Clinical Case Report

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Long term follow-up in a patient with prune-belly syndrome – a care compliant case report

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Abstract

Rationale: Malformative uropathies represent a major cause of Chronic Kidney Disease (CKD) in children. Genitourinary system is the most frequent and sever affected in Prune-Belly syndrome cases. That is why the findings of early diagnosis and vigilant monitoring for these situations remain a major challenge for the medical team.

Patient concerns: We present the clinical course of a 10 years old child with diagnosis of Prune-Belly syndrome. A urinary tract abnormality was suspected starting 25 weeks of gestation, when a routine ultrasound showed oligohydramnios, increased size urinary bladder, bilateral hydronephrosis and megaureters, thin abdominal wall.

Diagnosis: Prenatal suspicion of Prune-Belly syndrome plays a deciding role in renal disease progression. A detailed clinical exam at birth established the diagnosis of Prune-Belly syndrome. Renal ultrasound confirmed bilateral grade III hydronephrosis and megaureters, with empty bladder, suggesting an obstruction at this level. A persistent urachus was confirmed by catheterization. Later it was used for imaging study that showed bilateral high grade reflux.

Interventions: The main goal of any treatment is to preserve kidney function. Treatment options depend on the clinical picture. The pregnancy was closely monitorized, but fetal distress appeared so early labor was induced at 32 weeks. At beginning a temporary catheter was placed into the urachus which expressed urine. The urachus drain was left in place until the age of 6 weeks, when a bilateral ureterostomy was performed. Skeletal and genital malformations were present too; the child has undergone several surgeries to solve these abnormalities.

Outcomes: At the age of 10 years, he is a well-adapted child. He has had fewer than 3 urinary tract infections per year. Long term follow-up showed a relatively slow decline in the estimated Glomerular Filtration Rate in our child (62 ml/1.73m^2/min).

Lessons: This case suggests that induced early labor could prove beneficial for early upper urinary tract decompression through earlier access to surgery. This is an option especially in situations or region where vesicoureteric or vesicoamniotic shunt placement is not available.

Abbreviations: CKD = chronic kidney disease, CRP = C reactive protein, DTPA = diethylene-triamine-pentaacetate, eGFR = estimated Glomerular Filtration Rate, EPO = erythropoietin, ESRD = end-stage renal disease, MRI = magnetic resonance imaging, PBS = Prune-Belly Syndrome, UTI = urinary tract infection, VCUG = voiding cystourethrogram, VUR = vesicoureteral reflux.

Keywords: child, prune-belly syndrome, urachus, ureterostomy

1. Introduction

Prune-Belly Syndrome (PBS), also known as Eagle-Barrett syndrome or triad syndrome, is a rare congenital disorder with a wide spectrum of severity consisting of abdominal wall defects, urinary tract malformations and bilateral intra-abdominal testes, associated with pulmonary, cardiovascular and musculoskeletal malformations.[1–3] Nearly 10% to 25% of newborn infants die in the perinatal period.[4] The male predominance is overwhelming (95%) and unexplained.[5] Diagnosis is performed through prenatal ultrasound, in the second trimester sometimes as early as 12 weeks, depending on the severity of the urinary tract obstruction and oligohydramnios and last but not least influenced by other factors like examiner experience.[3] Skeletal involvement is less common (30–40%) (mainly vertebral defects and dysplastic hip), while anomalies of the gastrointestinal tract (20–30%) and, more rarely, heart malformations (10%) can be seen.[1,3,5] The mainstay therapy is surgical decompression of the upper urinary tract through ureterostomies or vesicostomy.[1,2]

Herein, we reported a 10-year-old male, who was diagnosed early during pregnancy with PBS. Long term follow-up showed a

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Written informed consent was obtained from the parents of child for the publication of this case report.

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relatively slow decline in the estimated Glomerular Filtration Rate (eGFR) in our child due to the interdisciplinary approach. Our patient is one of the few follow-up cases reported in our country population. Written informed consent was obtained from the parents of child for the data related to this case to be submitted for publication. This case report was approved by the ethics committee of the hospital.

2. Clinical case

We present the clinical course of a 10 year old boy admitted in Pediatric Nephrology Department for the first time at age 3 days with suspicion of PBS. The baby came from healthy parents, without any known medical family history, like genetic disease or kidney abnormalities. A renal malformation was suspected starting 25 weeks of gestation, when a routine ultrasound showed oligohydramnios, increased size urinary bladder, bilateral hydronephrosis and megaureters, thin abdominal wall (Fig. 1A). Because of fetal distress, labor was induced at 32 weeks, APGAR scores were 5 at 1 minute and 8 at 5 minutes, birth weight 2200 grams. Clinical examination showed: mild respiratory distress syndrome, absence of anterior musculature of the abdominal wall, loose and crinkled skin while urine was expressed through an orifice below the umbilicus. The scrotum was hypoplastic and the testes were absent. Based on these data a diagnosis of PBS was established. This was confirmed by a renal ultrasound showing bilateral grade III hydronephrosis and megaureters. The bladder was empty and the juxtaposed ureters were clearly visible suggesting an obstruction at this level. Due to the medium grade hydronephrosis and the persistence of a renal function (albeit decreased) we supposed the existence of a persistent urachus. We failed to catheterize the urethra but we succeeded to place a temporary catheter into the urachus in the 5th day of life, which expressed urine. Two weeks later, the catheter was used for a retrograde injection of an iodine based contrast (Fig. 1B) that showed bilateral high grade reflux into the dilated ureters and hydronephrotic kidneys. A small amount of contrast entered the bladder suggesting that the ureteral obstruction was not complete. Antibiotic prophylaxis was started. The urachus drain was left in place until the age of 6 weeks, when a bilateral

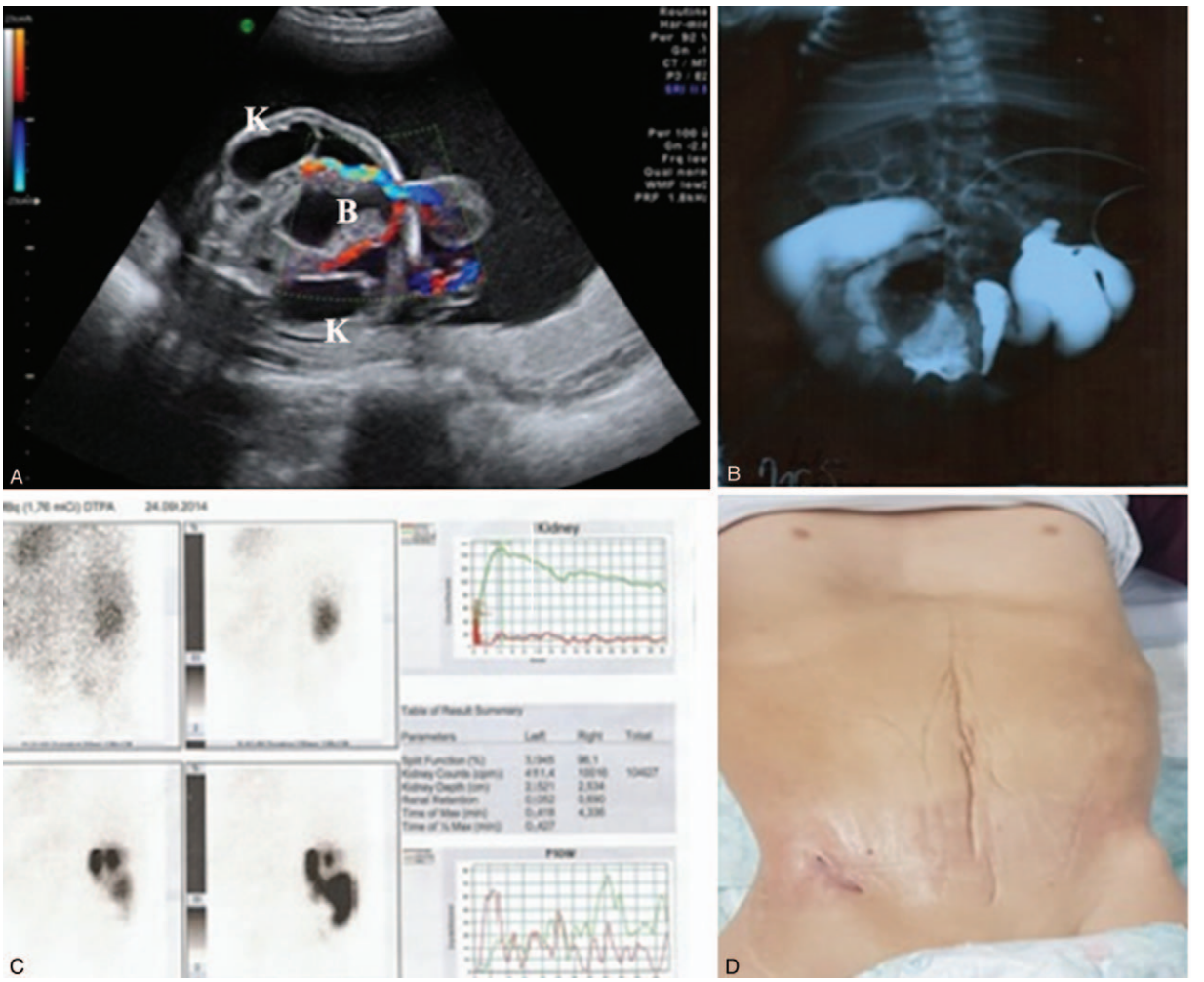

Figure 1. A. Prenatal ultrasonography showing an enlarged bladder (B), dilated ureters and hydronephrosis, kidneys with reduced parenchymal thickness (K); B. Voiding cystography: contrast agent introduced trough the uracha into the bladder showing high degree bilateral vesicoureteral reflux (IV grade); C. Dynamic renal scintigraphy 99mTc-DTPA showing no glomerular function on the left side, the right side: no obstruction but with significant pooling in the right ureter; D. Photo of the patient at age of 10 showing the abdominal wall defect and right iliac fossa ureterostomy opening.

ureterostomy was performed. Soon after the surgical intervention, upon the placement of the ureteral catheters the left stomy yielded grossly cloudy urine and the child became febrile. The culture grew Pseudomonas maltophila. The clinical examination also showed bilateral hip displacement, confirmed by ultrasonography. The renal ultrasound showed bilateral moderate hydronephrosis, left kidney of 32 mm in length, hyperechoic cortex, right kidney of 37 mm, normal cortex, and decreased paranchymal index on both sides. The ureters had a maximal diameter of 12 to 14 mm on both sides. The urinary bladder was empty. Blood work showed leukocytosis (16.000/mm^3) with neutrophilia predominance (70%), increased CRP (12 mg/dl – cut-off 0.8 mg/dl), elevated urea (78 mg/dl, cut-off 40 mg/dl) and creatinine (0.99 mg/dl, cut-off for age – 0.4 mg/dl), metabolic acidosis, severe normocytic, normochromic anemia (Hb = 6.8 g/dl, Ht = 20.4%). We interpreted the case as left kidney pyonephrosis with secondary anemia and Ceftriaxone treatment was started. Baby was transfused with packed red blood cells (RBCs) typed and cross-matched. He was later switched to Meropenem according to the antibiogram. The immediate outcome was favorable. The creatinine stabilized at 0.6 mg/dl, showing the development of chronic kidney disease (CKD). The metabolic acidosis required constant NaHCO3 administration for appropriate correction. The child was put on chronic antibiotic prophylaxis. Long-term 5 year follow-up revealed recurrent nonfebrile urinary tract infections (UTIs) and a decrease in the left ureter urine output. Clinical examination showed moderate dextroconvex dorsolumbar scoliosis, pectus excavatum, distended abdomen, with visible peristalsis and palpable kidney in the right flank. Ureterostomies looked normal, no signs of inflammation. Leg length asymmetry was observed. Blood work established a second degree CKD, without proteinuria. Chronic, intermittent erythropoietin (EPO) administration had been necessary to maintain a normal level of hemoglobin. Compensated metabolic acidosis persisted despite oral $NaHCO_3$ therapy. Renal ultrasound yielded a small left kidney (4 cm in length), with severely decreased parenchymal index; the right kidney was 5.8 cm in length with grade II hydronephrosis. Both ureters remained dilated, with diameters ranging between 8 and 12 mm. The reduced size of the left kidney and the decreased urine output on the same side led to the need to evaluate renal excretion. We used a dynamic renal scintigraphy with Tc-99m DTPA (diethylene-triamine-pentaacetate) (Fig. 1C). This showed no glomerular function on the left side. The right side showed no obstruction, but there was significant pooling in the right ureter. Pelvis and inferior limb X-rays showed asymmetrical femoral diaphysis secondary to bilateral hip arthroplasty, which had been performed at ages 1 and 3 years. At the age of 10 years he is a well-adapted child. Ureterostomy is still in place (Fig. 1D); he had no corrective surgery for the abdominal wall defect. Unilateral left orchidopexy and right orchiectomy have been performed. He has had fewer than 3 UTIs per year, all of them without fever while on antibiotic prophylaxis. Blood pressure is within the normal range. His renal function is stable (eGFR 62 ml/1.73m^2/min). Hemoglobin levels have been stable for the last 6 months, but EPO analogues were needed. Renal ultrasound shows an 8.1 cm right kidney, with grade 2 hydronephrosis, normal parenchymal index, and a 4 cm left kidney with decreased parenchymal index. His current medication consist just of oral $NaHCO_3$ 8.4% 4 ml qid. We envisage a cystoscopy and ureteral reimplantation and a conservative management of his CKD.

3. Discussion

Urinary tract abnormalities require multidisciplinary approach regarding the diagnosis, treatment and prognosis.[6–8] PBS can be a life threatening disease, especially when the urethral atresia is not compensated by a patent urachus, thus leading to oligohydramnios and pulmonary hypoplasia.[3] The latter variant is the most severe (grade 1). Grade 2 comprises the classic triad and minimal unilateral renal dysplasia, whereas cases that do not meet the triad are considered grade 3. The increased abdominal wall pressure, due to the enlargement of the urinary tract is seen as a probable cause for the abdominal muscle hypoplasia.[1] This pathogenic theory also regards the massively distended bladder as a potential cause that hinders the descent of the testes, thus causing cryptorchidia.[1] Another pathogenic theory suggests a developmental mesodermal defect between weeks 6 to 10 of gestation. This leads to aberrant formation of the urinary tract and anterior abdominal wall.[1] Diagnosis is usually made antenatally, through uterine ultrasound. Anatomical information regarding ureters and bladder can be obtained using a voiding cystourethrogram (VCUG), with contrast injected through any type of urine outlet or intravenous pyelogram or if possible better with abdominal contrast MRI. Kidney function can be monitored by estimating glomerular filtration rate (GFR) and renal Tc-99m DTPA excretion scyntigraphy. Our case presents the classic triad of PBS and the common association of orthopedic malformations. Amnioinfusion may be a treatment option, but it should be performed just in centers specialized in invasive fetal medicine.[9] Because of fetal distress labor was induced at 32 weeks, with mild respiratory distress syndrome. We regarded this as the best option for fetal distress management and for early decompression of the upper urinary tract through bilateral ureterostomy. Literature data suggests in utero placement of a vesicoamniotic shunt as a possible decompression solution.[1,10] This was unavailable at the time in our center and the procedure is known to have an important infectious risk. Antenatal corticosteroid therapy was given for reducing well-known neonatal consequences associated with early birth, like respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis and perinatal death.

PBS is a clinical entity with a broad spectrum of severity; around 25% of newborns die within the perinatal period, and nearly 25% to 30% of those affected by PBS go on to develop CKD of ranging grades outside the postnatal period.[4] Long term follow-up showed a relatively slow decline in the eGFR in our child. According to recent data, in case of unfavorable evolution to end-stage renal disease (ESRD) renal replacement therapy should be offered to all PBS patients until renal transplantation, which appears to be a treatment option in 15% of PBS children.[2,4] Transplanted patients necessitate a follow-up program in order to avoid severe complications like infections or limphoproliferative disorder.[11] The presence of patent urachus or vesicocutaneous fistula is compulsory in case of urethral atresia or hypoplasia that is found in many cases (18%),[9] similarly with our case. The management of this case proved challenging, it involved a team of urology and orthopedic surgeons alongside pediatric nephrologists. The most difficult task was to devise a coherent long-term plan to preserve kidney function. The mainstay surgical approach is bilateral ureterostomy to prevent severe VUR, reduce the frequency of UTIs and slow or stop the decline of the GFR. Resection of a posterior urethral valve or bladder reconstruction with maintaining a patents urachus is the most common solution for the lower part of

the collector system. Reconstruction of the abdominal wall and orchidopexy or orchiectomy is usually performed during the next surgical step, as well as an antireflux reimplantation of ureters. Our case required extensive orthopedic surgery as well, to correct the lower limb asymmetry and hip displacement. Until the abdominoplasty the use of a corset can be recommended, as other authors proposed it to improve bladder emptying and reduce gastrointestinal problems.[2,12] Urinary tract tuberculosis should be considered in case of persistent hematuria or when UTI fail to respond with proper antimicrobial treatment.[13] Abdominoplasty and urinary tract reconstruction are recommended as they may have a positive effect on both parental and patient's quality of life.[2,14] Recent data highlight that abdominoplasty no longer plays the decisive role in surgical therapy.[5] Life quality is severe influenced by associated anatomic abnormalities and complicated and numerous surgeries as well as related comorbidities.[2,5,14]

Due to the rarity of the condition, there are only a few publications that describe such cases, especially regarding the long-term follow-up. We did not find any publication regarding early induced labor as a viable alternative to slow chronic kidney disease progression in PBS.

Prenatal diagnosis of PBS plays a deciding role in renal disease progression. Induced preterm labor could prove beneficial for early upper urinary tract decompression through faster access to surgery, especially when vesicoureteral shunt placement is not available. Our patient is one of the few follow-up cases reported in our country population. The long-term follow-up showed a well conserved GFR due to the interdisciplinary approach.

Author contributions

Conceptualization: Aldea Cornel, Dan Delean, Bogdan Bulata.
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