A rare case of cloacal exstrophy – prenatal diagnosis

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SUMMARY

This report describes a case of pregnancy complicated by a rare defect of cloacal exstrophy. The defect in the fetus was diagnosed in the second trimester of pregnancy as omphalocele with bladder exstrophy and an abnormal image of the anus. Detailed ultrasound scanning supported by genetic tests allowed the patient to decide to continue the pregnancy and prepare of both medical personnel and the pregnant woman with her family for birth.
Key words: ultrasound; fetus; pregnancy; cloacal exstrophy

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INTRODUCTION

A fetus begins to produce urine in approximately week 10 of gestation. The urinary bladder can be seen as early as in week 11–12 [1,2]. Failure to visualize the bladder after longer examination in a fetus older than 15 weeks should be treated as an anomaly. The inability to visualize the urinary bladder can be caused by agenesis or impaired renal function, but when the renal structure and the amount of amniotic fluid are normal, bladder or cloacal exstrophy should be suspected. Bladder exstrophy is a rare congenital anomaly occurring once per every 30,000–50,000 live births with male to female ratio of 2,3:1. This defect can be isolated or coexist with other abnormalities. If there are other coexisting defects, including anal atresia and omphalocele, the term *cloacal exstrophy* should be used. Its prevalence is estimated at 1:200,000–400,000 live births [3,4]. In the literature on prenatal diagnosis, cloacal exstrophy is referred to as OEIS (O-*omphalocele*, E-*exstrophy of the bladder*, I-*imperforate anus*, S-*spinal anomalies*) [5].

This report describes a case of pregnancy complicated by a rare defect of cloacal exstrophy and reviews literature on this problem.

CASE PRESENTATION

A 27-year-old patient in her first pregnancy reported to a physician in week 7 of gestation. Up to week 19, no ultrasound scans were conducted. The family interview was not significant. Before pregnancy, the patient smoked approximately 10 cigarettes daily and did not use folic acid supplementation. She worked in a printing house. The first fetal US scan was conducted at week 19+6 days. US showed a single fetus with biometrics appropriate to the gestational age calculated based on the last menstruation. The cerebral, facial and thoracic anatomy, including the heart, was normal.

However, an abnormal image of the umbilical cord attachment with herniation that encompassed the liver drew attention (Fig. 1). The umbilical cord was trivascular, but the umbilical arteries were significantly separated (Fig. 2). During an over 30-minute examination, the urinary bladder echo could not be found; the only findings were an uneven bulging outline of the lower fragment of the anterior abdominal wall and the absence of the pubic symphysis bones (Fig. 3). The anatomy of the kidneys was normal, as was the amniotic fluid index, which equaled 136 mm. Sex determination was difficult. A male fetus was suspected, but the image was not unequivocal. The anal echo raised further concerns. It suggested imperforate anus. Moreover, the absence of physiological curvature in the sacral spine was noted (Fig. 4). Based on these findings OEIS was diagnosed.

After the examination, genetic consultation and genetic amniocentesis were ordered. The karyotype was normal, male 46 XY. Due to the presence of a severe fetal defect, the parents were informed about the right to terminate pregnancy, but they expressed the will to continue it.

Subsequent ultrasound examinations were performed at the Clinic of Obstetrics and Perinatology in week 25, 29, 32 and 35 of pregnancy. Slower fetal growth was observed. The amniotic fluid index ranged from 204 mm in week 25 and 135 mm in week 35.

The biophysical profile of pregnancy in the second and third trimesters was normal. The patient was consulted by neonatologists and pediatric surgeons from the University Pediatric Hospital in Krakow and from a center with the greatest experience in this respect, i.e. the Department of Pediatric Urology at the Children's Memorial Health Institute in Warsaw. It was agreed that pregnancy would be concluded in the Clinic of Obstetrics and Perinatology in Krakow, after which the child would be transported to the Department in Warsaw.

In week 37, the cervix began to contract. Due to the nature of the defect, cesarean sec-

Fig. 1. Omphalocele (*przyczep sznura pępowinowego* – umbilical cord attachment; *wątroba* – liver)

Fig. 2. Abnormal course of the umbilical arteries. No urinary bladder echo between the arteries which are run in significant separation (*tętnice pępowinowe* – umbilical arteries)

tion was performed. During the surgery, the amniotic fluid was found green. The patient had a live boy, 2240 g and 46 cm with 10 points in the Apgar scale at 1, 3 and 5 minutes. After birth, the suspicious defect was confirmed (Fig. 5).

On the second day of life, after securing the defect with a sterile dressing saturated with physiological saline and an antibiotic wrapping, the boy was transported to the Department of Neonatology, Pathology and Intensive Care of the Children's Memorial Health Institute in Warsaw. On day 15 of life, a team of pediatric urologists conducted the first stage of surgery, i.e. separation of the digestive system from the urogenital tract (Fig. 6).

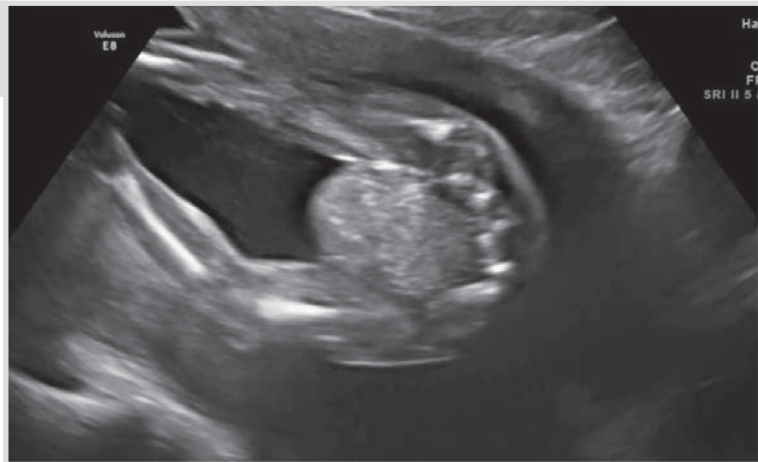**Fig. 3.** Abnormal image of the pelvic girdle with absence of the pubic bones
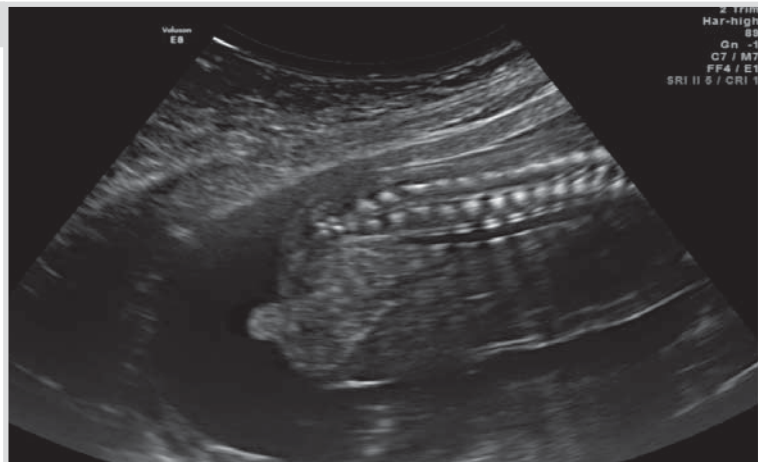

Fig. 4. Fetal lumbosacral spine

Fig. 5. Cloacal exstrophy after birth

From the cloacal exstrophy complex, an intestinal part was separated and terminal colostomy was performed. The omphalocele membrane was removed. Both halves of the urinary bladder were joined in the midline, thus changing cloacal exstrophy into bladder exstrophy. The second stage of surgery is planned at the end of the first year of life (closure of the exstrophied bladder with bilateral osteotomy of the iliac wings and reconstruction of all abdominal walls). The subsequent stages of surgery will be implemented as needed. Unfortunately, total correction of this defect is not possible.

DISCUSSION

In normal conditions, in week 4 of gestation, the cloaca is separated from the amnion by the cloacal membrane made of ectoderm and endoderm. The penetration of the mesoderm between the ecto- and endoderm of the cloacal membrane initiates the development of bones and muscles of the lower abdomen. At the same time, the urorectal septum, which grows caudally, divides the cloaca into the urinary part (anterior) and anorectal part (posterior). Subsequently, by perforation, the cloacal membrane creates the anus and the urogenital orifice. Genital tubercles migrate medially and fuse before the cloacal membrane perforates, thus initiating the development of the external genital organs.

The most feasible theory of embryonic defects observed in the exstrophy and epispadiasis syndrome has been formed by Marshall and Muecke [6]. It indicates that the major cause of this anomaly is cloacal membrane hypertrophy that prevents the mesoderm from entering between the ecto- and endoderm as well as hinders the medial migration and fusion of the genital tubercles. This leads to abnormal development of pelvic bones with varying degrees of pubic symphysis diastasis, separation of the smooth muscles in the lower abdomen and separation of the pelvic diaphragm in its anterior part. It also leads to abnormal development of the external urogenital organs. Early cloacal membrane perforation, i.e. before the urorectal septum divides the cloaca into the urinary and anorectal parts, leads to cloacal exstrophy. Perforation after the division results in bladder exstrophy, and failure of tubercle fusion is responsible for epispadiasis.

In cloacal exstrophy, the separation of the pubic symphysis and the defect in the abdominal integuments are considerable. Within the exstrophy complex, the medial part is occupied by the open cecum with small intestine prolapse through the ileocecal valve, two appendices and an invisible short and blind fragment of the large intestine (usually several centimeters long). At both sides of the intestinal part, there are two halves of the exstrophied bladder. Above the exstrophy complex, omphalocele of variable sizes is visible. The penis is usually very poorly developed and divided completely into two halves located far from each other. The scrotum is similarly altered with no palpable gonads (cryptorchidism).

In girls, there is vaginal and uterine duplication with their transverse location and lateral transposition. The clitoris and labia are also separated completely and their poor development sometimes makes them difficult to notice.

Despite various theories concerning the formation of these anomalies, the ultimate cause still remains unknown [7]. According to Mar-
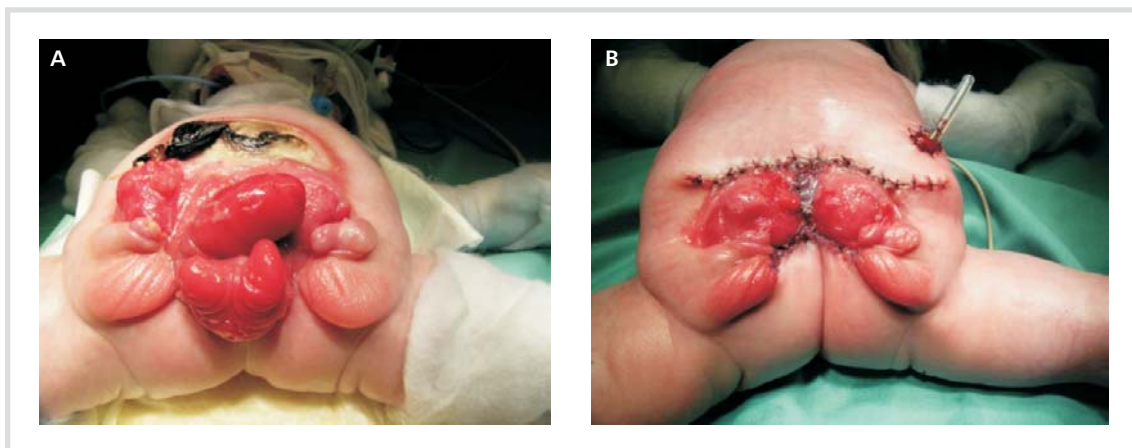
Fig. 6. Patient with cloacal exstrophy before surgery (A) and after stage I of reconstructive treatment (B)

tin et al. [8], there may be a relationship between the development of bladder exstrophy and pesticides. The authors presented a case of a pregnant patient exposed to pyrethroids and pyriproxyfen who had a child with this abnormality. Toxic pesticides were present in the child's urine sample. It is also indicated that this anomaly may have genetic background. It can be associated with unbalanced translocation between the long arm of chromosome 9 and Y as well as HLXB9 and HOX mutations [9]. Moreover, the risk of this defect is higher in pregnancies resulting from the use of assisted reproductive technology [10]. In this case, the family history of both the mother and father was insignificant. The karyotype of the fetus was normal, but the patient was exposed to printing ink at work.

Despite a considerable spectrum of structural abnormalities, cloacal exstrophy is still rarely identified prenatally and is frequently mistaken for omphalocele or gastroschisis. Bladder exstrophy is much easier to detect in prenatal diagnosis. Gearhart et al. [11] described five ultrasonographic features of bladder exstrophy based on a retrospective analysis: 1) inability to visualize the urinary bladder, 2) presence of a solid mass in the lower abdomen, 3) low attachment of the umbilical cord, 4) broad arrangement of the pubic bones and 5) difficulty in sex determination [11]. Bladder exstrophy should always be suspected when the amount of amniotic fluid is normal but the urinary bladder cannot be located.

Diagnostic criteria for cloacal exstrophy in prenatal diagnosis are not that precise. By contrast with bladder exstrophy, cloacal exstrophy is always concomitant with imperforate anus and is usually accompanied by omphalocele and spinal defects, particularly in the lumbosacral segment. It is proposed to adopt so-called major and minor criteria [12]. Major criteria, seen in over 50% of cases, include: nonvisualization of the bladder (91%), anterior abdominal wall defect or the presence of a cystic structure on the anterior wall (82%), omphalocele (77%) and myelomeningocele (68%). Minor criteria, present in less than 50% of cases, include: lower extremity defect (23%), renal anomalies (23%), widened pubic arches (18%), narrow thorax (9%), hydrocephalus (9%) and single umbilical artery (9%).

In the case reported herein, bladder exstrophy was accompanied by omphalocele, which was more prominent in week 19 of gestation than in the third trimester, as well as anal atresia. Moreover, abnormal arrangement of the pubic bones and absence of physiological lumbosacral curvature without signs of cleft drew attention.

Despite the fact that ultrasonographic features typical of bladder or cloacal exstrophy have been described on many occasions, only approximately 25% of cases are identified prenatally [13]. It seems that magnetic resonance imaging (MRI) is a more sensitive tool to diagnose urogenital defects in fetuses [14–16]. MRI delivers more anatomic information, enables more accurate sex determination and allows one to evaluate the neural tube, thus facilitating prognosis. In doubtful cases concerning prenatal sex determination, the fetal karyotype should be examined, which was conducted in the case reported above. Extending the diagnostic process by including MRI was offered, but the patient did not consent.

Early prenatal diagnosis and presentation of the complexity of the pathology associated with cloacal exstrophy gives parents time for making a decision concerning continuation or termination of pregnancy. Moreover, it enables to plan and implement appropriate management of a neonate shortly after birth. Some authors recommend early reconstruction procedures to minimize bacterial colonization of organs remaining beyond the abdominal cavity [17,18]. However, the management in the first days of life should be primarily adjusted to the state of the child. It is the most important to normalize the acid-base balance and water-electrolyte metabolism, which might be impaired due to large losses of intestinal contents by the congenital fistula in the small intestine (opening at the level of the ileocecal valve). Stepwise surgical treatment should be implemented once the neonate's state is stable [19]. Until then, the exstrophy complex must be secured by a dressing saturated with saline and the skin around it amply lubricated with a silicone ointment.

Huge progress that has recently taken place in the field of prenatal diagnosis, also in surgery, surely contributes to reduced mortality and improved quality of life of patients with these defects.

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