

Journal of Nephrologist



Prune-Belly syndrome; kidney injury in a rare disorder

Catarina Isabel Ribeiro*^{ID}

Nephrologist Department, Vila Nova de Gaia-Espinho Hospital Center, Vila Nova de Gaia, Porto, Portugal

ARTICLE INFO

Article type:
Mini Review

Article history:
Received: 2 September 2020
Accepted: 25 September 2020
Published online: 7 October 2020

Keywords:
Prune-Belly syndrome, End-stage renal disease, Renal replacement therapy, Cryptorchidism

ABSTRACT

Prune-Belly syndrome (PBS) is a rare congenital disease characterized by a clinical triad; abdominal muscle's hypoplasia, severe urinary tract abnormalities and cryptorchidism. PBS consists of a multisystem disease, which includes cardiopulmonary, gastrointestinal, musculoskeletal and urinary anomalies in varying degree. The cause and pathogenesis of PBS is unknown and the severity of symptoms can diverge greatly. On one hand, this condition may cause severe renal and pulmonary disorders, sometimes incompatible with life; on the other hand, it may origin few and tenuous urological abnormalities. Treatment is variable; it usually includes surgical management of symptoms. Renal replacement therapy for those patients with end-stage kidney disease may be necessary and it includes dialysis and kidney transplantation. The kidney failure is the main cause of postnatal death.

Implication for health policy/practice/research/medical education:

The PBS is a rare congenital disease. It is a multisystem disease, which includes cardiopulmonary, gastrointestinal, musculoskeletal and urinary anomalies. The severity of renal disease is the primary factor that affects the clinical manifestations and the kidney failure is the main cause of postnatal death.

Please cite this paper as: Ribeiro CI. Prune-Belly syndrome; kidney injury in a rare disorder. J Nephrologist. 2021;10(3):e22. DOI: 10.34172/jnp.2021.22.

Introduction

The Prune-Belly syndrome (PBS) is also known as Eagle-Barrett disease. It is a congenital disease characterized by abdominal muscle deficiency, severe urinary tract abnormalities and cryptorchidism in males' patients (1,2). The exact pathogenesis and cause of PBS is unknown. It may be caused by abnormalities in the bladder in fetal maturity. The severity of renal disease is the primary factor that affects the clinical manifestations. The main renal anomaly of PBS is the dysplasia, and it is manifested by incomplete nephron differentiation and tubules dilatation. Approximately one-half of patients have severe dysplasia and develop end-stage renal disease, with renal replacement therapy necessity (3).

The remaining clinical manifestations include "Prune-Belly" appearance due to aplasia or deficiency of abdominal muscles, impaired kidney function, bilateral cryptorchidism, and aplasia or hypoplasia of abdominal muscles. Pulmonary hypoplasia due to severe oligohydramnios resulting in maldevelopment of the lungs is the most severe finding associated with PBS.

Other findings include gastrointestinal malformations and skeletal abnormalities (1,4).

The PBS diagnosis is made clinically with the identification of characteristic features of abdominal muscle deficiency, severe urinary tract abnormalities and cryptorchidism. This diagnosis may be made by ultrasonographic examination between 20 and 30 weeks' gestation, or at birth or in early childhood by clinical recognition of the syndrome (5,6).

In spite of the survival rate has improved for PBS with earlier diagnosis and management, the mortality rate still at approximately one third. The majority of deaths happening at antenatal and perinatal time due to renal and pulmonary insufficiency (7,8).

Methods

A search for clinical guidance standards, review articles, systematic reviews, meta-analyses and randomized controlled clinical trials on Medline, evidence-based medicine sites, index of Portuguese medical journals and bibliographic references of selected articles published

*Corresponding author: Catarina Isabel Correia Dias Ribeiro,

Email: catarina.isabel.ribeiro@gmail.com, catarina.dias.ribeiro@chvng.min-saude.pt

between 2000 and 2019, in Portuguese, English and Spanish, using the keywords (MeSH terms) “Prune-Belly Syndrome”, “Urologic Diseases” and “Kidney Failure”.

Epidemiology and genetic

The estimated incidence of PBS is 3.8 cases per 100 000 births. According based upon from the Kids' Inpatient Database in the United States of American from 2002, 2003, and 2006 approximately 50% of affected patients were white, 30% black and 10% Hispanic. Boys are primarily affected, although there are described rare cases in females (less than 5%) (1,9).

The genetic basis of PBS remains unidentified. The predominance of affected male patients suggests a recessive X-linked deficiency. This syndrome has also occurred in association with another chromosomal anomalies and a report of large deletion in the long arm of chromosome 6 in a male fetus. Further evidence for a genetic basis of PBS includes a report of 2 cases of concordant PBS in monozygotic twins, and a report of 2 non-twin brothers. Isolated abdominal wall muscular hypoplasia, without evidence of urinary tract or renal pathology, has also been described in a family with apparent autosomal dominant or mitochondrial inheritance (6,10,11).

Pathogenesis

In spite of the exact pathogenesis of PBS is unidentified, there are many hypothesis, some controversial. PBS could be caused by a bladder's defect occurred during fetal maturity. Urine retention can distend bladder, ureters and kidneys (1,6). Retention of the testes in the abdomen may be attributed to obstruction by an unusually large bladder or to obliteration of groin canals. Other authors consider that incomplete emptying of the bladder leading to urinary retention and infection can occur as a result. Since the abdominal muscles are important for respiration, deformity of the chest could be explained by their absence. Another possibility is that the muscle deficiency and the urinary tract defects have a common cause that hasn't yet been revealed. A congenital open spinal canal has been too recognized in a few patients. A nervous system deficiency responsible for failure of abdominal muscles may be a hypothesis. (3,12).

Clinical manifestations

The characteristic findings of PBS include lack of abdominal muscle wall, kidney and urinary tract abnormalities, and in affected males, bilateral cryptorchidism (1,6). The severity of urinary tract defects and the pulmonary hypoplasia are the two main characteristics that determine outcome among patients with PBS. These disorders may result of repeated urinary tract infections, varying degrees of renal and respiratory insufficiency and other manifestations

of the disorder. Gastrointestinal malformations can also occur (1,4). Approximately 50% of patients surviving babyhood time will develop chronic kidney disease in childhood or adolescence period. Findings of bilaterally abnormal kidneys, a serum creatinine greater than 0.70 mg/dL, and episodes of clinical pyelonephritis appear to predict the eventual development of chronic kidney disease. Some patients present the least severe PBS form and they experienced either no or only mild impairment of renal function. The severity and timing of onset of renal insufficiency may reflect the degree of renal dysplasia. End-stage kidney disease in these patients was thought to be due to pyelonephritis and obstruction, not renal dysplasia (3,13,14). There may be a striking discrepancy between the deformed appearance of the urinary tract on renal ultrasonography and the often surprisingly good renal function. In most affected males, bilateral undescended testes and an empty scrotum are typical findings. Owing to early orchiopexy, there are case reports of successful paternity by aspirated sperm retrieval and in vitro fertilization. In addition, hypoplastic or dysplastic prostate leads to prostatic urethral dilation, which may cause urinary obstruction. Urinary tract infections, including recurrent episodes of cystitis and pyelonephritis, are common, occasionally resulting in urosepsis. Megaureters, hydronephrosis and polycystic or dysplastic kidneys are also commons (1,3,4). Pulmonary hypoplasia is the most significant complication in PBS. It is caused by oligohydramnios in the first half of gestation due to lack of sufficient urine production. Without amniotic fluid entering the airways, the lungs remain hypoplastic. In addition, thoracic cage deformities and irregularly movement of the abdomen during respiration may predispose affected patients to mechanical restriction, thereby explaining their susceptibility to impaired cough mechanism, recurrent bronchitis, and respiratory depression following anesthesia. Other manifestations include: chronic constipation, is a common feature of PBS, impaired exercise tolerance in adolescents and adults due to irregularly motion of abdomen during respiration, expansion retardation occurs in up to one-third of cases, anorectal malformations have been described in children with PBS including imperforate anus, anorectal agenesis, or congenital pouch colon, splenic torsion may occur due to intestinal malrotation, musculoskeletal anomalies are numerous and included dislocated hip, kyphoscoliosis, polydactyly, torticollis and pectus excavatum (1,2).

Diagnosis

PBS diagnosis is frequently evident from birth. Nevertheless care and time are essential to identify the anomalies (1). The diagnosis is made clinically with the identification of the characteristic features. PBS is most often recognized at

birth or in early childhood by the peculiar appearance of the abdominal wall, cryptorchism in males, and identified urogenital abnormalities by ultrasound. PBS occasionally presents later in life as a rare cause of renal failure in the adult. Antenatal diagnosis may be made by routine ultrasonographic examination of the fetus between 20 and 30 weeks' gestation. In some cases, it may be difficult to differentiate posterior urethral valves from PBS in utero, as both may present with antenatal ultrasound findings of a dilated bladder and bilateral hydronephrosis. In the rare cases of in utero intervention, patients with PBS have a better prognosis than those with posterior urethral valves (5,6).

Treatment

Treatment will depend ahead on the severity of the presented symptoms. Many patients will need rather modest surgical interventions such as vesicostomy (that will facilitate voiding of urine) or orchiopexy. More complex surgical procedures (such a bladder reconstruction or a urethra surgical widening) have been successfully undertaken (2,6). Other patients may reach adult life with only a minor degree of chronic kidney disease, and, therefore, require only minimal early intervention. Furthermore, as the progression of the renal insufficiency in childhood and adolescence is primarily due to recurrent pyelonephritis and reflux nephropathy, adequate antibiotic including antibiotic prophylaxis and, in rare cases, surgical intervention may prevent or delay end-stage renal disease. Kidney transplantation has been successfully presented in PBS and it is the favorite management for end-stage renal disease, either as preemptive therapy or dialysis. Long-term outcome is very good and is comparable to other reasons of end-stage renal disease. There also may be rare complications of transplantation intrinsic to this syndrome, such as acute torsion of the kidney transplant (7,14). In some cases when the native bladder is unsuitable, successful drainage of the kidney transplanted into a urinary conduit or augmented bladder has been performed. Maintenance hemodialysis and peritoneal dialysis are equally effective in the management of end-stage renal disease. Children with PBS who are initially treated with peritoneal dialysis have similar complication rates as patients with other causes of renal insufficiency (1,13).

Prognosis

Patients with PBS had generally poor prognosis. In older reports, 20% of all affected kids were said to be stillborn, and more than 50% did not survive 2 years. The majority of deaths occurring at antenatal and perinatal time, and it is due to pulmonary insufficiency. The kidney failure is the main cause of postnatal death (6-8).

Conclusion

PBS is a complex clinical entity with a kidney injury that can have an unfavorable outcome if not diagnosed early. It is important to highlight the commitment to intrauterine diagnosis, which requires strict surveillance by the obstetrician and multidisciplinary monitoring during and over there the prenatal period.

Author's contribution

CIR is the single author of the manuscript.

Conflicts of interest

The author reports no conflict of interest.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the author.

Funding/Support

None.

References

1. Seidel NE, Arlen AM, Smith EA, Kirsch AJ. Clinical manifestations and management of Prune-Belly Syndrome in a large contemporary pediatric population. *Urology* 2015; 85:211. doi: 10.1016/j.urology.2014.09.029
2. Hassett S, Smith GH, Holland AJA. Prune Belly Syndrome. *Pediatr Surg Int*. 2012;28:219-228. doi: 10.1007/s00383-011-3046-6
3. Arlen AM, Nawaf C, Kirsch AJ. Prune Belly Syndrome: current perspectives. *Pediatric Health Med Ther*. 2019; 10: 75-81. doi: 10.2147/PHMT.S188014
4. Smolkin T, Soudack M, Goldstein I, Sujov P, Makhoul IR. Prune belly syndrome: expanding the phenotype. *Clin Dysmorphol*. 2008; 17:133-135. doi: 10.1097/MCD.0b013e328263083b
5. Achour R, Bennour W, Ksibi I, et al. Prune Belly Syndrome: approaches to its diagnosis and management. *Intractable Rare Dis Res*. 2018;7(4):271-4. doi: 10.5582/irdr.2018.01094
6. Tonni G, Ida V, Alessandro V, Bonasoni MP. Prune-Belly Syndrome: case series and review of the literature regarding early prenatal diagnosis, epidemiology, genetic factors, treatment, and prognosis. *Fetal Pediatr Pathol*. 2013;31(1):13-24. doi: 10.3109/15513815.2012.659411
7. Yalcinkaya F, Bonthuis M, Erdogan BD, van Stralen KJ, Baiko S, Chehade H, et al. Outcomes of renal replacement therapy in boys with Prune Belly Syndrome: findings from the ESPN/ERA-EDTA registry. *Pediatr Neph*. 2018;33(1):117-124. doi: 10.1007/s00467-017-3770-9
8. Arlen AM, Kirsch SS, Seidel NE, Garcia-Roig M, Smith EA, Kirsch AJ. Health-related quality of life in children with Prune Belly Syndrome and their caregivers. *Urology*. 2016;87:224-227. doi: 10.1016/j.urology.2015.09.028
9. Routh JC, Huang L, Retik AB, Nelson CP. Contemporary

- epidemiology and characterization of newborn males with Prune Belly Syndrome. *Urology*. 2010;76:44-48. doi: 10.1016/j.urology.2009.12.072
10. Ramasamy R, Haviland M, Woodard JR, Barone JG. Patterns of inheritance in familial Prune Belly Syndrome. *Urology* 2005; 65:1227. doi: 10.1016/j.urology.2004.12.050
 11. Balaji KC, Patil A, Townes PL, Primack W, Skare J, Hopkins T. Concordant Prune Belly Syndrome in monozygotic twins. *Urology* 2000; 55:949. doi: 10.1016/s0090-4295(00)00452-0
 12. Woolf AS, Lopes FM, Ranjzad P, Roberts NA. Congenital Disorders of the Human Urinary Tract: Recent Insights From Genetic and Molecular Studies. *Front Pediatr* 2019; 7:136. doi: 10.3389/fped.2019.00136
 13. Dharnidharka VR, Fiorina P, Harmon WE. Kidney transplantation in children. *N Engl J Med*. 2014;371:549-58. doi: 10.1056/NEJMra1314376
 14. Penna FJ, Elder JS. CKD and bladder problems in children. *Adv Chronic Kidney Dis*. 2011;18:362-9. doi: 10.1053/j.ackd.2011.08.001
 15. Zugor V, Schott GE, Labanaris AP. The Prune Belly Syndrome: urological aspects and long-term outcomes of a rare disease. *Pediatr Rep*. 2012;4:e20. doi: 10.4081/pr.2012.e20

Copyright © 2021 The Author(s); Published by Society of Diabetic Nephropathy Prevention. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.