstrophy

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ABSTRACT
Bladder exstrophy is a rare congenital malformation that consists of external exposure of bladder's mucosa, ureteral orifices, bladder neck, and urethra, as a consequence of a failed abdomen wall closure. Although the cause of this kind of malformation is unknown, we can distinguish the isolated bladder exstrophy from those associated with other anomalies, especially in the pelvic area, and the diagnosis is mainly made after the birth. The correction of bladder exstrophy anomalies should be performed using different and specific surgeries, allowing people affected by this disease to reach an almost healthy life. In particular, women with corrected bladder exstrophy may obtain a regular sexual activity, and the possibility of getting pregnant. Monitoring this category of patients for the whole pregnancy, delivery and post-partum represent the most critical moments to manage to avoid several complications. In this article, we present the case of a woman that got pregnant after several corrective interventions for bladder exstrophy. Thanks to strict monitoring during pregnancy and good management of the delivery, she had a baby in good condition. Any adverse events were reported during the post-partum.

Keywords: bladder extrophy; pregnancy; delivery; post-partum; management.

SOMMARIO
L'estrofia vescicale è una rara malformazione congenita che consiste nell'esposizione esterna della mucosa della vescica, degli orifizi ureterali, del collo vescicale e dell'uretra, come conseguenza di un fallimento della chiusura della parete addominale. Sebbene la causa di questo tipo di estrofia sia sconosciuta, possiamo distinguere un'estrofia isolata da quella associate ad altre anomalie, specialmente nell'area pelvica. La diagnosi viene posta principalmente dopo la nascita. Al giorno d'oggi, la correzione delle anomalie dell'estrofia vescicale dovrebbe essere eseguita utilizzando interventi chirurgici diversi e specifici, consentendo alle persone colpite da questa malattia di raggiungere una vita quasi normale. In particolare, le donne con un'estrofia vescicale corretta possono ottenere una normale attività sessuale e la possibilità di rimanere incinta. Il monitoraggio di questa categoria di pazienti per tutta la gravidanza, il parto e il post-parto rappresenta l'elemento più importante nella gestione delle donne con estrofia vescicale al fine di evitare diverse complicazioni che possono verificarsi. In questo articolo, presentiamo il caso di una donna rimasta incinta dopo diversi interventi correttivi per l'estrofia vescicale. Grazie a un rigoroso monitoraggio durante la gravidanza e una buona gestione del parto, ha avuto un bambino in buone condizioni. Eventuali eventi avversi sono stati segnalati durante il post-partum.

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DOI: 10.14660/2385-0868-136

INTRODUCTION

Bladder exstrophy (BE) is a rare congenital malformation that occurs when the lower abdominal wall does not correctly close, and the bladder's mucosa, the ureteral orifices, the bladder neck, and the urethra result exposed externally. It has an incidence of about 1:30000 to 1:50000 live births, and it is more frequent in men than in women, and in Caucasians than in other races[1-4]. BE could occur as an isolated syndrome or in association with other anomalies, such as pubic bone anomalies (for example, diastasis)[1, 2], epispadias, omphalocele, anal defects (imperforate anus), neural tube defects, skeletal defects, cloacal exstrophy[1-2-5-6]. In rare cases, it may occur in association with gynecological cancer, such as borderline ovarian tumors[7-9]. The isolated form is the most frequent[1-5]. We could also see defects in muscles and genitalia[1-10].

BE pathogenesis remains unknown. It has been supposed that the infraumbilical mesenchymal tissue fails to migrate between the ectodermal and endodermal layers of the cloacal membrane. It is not clear if factors as environment, gene mutations, or drugs could influence BE development[1-3].

Diagnosis is mainly made at birth because children with BE usually show an abdominal mass that comes out from the abdomen, often beneath umbilical cord insertion, associated with the separation of rectus muscles and pubic bones. We can also see dribbling urine. Other anomalies that could be observed are the absence of belly button, epispadias, inguinal hernias, or other genitalia anomalies[11]. Conversely, less often, the BE diagnosis is made during pregnancy by ultrasounds[11]. The high-resolution ultrasonographic scan could allow a diagnosis of BE even at the 15th week of gestation: it is possible to observe the absence or low-set umbilicus, a lower abdominal mass, and the absence of bladder inside the abdomen[1]. Nevertheless, BE represents a rare form of abdominal wall defects and is not simple to identify. Moreover, only recently, genetic and developmental basis start to be elucidated, with a limited utility of prenatal screening[12-14].

If BE is not treated, it can cause some complications that include urinary recurrent infections and incontinence, renal calculi, bladder cancer, and prolapse of abdominal organs[2-3]. It is also essential to consider the psychological impact of this illness in children and adult life[3]. Therefore, it is mandatory to start surgical therapy since the neonatal age. The aim of surgical treatment is the closure of the abdomen to recover bladder position and urinary tract functionality and continence, with preservation of kidneys, and to avoid complications as infections. The surgical options are two: complete primary repair and staged reconstruction. In the first option, we have the simultaneous repair of all urinary abnormalities. In the second option, we have a succession of surgical treatments that have the aim of bladder's closure, its placement in the abdomen, reconstruction of abdominal wall, urethra and bladder neck, and repair of other defects, such as epispadias and genitalia alterations. It is often necessary to resort to pubic bone osteotomy to help pelvic ring closure.

Furthermore, an extension of the bladder can be done, creating a connection with the bowel and temporary with the skin (for example, colocystoplasty or ureterosigmoidostomy) to gain continence[2-6-11]. In a second time, the upper and the lower part of the urinary tract can be connected as in healthy people. In some cases, it is possible to use Mitrofanoff's procedure, where bladder or its extension is connected to the skin thanks to the appendix[6].

Surgical complications include wound dehiscence, bladder prolapse, urethral outlet obstruction, urinary tract calculi, pubic separation, persistence of urinary incontinence, urinary and surgical site infections, urethral-cutaneous fistulas[3].

As regards women, BE can cause many problems with sexuality, fertility, and pregnancy[15]. Some studies demonstrate that BE can be associated with some genitalia's abnormalities, such as septate uterus, bifid clitoris[1], wide separated labia[2], double vagina and didelphys uterus[6], and uterus prolapse[3].

It is necessary to correct abnormalities with previously described surgeries to allow women with BE to have an almost healthy life and to have a pregnancy. It is also possible to proceed with corrections of the reproductive system, even if complications are common (as pelvic adhesions, urinary stones, UTIs, and vaginal, uterine and rectal prolapse) and there is the risk of persistence of defects (incontinence, sexual dysfunction, missed pelvic closure) that can cause infertility and high-risk pregnancy[2-16].

We present the case of a woman that carried out a pregnancy after BE correction.

CASE REPORT

The patient was born by natural childbirth. At birth, she exhibited poor general conditions. At the lower third of the abdomen, in the median region,

she had a red swelling of 5 cm that extended from the suprapubic region to two fingers above the umbilical area. It could be pressed in the abdominal cavity, and in its inferior part, there were two orifices whence urine drops came out. Furthermore, urethra and belly button were absent, and at the genital level, labia minora were rudimentary.

After a month from the birth, the patient was operated to close the bladder and to replace it in the abdomen.

At the age of 5 years, she was operated for an ureterosigmoidocutaneostomy, with colon conduit packing (external urinary derivation that is obtained with a ureteral anastomosis connected with an isolated sigma handle exteriorized from the abdominal wall and connected with skin). After surgery, the patient showed a limited bladder capacity and bladder-ureteral reflux. Thanks to the medical examinations carried out during recovery, a double vagina with closed-end was discovered.

When the patient was 10 years old, she was operated for urinary diversion, so ureters were reconnected to the bladder. At the age of 11 years old, the patient was operated for a bladder neck reconstruction according to the Young-Dees technique, with the construction of a neourethra from the posterior surface of the bladder wall and trigone.

When the patient was 18 years old, the reconstructed bladder was extended with an ileal pouch. After five years, the patient was operated for an abdominoplasty, reconstruction of the belly button, and genitoplasty (reconstruction of the mons pubis, clitoris, and labia minora).

After all surgeries, urinary functionality was regular by mechanic and laboratory point of view. She started an almost regular sexual life too.

In 2017, the patient had a spontaneous miscarriage. At the age of 43 years old, she became pregnant by assisted reproduction, an ICSI technique with embryo transfer. Pregnancy examinations and exams were regular (I trimester screening, II-III trimester ultrasonographic scan, blood and urinary exams).

The patient came to the emergency department of our hospital at 36+1 weeks of gestation for hyperpyrexia (38 °C). She was in good general conditions; her BMI was normal. During pregnancy her weight increased by 12 kg. At first obstetric examination, cervix was closed but centralized and shortened. Amniotic membranes were unbroken, and there were not blood traces.

During the ultrasound exam, the fetus was in a longitudinal situation and breech presentation, with a normal heartbeat and regular movements. Biometric data corresponded to the 25th percentile. Amniotic fluid was reduced (AFI = 5), and the placenta was in the anterior part of the uterus. Behind the placenta, there were two myomas, the first one was antero-fundic and intramural, and its diameter was 9 cm; the second one was subserous, between the cervical and isthmic regions, and its diameter was 5 cm.

The patient was hospitalized and monitored with different examinations and ultrasound exams. At the beginning, some blood exams were altered: Haemoglobin level was 10.4 g/dl; the red blood cells count was 3.45x10^6/ uL; the platelets were 168x10^3/ uL; white blood cells were 18.60x10^3/ uL with an increase of neutrophil rate. Even urine exams showed some alterations and signs of infection, with traces of red blood cells (281), white blood cells (861), bacteria (1638), and casts (52,62). C-reactive protein (PCR) and procalcitonin (PCT) levels were altered (respectively, 7.1 mg/dl and 1.37 ng/ml).

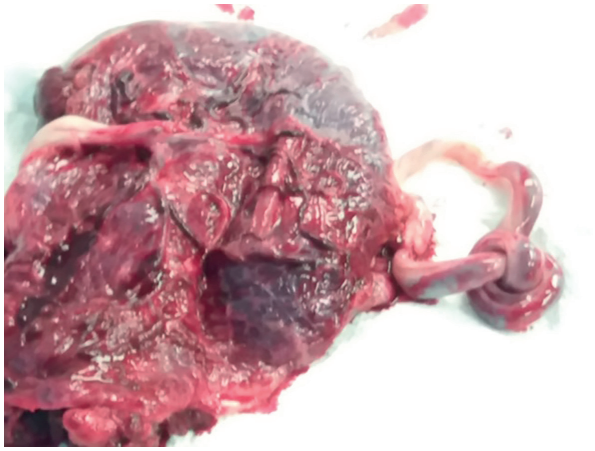
When vaginal and rectal swabs were performed, they were negative for S.Agalactiae but positive for Proteus Mirabilis. Antibiotic therapy with cefazolin was thus started, and corticosteroids prophylaxis was administrated to help fetal lungs development. Paracetamol was also used to solve hyperpyrexia, obtaining a normal body temperature after two days.

Thanks to antibiotic therapy, blood exams values got better (for example, PCR was 1.36, PCT 0.38 and with blood cells 7.4), and urine alterations improved too.

When the patient was at 37 weeks of gestation, because of her clinical history, the progressive reduction of amniotic fluid, the fetus breech-presentation and myomas' presence, a Caesarean section was performed to safeguard mother and baby lives. The medical equip was composed of three gynecologists, a urologist, and an anesthetist. A longitudinal navel-pubic laparotomy was done. When the abdomen was opened, extended and tough adhesions for previous surgeries were noticed. The two bladder extensions, from sigma at the left side and from ileum at the right side, were closely connected with lateral uterus walls.

Opening the abdomen and extracting the baby was very difficult, and so the uterus initial transversal incision was modified with a longitudinal corporal hysterotomy. When

Figure 1. *The placenta with the true knot of the umbilical cord*



the baby was extracted, the umbilical cord was around the neck and presented a true knot **(Figure 1)**.

The baby was alive and in good condition with an Apgar score of 9/10. During the cesarean section, two main myomas were removed because massive, near hysterotomy, and symptomatic[17-19].

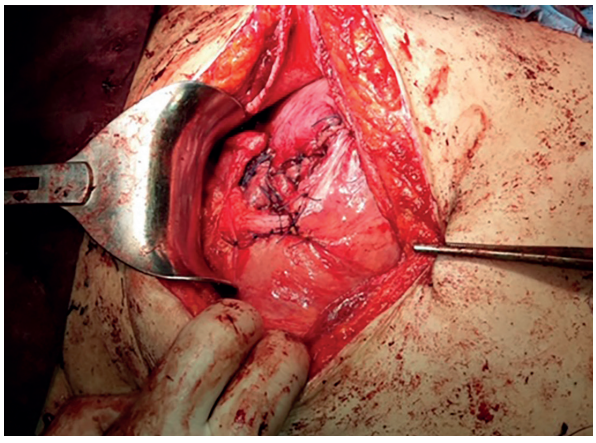
Moreover, it was necessary to repair a break to the continuity of 1.5 cm in the sigma neobladder, due to extraction maneuvers.

Spinal anesthesia was performed at the beginning of the cesarean section, but it was converted to general anesthesia in order of the surgery's length **(Figure 2)**.

The patient remained in our department for about fifteen days. She had a new increase in body temperature, which was controlled using ceftriaxone for twelve days and anti-inflammatory drugs.

In post-operative days blood exams showed new alterations, as Haemoglobin level decrease (8.7 in the Caesarean day and 7.5 in the first day of post-op.), a decrease of red blood cells (2.95) and an increase of white blood cells (12.5). An iron ad folic acid therapy was started. It was not necessary to do a blood transfusion because of the relatively steady Haemoglobin level (7.8). White blood cells values decreased thanks to therapy.

Figure 2*. Final result after uterine suture.*



The urinary function was monitored with temporary catheterization for fifteen days. When the catheter was removed, the urination was spontaneous and regular. Neither urinary infections nor urinary obstructions were observed. The same was for urinary retention or incontinence.

On the 18th day after the cesarean section, the patient was discharged from the hospital in good conditions, and successive controls were performed by her gynecologist. Prolapse or other complications were not registered until now.

DISCUSSION

It has been demonstrated that pregnancy can occur in women with treated BE, but it is not free from risks and complications. Several studies reported the risk of miscarriages[1-20], hydronephrosis, UTI's[1-3-21], urinary tract obstruction[15-20], prolapse[1-2-15], premature labour[3], preeclampsia[2-15-20-22-23], baby breech-presentation[20], placental abruption[10], temporary incontinence or urinary retention[3-20], venous obstruction and stasis at cervical level with oedema and ulceration[3].

Optimal management of pregnant BE women includes strict monitoring of the obstetric and urological conditions[1] with great attention to possible urinary complications such as infections, performing urine and culture test as well as eventually using antibiotics and hydration[20].

In cases of prolapse, a pessary placement could temporarily solve the problem[1-15-24-25]; it is useful to use temporary catheterization for urinary retention or incontinence; ultra-sonographic monitoring of pregnancy is necessary to control fetal health, placenta position, and cervix length.

The cesarean section is the recommended choice in the most significant part of cases[1-3-6-10-11-15-16-20-21].

In some cases, this choice is guided by obstetric conditions (pre-term labor, cervical shortening, breech-presentation, preeclampsia). However, in other cases, cesarean section seems to be the best method to avoid prolapse and possible adverse effects of vaginal delivery on bladder reconstruction (even when the bowel is involved) and urinary continence[3-20].

However, the cesarean section may report some complications, such as multiple pelvic adhesions,

ureteric transection, fistulas insurgence, that make the surgery more difficult[2].

As far as the cesarean section technique is concerned, although the most used is the transverse laparotomy[10], the recourse to a height incision or the use of a high midline incision should be needed to avoid the damage of possible stomas (Mitrofanoff) or the new bladder, also taking into account previous abdominal scars and organs adhesions[6]. These patients represent a high-risk population for bladder or new-bladder damage during cesarean section, and expert equip is mandatory[26-27].

After birth, it is necessary to keep attention to possible complications, like prolapse, incontinence, and urinary infections that can occur in a second moment. Our study focused on the possibility for women with a previous bladder exstrophy correction to obtain and carry out a physiological pregnancy. As discussed in our paper, strict monitoring in the prenatal period, a thoughtful choice of the optimal type and time of delivery, and specific controls in the post-partum period is mandatory. A multidisciplinary approach is thus required to manage these cases, especially considering the whole urological, obstetrics, and laboratory elements.

DECLARATION OF INTEREST

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper. No specific funding was obtained.

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