The Prune Belly syndrome: urological aspects and long-term outcomes of a rare disease

Vahudin Zugor,[1] Günter E. Schott,[2] Apostolos P. Labanaris[1]

[1]Department of Urology and Pediatric Urology-Prostate Center Northwest, St. Antonius Medical Center, Gronau; [2]Deparment of Urology, University of Erlangen Medical Center, Erlangen, Germany

Abstract

Prune-Belly syndrome is a disorder characterized by the following triad of symptoms: deficiency of the abdominal muscles, malformations of the urinary tract and bilateral cryptorchidism. This study included a total of 16 patients. The findings included clinical characteristics, diagnostics, therapy and long-term clinical outcomes. All patients were asked to complete a questionnaire and, in some cases, were given further examination. All patients were diagnosed with congenital aplasia of the abdominal wall and a variety of urogenital malformations. Cryptorchidism was present in 11 patients (68.8%), malformations of the prostate in 3 (18.8%), urethral malformations in 8 (50%) and mega-ureter in 14 patients (87.5%). A mega-bladder was observed in 13 patients (81.3%). Distinctive renal malformations, such as renal dysplasia, in 3 patients (18.8%) and hydronephrosis in 9 patients (56.3%), respectively. Abdominoplasty was performed on 4 patients (25%). Urethral surgery was performed in 10 patients (62.5%). Seven patients (43.8%) required ureter surgery, most of which involved re-implantation of the ureter and, in some cases, additional ureter modeling. Renal surgery was performed on 5 patients. Four patients with non-functioning kidneys with hydronephrosis underwent a nephrectomy and one patient pyeloplasty. We demonstrate that successful treatment is possible even in cases of serious and complex malformations, such as those of the Prune-Belly syndrome. Treatment must be tailored to the individual patient. The severity of the renal dysplasia is the main prognostic factor.

Introduction

Prune-Belly syndrome (PBS) is a rare malformation disorder (1 in 40,000 live births), affecting almost exclusively males (>95%), and characterized by a triad of clinical features including urinary tract anomalies, abdominal wall deficiency and bilateral cryptorchidism. Nowadays, not as many children with PBS are seen in clinical practice as in the past, mainly due to prenatal ultrasound and subsequent pregnancy termination of affected cases.

The protruding hypoplastic abdominal wall looks like a dried prune, hence the name Prune-Belly.[1-5] However, abortive forms are often also presented in which hypoplasia of the abdominal wall is not particularly severe. Malformations of the urinary tract are due to dysplasia of the smooth muscles of the renal pelvis and of the ureters, as well as of the prostatic part of the urethra. Depending on type and severity, the syndrome presents with three different clinical manifestations: i) the non-viable oliguric form with severe kidney dysplasia; ii) a serious form consisting of marked renal dysplasia, with mega-ureters, mega-vesicles, and progressive renal failure; and iii) the more favorable form with moderate renal dysplasia and different degrees of enlargement of the ureters and bladder.[1,3,5]

Prune-Belly syndrome is a complex malformation disorder with wide variability in severity and clinical manifestations. A thorough examination, usually as regular follow-up analyses, should establish the diagnosis and determine the perinatal management. This diagnosis should be considered when prenatal abdominal wall deficiencies have been confirmed.[6,7]

The purpose of this study is to present our clinical experience with children proven to have Prune-Belly syndrome, as well as to outline the surgical treatment options that can be used.

Materials and Methods

All clinical records of patients with Prune-Belly syndrome who were treated at the Erlangen Pediatric Urology department between 1970 and 2006 were again analyzed retrospectively. Questionnaires were sent out to all patients, some of whom (7 children) underwent further examination. Statistical analysis was carried out with the SPSS program. A total of 16 patients were included in the study. Findings cover clinical characteristics, diagnostics, therapy, and long-term clinical outcome.

Results

The sample population consisted of 16 patients in whom Prune-Belly syndrome had been clinically verified. There were 14 male (86.7%) and 2 female (13.3%) patients. Survival rate after ten years was 93.7%. At the time of diagnosis, average age was 7.4 years and median age 9.3 years. The youngest patient was 1.2 years old and the oldest 12.9 years old. Mean follow-up time was 17 years. Prune-Belly syndrome had been clinically confirmed in all patients. All children had been diagnosed with congenital aplasia of the abdominal wall and a variety of urogenital malformations. Cryptorchidism was present in 11 children (68.8%), malformations of the prostate in 3 (18.8%), urethral malformations in 8 (50%) and mega-ureter in 14 (87.5%) children. A mega-bladder was observed in 13 children (81.3%). Distinctive renal malformations, such as renal dysplasia in 3 children (18.8%) and hydronephrosis in 9 children (56.3%) (Table 1). Other related malformations, such as atrial septum defect (ASD), patent ductus arteriosus (PDA), spina bifida occulta and club-foot were found in a total of 5 children (31.2.%) (Table 1).

These patients did not receive homogeneous treatment and they were treated over different time periods. Our methodology was often individually targeted, geared towards treating the clinical symptoms and congenital urogenital malformations according to severity and form. Abdominoplasty was performed in 4 children (25%). Urethral surgery was performed in 10 children (62.5%). We first carried out a variety of endoscopic procedures in order to ensure a regular urine flow (in 50% of cases). Open urethral surgeries, such as urethralplasty and correction of epispadia, were performed in 2 children (12.6%). Bladder surgery was necessary in 10 children (62.5%); bladder reduction surgery was the most common procedure performed (31.3%) (Table 2). Seven children (43.8%) had to undergo ureter

Correspondence: Apostolos P. Labanaris, Prostate Center Northwest, Department of Urology and Pediatric Urology, St. Antonius Medical Center, Moellenweg 22, 48599 Gronau, Germany.
Tel. +49.2562.915.7114 - Fax: +49.2562.915.2105.
E-mail: Labanaris@web.de

Key words: Prune-Belly syndrome, diagnosis, therapeutic options, surgical treatment.

Received for publication: 30 May 2011.
Revision received: 17 November 2011.
Accepted for publication: 18 November 2011.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright V. Zugor et al., 2012
Licensee PAGEPress, Italy
Pediatric Reports 2012; 4:e20
doi:10.4081/pr.2012.e20

surgery, mostly including ureter re-implantations and in some cases additionally ureter modeling. Five of the 11 children with cryptorchidism had to undergo orchidopexy (31.3% of patients) which in every case was via an inguinal incision. One patient developed a seminoma at an adult age, and an inguinal orchiectomy was performed, followed by post-surgical radiotherapy. We performed renal surgery in 5 children. Four children who had non-functioning kidneys with hydronephrosis underwent a nephrectomy and one patient pyeloplasty. Four children who had developed terminal renal insufficiency which required dyalisis treatment underwent a kidney transplant. These children now have stable kidney function. Two children (12.6%). developed postoperative complications (urethral fistula and extravasation). A suprapubic catheter was inserted temporarily in 14 children. One child died from pulmonary hypoplasia and an advanced stage of renal insufficiency.

Table 1. The clinicopathological characteristics.

	N.	%
Sex		
Male	14	87.5
Female	2	12.5
Age when diagnosed		
Minimum	1.2	
Median	9.3	
Maximum	12.9	
Other congenital malformations		
Yes	5	31.2
ASD, atrial septum defect	1	6.3
Funnel chest (pectus excavatum)	1	6.3
Spina bifida occulta	1	6.3
Club-foot	1	6.3
Funnel chest	1	6.3
No	11	68.8
Treatment		
Surgical	16	100
Conserative	0	0
Congenital urological malformations		
Abdominal wall aplasia	15	93.8
Cryptorchidism	11	68.8
Malformations of the prostate	3	18.8
Urethral malformations	8	50
Mega-bladder	13	81.3
Mega-ureter	14	87.5
Renal dysplasia	3	18.8
Hydronephrosis	9	56.3
Surgical procedures		
Urethral surgery	10	62.5
Bladder surgery	10	62.5
Testicular surgery	6	37.5
Renal surgery	5	31.2
Ureter surgery	7	43.8
Abdominoplasty	4	25
Post-surgical complications		
Yes	2	12.5
No	14	87.5

Table 2. Urological surgical procedures.

	N.	%
Urethral surgery	10	62.5
Urethroplasty	1	6.3
Internal urethrotomy	4	25.0
Atrioventricular valve fulguration	2	12.6
Epispadias correction	1	6.3
Meatotomy	1	6.3
Shincterotomy	1	6.3
Ureter surgery	7	43.8
Cutaneous ureterostomy	1	6.3
Ureterocystoneostomy	5	31.3
Sober	1	6.3
None	9	56.3
Testicular surgery	6	37.5
Orchidopexy	5	31.3
Inguinal orchiectomy	1	6.3
None	10	62.5
Bladder surgery	10	62.5
Hemicystectomy	5	31.3
Hemicystectomy YV-plastic	1	6.3
Young-dees bladder neck Reconstruction	1	6.3
TUR bladder neck resection	2	12.6
Cystostomy	1	6.3
Renal surgery	5	31.3
Nephrectomy	4	25
Pyeloplasty	1	6.3
None	11	68.8
Suprapubic catheter	14	87.4
Kidney transplant	4	25

Discussion

Although many theories have been put forth regarding the embryonic origin of Prune-Belly syndrome, it has not been possible to determine the original factors causing this complex anomaly. Etiologically, it is a mesenchymal developmental arrest during the 6th to 10th week of gestation.[3] The morbidity rate is approximately 1:40,000 births.[5-16] Ninety-five percent of cases affect male children and 5% affect girls who usually do not exhibit the characteristic urogenital dysplasia nor, of course, cryptorchidism. Conversely, there are cases of boys who show the urogenital dysplasia typical of the Prune-Belly syndrome but have normotopic testes and no abdominal wall weakness at all; a variation of the disorder known as the pseudo Prune-Belly syndrome which is largely identical to the megacystis-megaureter syndrome.[3,8]

Prenatal diagnosis plays a key role in early detection of Prune-Belly syndrome. In addition, regular ultrasound examinations are extremely important in providing an early sign of missing kidney function or of dysplasia. Examination and palpation of the abdominal musculature, as well as nuclear medicine tests to establish physiological function such as an excretory urogram or magnetic resonance imaging urography and micturating cystourethrogram, are key components of postnatal diagnosis.

Major features of this syndrome are the related malformations of a gastrointestinal, cardiac, pulmonary and orthopedic nature. Anomalies of the gastrointestinal tract are observed in 20-30% of patients. Most abnormalities such as volvulus colon, esophageal atresia or stenosis of the rectum or of the esophagus, as well as a variety of malrotations, result from an insufficient fixation of the mesentery to the back of the abdominal wall.[1,2] Children with PBS can suffer from serious respiratory problems which can be caused by pulmonary hypoplasia due to an oligohydramnios or to related spinal and thorax deformities.[9] Since the incidence of orthopedic malformations lies between 30-40%, the skeletal system is, after the urinary tract, the second system in the body most frequently affected by this disorder.[1] Hip dysplasia, missing extremities or club-feet are frequent problems with the limbs. Atrial and ventricular septum defects are found in 10% of the cases, and Fallot tetralogies can also be observed.[1,10]

A mixed nephropathy, partly obstructive and partly dysplastic, affects the kidney, yet often without any obstruction at all. The kidney pelvis calyx system is usually moderately dilated. Renal insufficiency in these patients is primarily characterized by renal parenchymal dysplasia prompted by an early embryonal obstruction. Alternatively, renal insufficiency can also develop as a result of a bladder dysfunction with hyperperistalsis or the Prune-Belly syndrome's characteristic dysergenic contraction of the megacyst. Renal dysplasia can only be diagnosed through histological testing. A number of kidneys examined post-mortem showed dysplastic changes in the majority of the patients.[1,11,12] Since these changes were often present only in segments of the kidney, biopsies of these organs could lead to incorrect interpretation.

The wrinkled, drooping abdominal wall is a sign of a different type of hypoplasia and dysplasia of the abdominal wall muscles, first and foremost of a paraumbilical nature in the lower

half of the abdomen. The defect is attributed to the first lumbar myotome. The coarse folds of the abdomen look like a dried prune.[3] Another distinct feature of this syndrome is cryptorchidism. The reason for the undescended testes remains unknown. Mechanical factors, such as the greatly overextended bladder or the faulty development of the inguinal canal, allegedly account for this.[11,13,14] The crytorchid testes have a favorable histology. Tissue in the testes of PBS patients is no different from that found in intra-abdominal testes. The stem cell count in the first year of age, in particular, is comparable to that of normal testes.[11,15]

In most cases, bladder capacity is two to four times larger, the detrusor muscle is thickened and, in cases of an objective infravesical obstruction, not trabeculated. The trigonum is enlarged in most cases, and has lateral and often refluxing ostia and paraostial diverticula. The bladder neck is open. In other cases, the deficient urodynamics are shown by the sheer presence of a high volume of residual urine. Vesicoureteral reflux is found in 75% of cases.[1,3,8]

The ureters are typically elongated, and the related dilatation is mostly more pronounced than when there are only obstructive megaureters. Obstructive ureteral kinks exhibiting additional stenoses and consecutive dilatation are often found. Peristalsis is underdeveloped and often inefficient. Histological analyses frequently confirm the existence of structural disturbances in the entire abdominal wall.[3] The alterations are typically more marked in the distal section of the ureter than in the proximal part.

Treatment of Prune-Belly syndrome is a subject of controversy. In earlier times, due to the lack of experience with this very complex disorder, a conservative strategy advocating surgery followed by a *wait-and-see* approach was the recommended line of action. The main goal of any treatment is, of course, preserving kidney function.[3,11,15,16] Treatment options depend on the clinical picture. They can range from maintaining a *wait-and-see* approach while conducting regular urine checkups, to performing primary major corrective surgery and procedures for temporary urine diversion, such as a cutaneous ureteroileostomy with subsequent surgical reconstruction. However, as is well-known, reconstruction in the case of newborns makes no sense or is actually contraindicated since at this age the bladder is not yet fully developed, thus increasing the risk of obstruction after the uretero-cystoneostomy has been performed. Greater stabilization of the upper urinary tract can be achieved in many cases by performing procedures for more prolonged drainage at the bladder level, preferably a cystostomy.[5,16] The timing of surgery must be assessed on an individual basis and determined as part of the patient's clinical progress. These procedures can be considered in cases of, for example, vesico-urethral reflux and/or obstructive uropathy, in which there is the risk of further deterioration in renal function. Some authors advocate performing a urethrocystoscopy, if necessary, with urethrotomy in order to rule out an infravesical obstruction.

Abdominoplasty no longer plays the decisive role in surgical therapy that was presumed in former times. Physical therapy can indeed achieve equally good or bad results.[17-18] If necessary, tapering with reimplantation of the two dilated ureters should be performed, and both cryptorchid testicles mobilized during the orchidopexy that takes place during abdominal wall surgery.[12-19] Woodard, who has made a significant contribution in this field, advocates infravesical desobstruction wherever one may occur, excision of the surplus parts of both mega-ureters, modeling, antirefluxing neostomy in the bladder, and, likewise, excision of the diverticular upper half of the bladder. Orchidopexy completes this extensive major surgery. However, although this treatment, known as total reconstruction, has been broadly accepted, it is a very aggressive procedure and requires a great deal of surgical experience in pediatric urology. In fact, this approach has now been abandoned, even by Woodard himself, due to the high morbidity and mortality rate in infants undergoing total reconstruction.

Little is known about which children with PBS can benefit from extensive reconstructive procedures. Some authors advocate a purely conservative approach, given that the morphology and function of the urinary tract, as well as the abdominal wall malformations, may improve with age. Many pediatric urologists would agree that PBS represents a low pressure, dialated, non-obstructed system that in many cases does not require surgery. This point needs to be stressed; we have moved from aggressive surgery to medical management for many of these children. Of course, some children will need surgery for obstruction, but this is becoming less common than in the past. Many studies confirm that treatment for PBS should be tailored individually. A major study in Brazil has confirmed that various urologically invasive procedures performed in 32 children with PBS achieved good long-term results.[20-21] Renal transplants also secure good results in terms of function, as reported in a Japanese study of children with PBS.[22]

Conclusions

Our experience has shown that, with a sound diagnosis and depending on the clinical progress, adequate, effective treatment can be offered even in cases of serious and complex malformations, such as Prune-Belly syndrome. If the disorder follows a progressive course, an aggressive surgical approach has proven to be clearly more effective than a *nihilistic* treatment path or a *wait-and-see* strategy. Treatment, however, has to be tailored individually and specific indications for surgery assessed accordingly.

In the light of the comparatively sparse literature available and of the great diversity of phenotypes these malformations have, it is not possible to determine with certainty whether the surgical procedures adopted do indeed have a decisive impact on the long-term outcome of these children in terms of renal prognosis or, for that matter, *quoad vitam* prognosis.

References

1. Duckett JW, Snow BW. Prune-Belly-Syndrom. In: R Hohenfellner, JW Thüroff, H Schulte-Wissermann (eds.) Kinderurologie in Klinik und Praxis, Stuttgart, 1986, pp 348-65.
2. Shah D, Sharma S, Faridi MM, Mishra K. VACTERL association with Prune-Belly syndrome. Indian Pediatr 2004;41:845-7.
3. Schott G, Herrlinger A, Willital G. The prune-belly syndrome. Urologe A 1982;21: 322-6.
4. Van Ahlen H, Brühl P. Current views of prune belly syndrome Urologe A 1988;27: 207-13.
5. Harley LM, Chen Y, Rattner WH. Prune belly syndrome. J Urol 1972;108:174-6.
6. Greskovich FJ 3rd, Nyberg LM Jr. The prune belly syndrome: a review of its etiology, defects, treatment and prognosis. J Urol 1988;140:707-12.
7. Woods AG, Brandon DH. Prune belly syndrome. A focused physical assessment. Adv Neonatal Care 2007;7:132-43
8. Sigel A, Schrott KM. Congenital megaureter and its implications Urologe A 1982;21:312-7
9. Crompton CH, MacLusky IB, Geary DF. Respiratory function in the prune-belly syndrome. Arch Dis Child 1993;68:505-6.
10. Adebonojo FO. Dysplasia of the anterior abdominal musculature with multiple congenital anomalies. Prune belly or triad syndrome. J Natl Med Assoc 1991;265: 1179.
11. Kamel MH, Thomas AA, Al-Mufarrej FM, et al. Deceased-donor kidney transplantation in prune belly syndrome. Urology 2007;69: 666-9.
12. Patil KK, Duffy PG, Woodhouse CR, Ransley PG. Long-term outcome of Fowler-Stephens orchiopexy in boys with prune-belly syndrome. J Urol 2004;171:1666-9.
13. Docimo SG, Moore RG, Kavoussi LR. Laparoscopic orchidopexy in the prune

belly syndrome: a case report and review of the literature. Urology 1995;154:1513-5.
14. Hutson JM, Beasley SW. Embryological controversies in testicular descent. Semin Urol 1988;6:68-73
15. Woodard JR, Parrott TS. Orchiopexy in the prune belly syndrome Br J Urol 1978;50: 348-51.
16. Grapin-Dagorno C, Boubnova J, Ulinski T, et al. (2007) Renal transplantation in children with lower urinary tract dysfunction Bull Acad Natl Med 2007;191:569-81
17. Levine E, Taub PJ, Franco I. Laparoscopic-assisted abdominal wall reconstruction in prune-belly syndrome. Ann Plast Surg 2007;58:162-5.
18. Monfort G, Guys JM, Bocciardi A, et al. A novel technique for reconstruction of the abdominal wall in the prune belly syndrome. J Urol 1991;146:639-40.
19. Bogart MM, Arnold HE, Greer KE. Prune-belly syndrome in two children and review of the literature. Pediatr Dermatol 2006; 23:342-5
20. Dénes FT, Arap MA, Giron AM, et al. Comprehensive surgical treatment of prune belly syndrome: 17 years' experience with 32 patients. Urology 2004;64: 789-93
21. Diao B, Diallo Y, Fall PA, et al. Prune Belly syndrome: epidemiologic, clinic and therapeutic aspects. Prog Urol 2008;18:470-4.
22. Fusaro F, Zanon GF, Ferreli AM, et al. Renal transplantation in prune-belly syndrome. Transpl Int 2004;17:549-52.