Prune-belly syndrome: an autopsy case report

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ABSTRACT

Prune-belly syndrome (PBS) is a rare congenital anomaly characterized by a spectrum of mild-to-severe presentations of urinary tract malformations, deficient abdominal wall musculature, and cryptorchidism in male newborns or genital abnormalities in the female newborns. Currently, antenatal diagnosis is feasible with ultrasound examination, and treatment is based on case report experience. More recently, intrauterine management has been undertaken with encouraging results. The authors report a case of PBS diagnosed at the seventeenth gestation week, when ultrasonographic examination revealed the presence of ascites, distended bladder, thickened bladder wall and posterior urethral valve. The fetus was submitted to an intrauterine intervention at the nineteenth gestational week. Delivery occurred at 34 weeks of gestation and the newborn examination was consistent with PBS. On the second day of life, the newborn was submitted to abdominoplasty, colostomy, and orchiopexy. However, the outcome was unfavorable with respiratory failure and death on the fifteenth day of life. The autopsy confirmed the diagnosis of PBS, but the immediate cause of death was attributed to aspiration pneumonia.

Keywords
Prune Belly Syndrome; Cryptorchidism, Urologic Diseases.

CASE REPORT

A premature male newborn with 34 gestational weeks was born through cesarean section, weighing 2850g with an Apgar score 8/9/10. During a prenatal consultation, ultrasonography, undertaken at the fourteenth gestational week, disclosed a distended urinary bladder with a thickened wall, ascites, flaccidity of the abdominal wall, and a possible posterior urethral valve (PUV). Therefore, he was submitted to laser intrauterine fulguration at the nineteenth gestational week. Six days after this procedure, the ultrasonographic findings still revealed bilateral hydronephrosis and megaureter. The fetal karyotype was 46XY.

The mother was 31 years old, para 3, previously healthy, and had 11 pre-natal appointments. The cesarean delivery at 34 weeks was uneventful, but the mother was admitted at the emergency room with ruptured amniotic membrane. Post-natal examination of the newborn depicted abdominal wall flaccidity, bilateral cryptorchidism, imperforate anus with a fistula to the inferior urinary tract, posterior urethral valve, club foot, and lateralized trachea. The newborn outcome was troublesome with respiratory failure requiring orotracheal intubation and mechanical ventilatory support. On the second day of life, he was submitted to an abdominoplasty, a double-barrel colostomy, and a bilateral orchiopexy. Postoperative

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ultrasonography revealed bilateral ureteral dilation and right hydronephrosis. Paralytic ileus, frequent vomiting, and right lung pneumonia accompanied the postoperative period. Septic shock ensued and death occurred on the fifteenth day of life.

AUTOPSY FINDINGS

At the corpse ectoscopy, abdominal distension was marked accompanied by the presence of a recent surgical scar surrounded by purplish skin (Figure 1A). At the opening of the abdominal cavity, bladder distension, bilateral ureteral tortuosity, right renal pelvis distension (Figure 1B), a fistula between the rectum and the urethra, and a blind end of the rectum were evidenced.

The anus was imperforate (Figure 2) and a left clubfoot was evident. The testicles were stitched within the scrotal sac (Figure 1A) and were winy-colored at gross examination (Figure 3A), which at microscopy showed ischemic necrosis (Figure 3B).

The thoracic cavity examination showed normal gross examination of the heart and lungs. The total pulmonary/body weight ratio was 0.036, which was consistent with normal lungs. At microscopy, a bladder (Figure 4A) and ureteral interstitial fibrosis, with atrophy and disorganization of the muscle fibers (Figure 4B), were found.

Rectus abdominis muscles showed fibrosis and atrophy (Figure 5). Renal parenchyma was adequate for the patient's age, with the presence of a nephrogenic zone, well-formed glomeruli, and tubules without dysplastic areas probably influenced by the early intrauterine intervention.

Pulmonary examination showed pneumonia with giant cell and foreign body reaction consistent with bronchoaspiration (Figure 6).

The remaining viscera were within normal limits for the patient's age.

DISCUSSION

Initially reported by Frölich in 1839,[1] the PBS was described in 1895-1896 by Parker and Guthrie and coined as Prune-bely syndrome by Osler in 1901.[2,3]
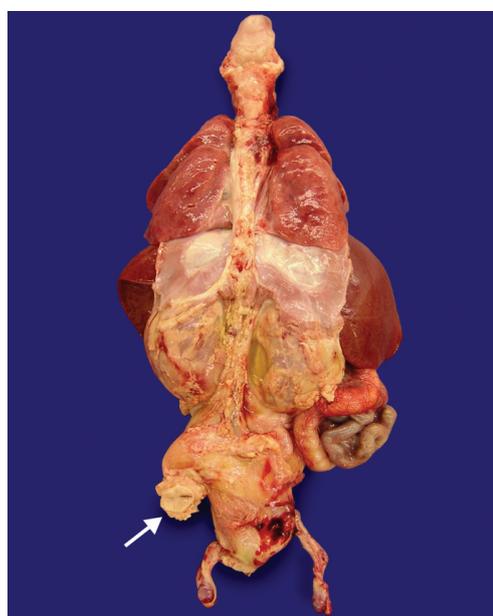
Figure 2. Posterior view of the entire eviscerated bloc. The arrow points the imperforate anus, where the rectum ends in a segment of skin.
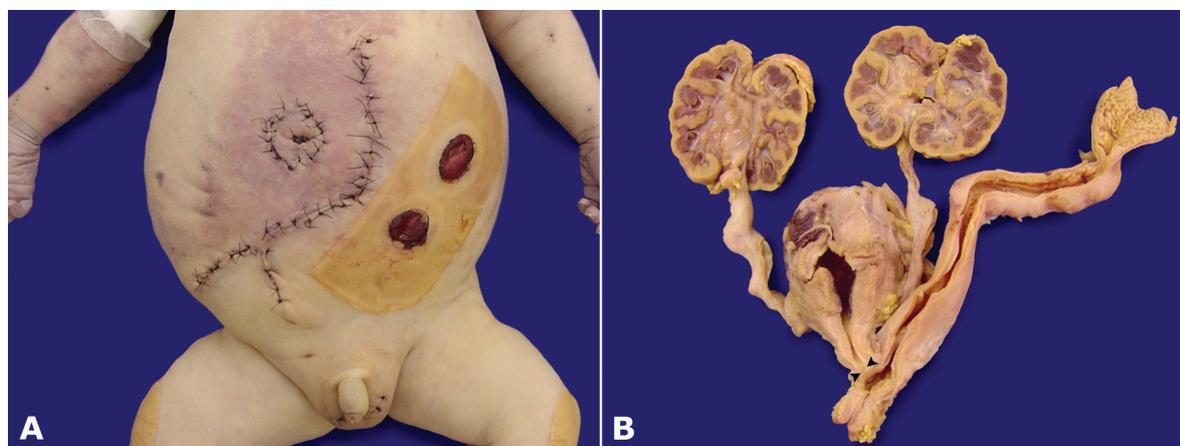
Figure 1. A - Ectoscopy of the corpse showing abdominoplasty surgical scar, double-barrel colostomy and stitches on the scrotal sac; **B** - Gross view of the dilated urinary system and a segment of the distal colon. The arrowheads points to a fistula between the colon and the urethra. Kidneys are grossly normal for the age.

This syndrome, also known as Eagle–Barrett syndrome or Triad syndrome is a rare congenital malformation, which is extremely morbid, and occurs predominantly in males (95-97%) with the incidence from 1 in 35,000 to 1 in 50,000 live births.[4] The incidence in twins is four times greater compared with single pregnancies.[4] Young mothers seem to have an increased risk to give birth to newborns with PBS.[3,4] However, in their observation, Ekwunife et al.[5] did not find any consistent maternal risk factor. Moreover, chromosome defects
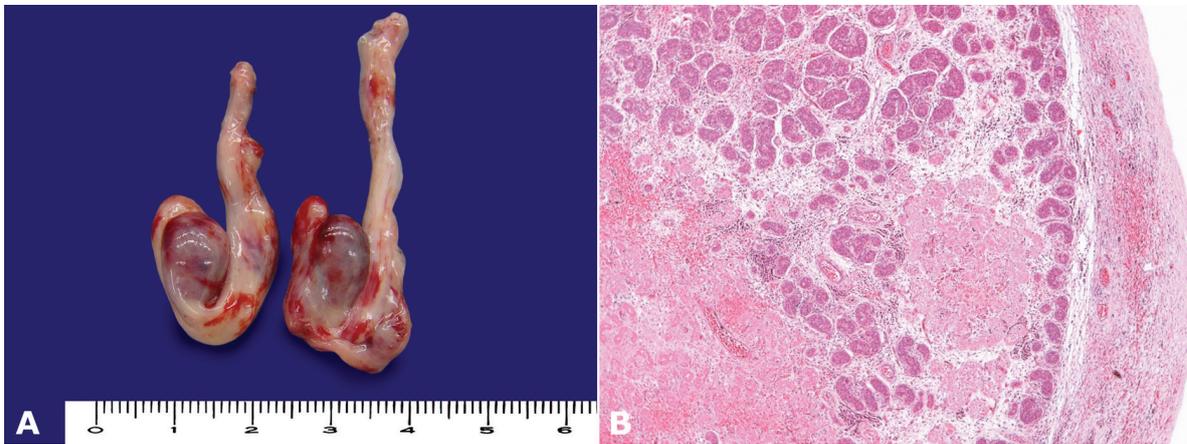

Figure 3. A - Gross view of the testicles showing their winy-colored appearance; **B** - Photomicroscopy of the testicular parenchyma showing an area of ischemic necrosis (HE, 200X).
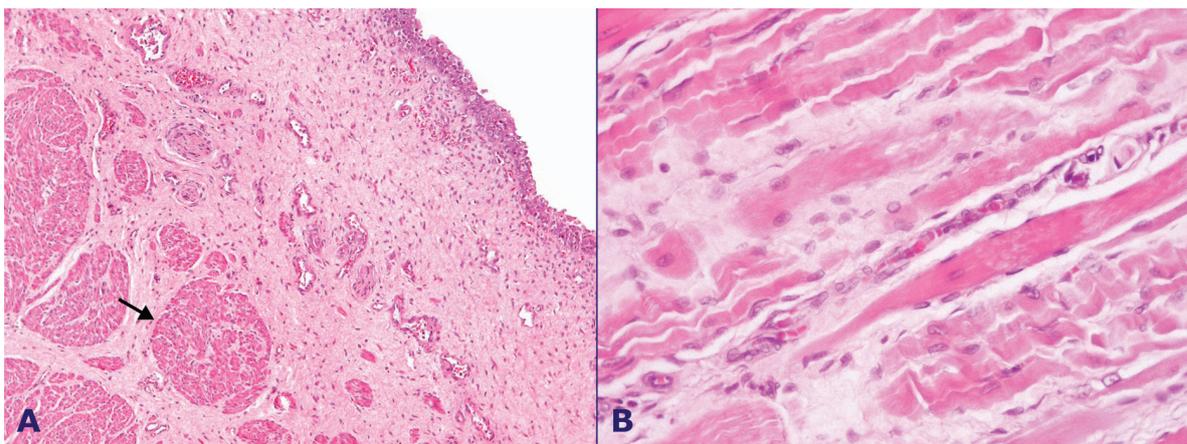

Figure 4. A - Photomicrography of the bladder wall showing fibrosis (arrow) (HE, 200X); **B** - Photomicrography of the rectum abdomini showing disorganized and atrophic muscle fibers (HE, 400X).
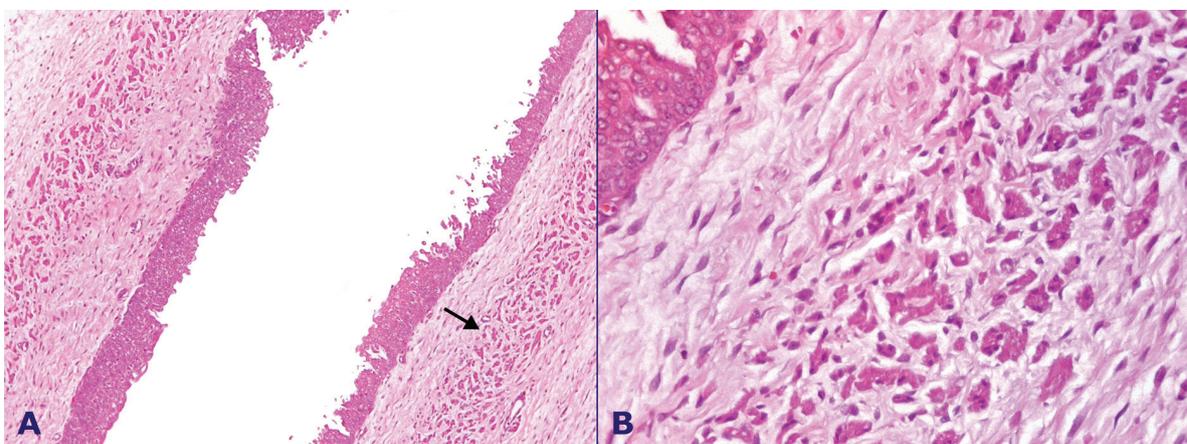

Figure 5. A - Photomicrography of the ureteral wall showing disorganized and atrophic muscle fibers (arrow) (HE, 200X); **B** - The detail of the area pointed in 5A (HE, 400X).
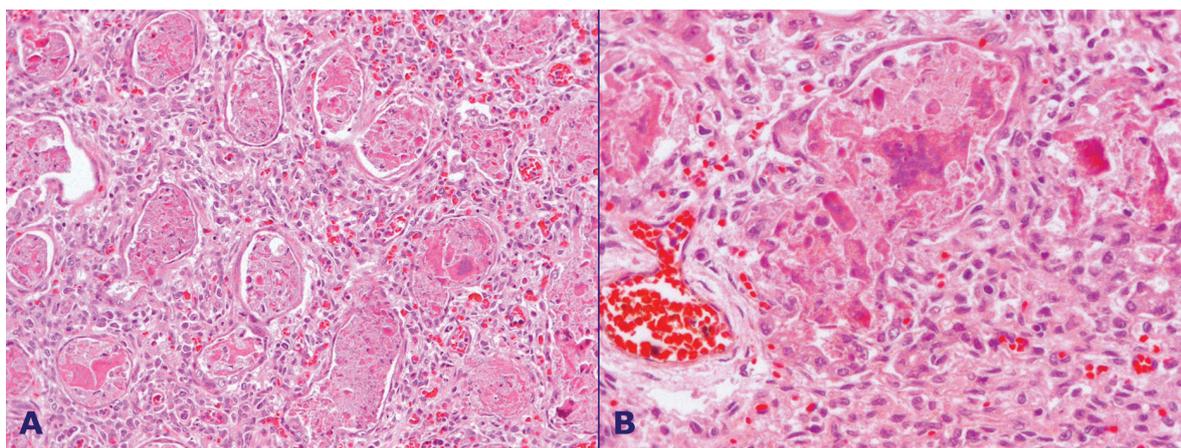
Figure 6. Photomicrography of the lung. **A** - Alveoli space filled by inflammatory cells and amorphous material (HE, 200X); **B** - Alveolar space, in detail, showing foreign body reaction with giant cell (HE, 400X).

associated with PBS are observed among advanced age mothers. The prognosis of fetuses varies substantially depending on the severity of the renal dysplasia and pulmonary hypoplasia.[6] Some forms are incompatible with life (50%),[7] 30% of the newborns die during hospitalization. Among those who remain alive, 50% have degrees of urinary pathology during their lifetime.[8]

PBS is characterized by a classic triad, which comprises absence or hypoplasia of the abdominal wall musculature, urinary tract anomalies, and in the case of males, bilateral cryptorchidism. Among the females, genital anomalies may also be present, such as vaginal atresia, bicornuate uterus, and urogenital sinus,[9] and the syndrome is typically more severe due to a higher incidence of urethral atresia.[10] The association with pulmonary malformations occurs in 58% of cases, which are mainly represented by pulmonary hypoplasia. Cardiovascular malformation occurs in 25% of cases and is represented by patent ductus arteriosus, tetralogy of Fallot, atrial septal defect, ventricular septal defect, and valvar anomalies. Skeletal muscle malformation occurs in 23% of cases and is represented by scoliosis, congenital hip dislocation, club feet, *pectus carinatum*, polydactylism, arthrogryposis, hemivertebrae, and bilateral cervical ribs. Gastrointestinal malformations occur in 24% of cases, which are represented by intestinal malrotation, atresia of the small bowel and colon, splenic torsion, imperforate anus, gastroschisis, omphalocele, and cloacal anomaly.[1,3,4,9]

The prognosis of the survivors depends on the severity of renal dysplasia and pulmonary hypoplasia.[9,11]

The etiology of PBS is not yet fully understood but a genetic influence is very likely to play a role, since familial cases have been reported.[12] Also, it has been suggested that a sex-linked recessive autosomic inheritance may be involved, since the majority of the cases occurs in males.[1,8,12] In sporadic cases, deletion of the hepatocyte nuclear factor 1beta (HNF1β), a transcription factor expressed in chromosome 17, required for visceral specification during embryogenesis including mesonephric duct derivatives, renal tubules of metanephros and the developing prostate, is observed.[13,14] According to Granberg et al.,[8] who studied genetic mutations in patients with PBS, only 1 case in 34 patients studied showed a remarkable mutation. However, this finding has to be carefully analyzed since only surviving patients were studied. Although few cases have been reported, PBS may be associated with other syndromes, such as trisomy 13, 18, and 21.[3,15-17]

The pathogenesis of PBS is uncertain. However, the theories include urethral obstruction and mesodermal development defect. The early urethral obstruction theory was based on postmortem observations and on the anatomy of infants with PBS. Urethral obstruction causes bladder and the remaining urinary tract distention. This distension impairs the abdominal muscle development, testicular descent, and renal dysplasia. This theory is supported by Gonzales et al.,[18] who demonstrated PBS in sheep that had undergone complete urethral obstruction.[18] Delayed canalization of the urethra,[19] transient urethral obstruction or the presence of a hypoplastic prostate may be responsible

for PBS development.[1,20] Since the urine production contributes to the amnion formation, the urinary tract obstruction results in oligohydramnios and consequently pulmonary hypoplasia and skeletal malformatioins.[1,4] The mesodermal development failure theory[21] involves an injury of the mesodermal layer during the early stages of gestation (between the sixth and tenth weeks of gestation). This theory is somewhat appealing since the urinary tract, abdominal wall musculature, kidneys, and prostate share a mesodermal origin. The presence of high amounts of fibrosis and connective tissue amidst the muscular layers of the urinary tract, without true obstruction, supports this theory. Both theories are linked to obstruction of the urinary flow with consequent damage to the urinary tract development.[4,22]

The first case of pre-natal PBS diagnosis dates from 1977, when an enlarged bladder was detected at 20½ weeks of gestation.[23] Currently, ante-natal diagnosis of PBS became feasible at around 12 weeks of gestation due to the sophistication of the ultrasonographic equipment. There are reports of PBS diagnosis between the eleventh and fourteenth gestational weeks, from when the fetal kidneys can be identified by ultrasonography.[1,4]

Ultrasonographic findings consistent with PBS suspicion are: hydroureter, bilateral hydronephrosis, bladder wall thickening, limb malformations, cryptorchidism, and oligohydramnios.[1,4] However, these findings are non-specific and cannot distinguish PBS from vesicoureteral reflux, urethra atresia, and other causes of urinary tract obstruction.[4,24,25] Definite diagnosis is only confirmed after birth.[26]

Recent technological advances in the pre-natal routine have an important role in the diagnosis and management of diverse urinary tract malformations, allowing early interventions and better prognosis.[4]

The potential benefits of the early interventions are improved fetal growth with respect to pulmonary and urinary tract development, thereby preventing chronic renal failure.[4,27,28] Intrauterine intervention criteria includes the second or third gestational trimester, progressive worsening of the hydronephrosis, oligohydramnios, the presence of megacysts, normal karyotype, as well as urinary sodium less than 100 mg/dL and urinary osmolarity less than 210 mOsm.[4,25]

Fetal minimally invasive intrauterine interventions include vesicoamniotic shunting (VAS), percutaneous cystoscopy with laser ablation, and the opened cistostomy.[4,28] However, these procedures are limited and represent palliative measures aiming for the amelioration of the fetal development conditions. Vesicoamniotic shunting has been recommended for obstructive uropathy for many years, postponing the definite treatment;[24] however, some complications may occur, such as shunt dislodgement, urinary ascites, premature labor, and corioamnionitis.[4] Although the improvement of the renal function is not fully established after intrauterine intervention, recent studies suggest that pulmonary function does ameliorate after this procedure.[11] According to Woods and Brandon,[4] the increment in the survival rate after early procedures is controversial.

In 1995, Quintero et al.[26] showed that percutaneous cystoscopy with laser ablation could be the better option for the treatment of PUV in fetuses with preserved renal function and when the PUV could be visualized,[28] although further studies are necessary to ascertain the better treatment.[26,28,29] However, Shimada et al.[22] studied 9 autopsies of fetuses with the PBS diagnosis, identifying no improvement in the development of the urinary tract musculature after early intervention.

The prognosis of the patients with PBS depends on the severity of the renal and pulmonary abnormalities.[9,11] In this setting, renal dysplasia and pulmonary hypoplasia are associated with 20% of intrauterine or neonatal death.[11]

After birth, the management of patients with PBS includes ventilatory support in case of pulmonary hypoplasia, and multiple surgical procedures namely: abdominoplasty, orchiopexy, and urinary tract reconstruction. The timing and the choice of surgical procedure are determined on a case-by-case basis.[9]

In the case reported herein, the prognosis seemed favorable since the PUV was treated early. The preserved renal function and the presence of normal lungs, as demonstrated at autopsy, most probably were due to the early intervention. However, clinical complications compromised the prognosis, which was expected to be favorable.

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