

## CASE REPORTS

## Morphological aspects in a urogenital malformation, complex and rare, in a child

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### Abstract

The aim of this study follows the detailed evolution of a child diagnosed with prune-belly syndrome. This syndrome is a complex dysplasia, a rare pathology in children, characterized by the triad – the classic – hypo- or aplasia of righteous abdominal, cryptorchidism, abnormality of the urinary tract; also, it can be associated with pulmonary, cardiac, digestive, osteoarticular, and other malformations. Diagnostic criteria and etiopathogeny aspects are presented showing embryopathy and X-linked hereditary transmission theories as the most plausible, as proofed by recent genetic studies. Analyzing therapeutic aspects, it is stressed that medical treatment precedes or follows surgery, which cannot resolve urinary infection unless dysplastic urinary reconstruction is performed. Serious forms of prune-belly syndrome have a development and poor prognosis. Intrauterine and neonatal mortality is 20% and 50% in the first two years of life. The risk of urinary infection and/or lungs burdens the patient's clinical condition, allowing further appreciation on evolution of the disease. For cases solvable by plastic surgical reconstruction, as those who respond to medical therapy, differentiation will be monitored in territory and check-ups by the specialized consulting room from Polyclinic Health Center. Urinary infection relapse danger is permanent, requiring differentiated supervision. These case interest practitioners, by at least two aspects: the rarity of the disease, and complexity of dysplasia constituent, which has serious implications on the body economy.

**Keywords:** prune-belly syndrome, presentation, clinical appearances, pathology.

### Introduction

Urinary tract infections in children rank third in the hierarchy of infectious morbidity after respiratory and digestive diseases [1–3]. Weinberg and Bergström have shown that they are not a single disease but a group of disorders that share significant bacteriuria in titer. Prune-belly syndrome, described by the Anglo-Saxon authors Frölich and Parker, is placed among the dysplastic pathology of a child with polymorphic polarity, predominantly in the urinary tract [3, 4]. Symptomatic triad, which outlines the diagnosis, consists of abdominal muscle hypoplasia or aplasia; abnormalities of the urinary tract and cryptorchidism [4–6].

Since the first descriptions of the disease between 1839–1895 several cases were mentioned in the literature (over 400 currently) [1, 6–8].

Urinary tract anomalies, accompanying illness, are by their complexity, a permanent risk factor for recurrent and dragged urinary infections, with adverse effects on kidney function, calling into question the future of sick children [7–10].

Prune-belly syndrome incidence is estimated at 1/40 000 babies born live [5]; boys are more frequently affected in proportion of 95–97% of the total cases, compared with only 3–5% girls [7, 8]. A pseudo prune-belly syndrome was also described, characterized by urinary tract dilation, but unaccompanied by the absence

of abdominal wall and/or cryptorchidism. Most cases occur sporadically in children with normal karyotype [9, 10].

Williams suggests, however, the association of chromosomal anomalies (trisomy 18, trisomy 21, Turner syndrome, and others), as well X-linked recessive possibility of transmitting the disease; the latter would explain the greater incidence of disease in males than in the female [11–14].

Prune-belly syndrome etiopathogenesis has not yet been fully elucidated, although several theories have been developed for this purpose [5–7]. Thus, for example, urethral obstruction theory cannot explain the complex morphological abnormalities occurring in prune-belly syndrome. Mesoderm-development deficit theory proposed by Stephens, suggest the intervention of an unknown contaminant that occurs in the mesoderm differentiation in weeks 6–10 of fetal life, resulting in the abdominal wall anomalies, genitourinary tract, and testes. Embryonic theory, proposed also by Stephens also tries to explain the complexity of morphological abnormalities of prune-belly syndrome; is, in turn, insufficient to elucidate the causes and mechanisms underlying abnormalities of the genital and upper urinary tract [8, 15].

### Patients and Methods

Study material was represented by three prune-belly

syndrome clinical cases of hospitalized children, diagnosed and cared for in our service. We will present those cases below.

B.O., child, male, aged two weeks, from urban environment (Arad), was transferred to our Infants Service Department from Hospital of Obstetrics and Gynecology, for diagnostic clarification.

Anamnestic information revealed the following: the baby came on first pregnancy carried to term; in the 7<sup>th</sup> week of gestation, the mother had a flu status. The birth took place in the natural way, in a breech delivery, resulting in a child weighing 3200 g, length 51 cm and Apgar score of 7–1, with good response to resuscitation maneuvers (clearing airways, heat, and oxygen).

At the first clinical examination, we observed: enlargement of the abdomen (abdominal area of 38 cm at birth); abdominal muscle aplasia; presence in flanks and hypogastrium of bosselated, flexible and mobile tumors; cryptorchidism; congenital clubfoot; abnormalities of the ear pavilions.

At 14 days of life, we detected hematuria and bacteriuria in significant titers and semi-consistent stools, with halo fluid, therefore sending the patient in the Pediatrics department.

Clinical examination revealed (Figure 1): a newborn in 2-week-old, weighing 2900 g, poor general condition, with peeling skin and visible multiple congenital malformations; abnormal ear pavilions; a left parasternal II/III degree heart murmur, congenital clubfoot, cryptorchidism. The abdomen is distended, bosselated, with perimeter of 40 cm, with anterior wall muscles aplasia and abdominal drawing content expressed. By palpation, we detected multiple tumor formations, mobile, flexible, distributed in flanks, in renal lodges and hypogastrium.



**Figure 1 – Newborn with prune-belly syndrome.**

## Results

Laboratory analysis revealed: normal blood count, serum urea 0.4 g%, serum creatinine 1.3 mg%, serum sodium levels 145 mEq/L, serum potassium 4.1 mEq/L; urinary urea 3 g%, natriuresis 56 mEq/L, chloride 20 mEq/L. Urine analysis reveals a cloudy urine, with a density of 1005, thick cloud of albumin, significant pyuria, hematuria, and posters of leukocytes; bacteriological test reveals the presence of strains of *Klebsiella* (over 100 000 germs per mL of urine), sensitive to Gram-negative, ampicillin, gentamycin, biseptol. Stool was negative; in pharyngeal exudate culture, *Streptococcus viridans* was evident.

Laboratory investigations were performed with diagnostic role. ECG shows the heart's electrical path in

sinus rhythm with a ventricular rate of 150 beats per minute and the QRS axis,  $-150^{\circ}$ , as of right predominantly elements. Radiograph of the chest shows the lungs and heart look normal for age. Instead, the empty abdominal radiography shows a flabby abdominal wall and dilated, with homogeneous opacities in the right flank and lower floor.

Ultrasound, both kidneys appear enlarged, globular, with medullo-cortical differentiation lost through increased echogenicity of Malpighi pyramids. The parenchyma is visualized with small transonic images, round-oval, thin walled, clearly delineated (cysts). It is obvious sinus-parenchyma differentiation, drawing pielo-pelvis is uneven, and there is basin stasis. Both ureters are visualized throughout their length; their sinuous paths are dilated and pleated (dolicho-megaureter). Bladder of normal size for age has thickened walls, more echogen.

By vein uro-tomography (Figure 2) urinary tract highlight loosely, tardy and partly; contrast substance appears in 180 minutes, and only on computed tomography. Ureters are more narrow and elongated, dilated, occupying the entire abdominal cavity. Pyelocaliceal anatomy is not individualized. Described appearance, of dolicho-megaureter, persists even after 24 hours.



**Figure 2 – Radiological prone-belly syndrome appearance (bilateral dolicho-megaureter, mega-bladder).**

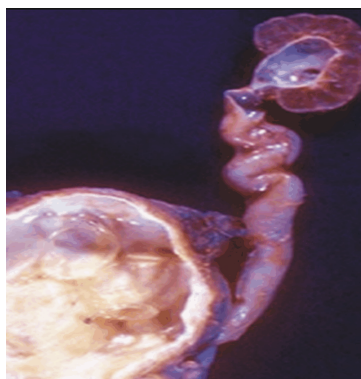
The presence of righteous abdominal aplasia, cryptorchidism, of urinary tract abnormalities and congenital clubfoot, say prune-belly syndrome diagnosis. Assigning also bacteriuria in significant titer and syndrome of nitrogenous retention completed biological diagnosis with urinary infection and kidney failure.

Etiological treatment was instituted, according to antibiogram (gentamycin associated with ampicillin, parenteral); endovenous perfusion; adjuvants; continued natural diet. Disease progression was unsatisfactory; newborn clinical condition worsens, appears oliguria, intravascular disseminated coagulation installing and the patient dies in the 9<sup>th</sup> day after admission at the age of 27 days.

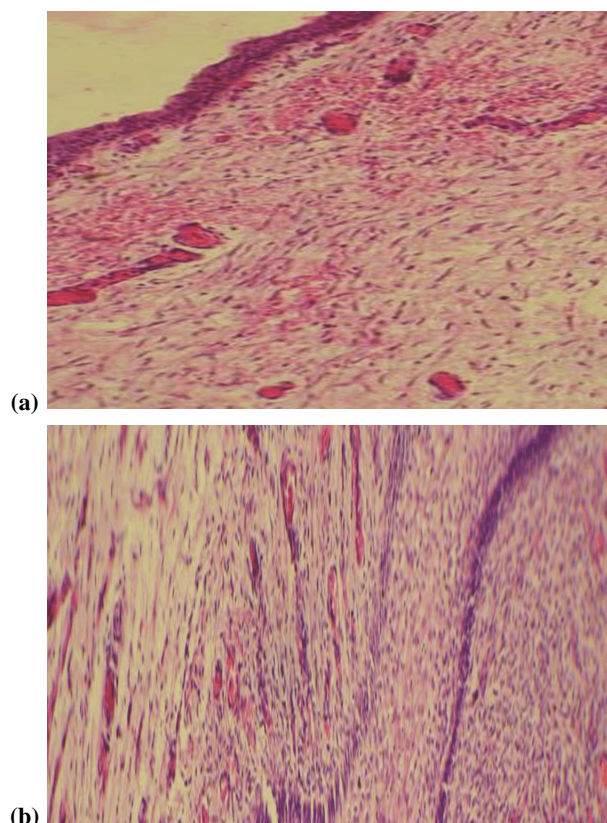
Necroptic examination (Figures 3 and 4) highlights the increased kidneys with multiple cortico-medullary cysts and basins filled with pus. Ureters are elongated, dilated, folded, wearing a dolicho-megaureter look. Bladder is normal, normal heart. Histologically (Figure 5, a and b), the structure of the kidney is largely wiped, cortico-medullary disseminated microcrystals occurs, mononuclear inflammatory infiltrates in vessels and the interstitium, glomerular and tubular atrophy,

dilated chalice, interstitial fibrosis with chronic inflammation aspect. Pathology diagnosis was confirmed as prune-belly syndrome associated with chronic pyelonephritis and acute urinary infection.

**Figure 3 – Necroptic appearance of a newborn with prune-belly syndrome (dolicho-megaureter, dysplastic kidney).**



**Figure 4 – Aplasia in all abdominal muscles.**



**Figure 5 – Focal mesenchymal collarettes found in the medulla. Hematoxylin–Eosin stain, original magnifications: (a) ob.  $\times 10$ ; (b) ob.  $\times 40$ .**

## Discussion

### Background

In 1830, Frölich and Parker, in 1895, describe a complex dysplastic syndrome with polymorphic polarity, predominantly in the urogenital [1, 3, 8–10].

Symptomatic classic triad, which outlines the diagnosis, consists of abdominal muscle hypoplasia or aplasia, abnormalities of the urinary tract, cryptorchidism.

Urinary tract anomalies, accompanying illness, are by their complexity, a permanent risk factor for recurrent and dragged urinary infections and so is difficult to control with medication. Vital prognosis in these patients is reserved and the risk of early mortality is real [3–6].

This dysplastic syndrome incidence is estimated at 1/40 000 babies born live; boys are more frequently affected in proportion of 90% of the total cases [5, 7].

Most cases occur sporadically in children with normal karyotype. There were authors (e.g., Williams) who have suggested an association with chromosomal abnormalities (trisomy 18, trisomy 21, and Turner syndrome) [14, 15].

### Genetics

Anglo-Saxon literature stated symptomatic triad was placed in the “wrinkled prune” dysplastic syndrome. Thus, this triad is known as prune-belly syndrome.

X-linked recessive transmission of the disease could explain the male predominance net (sex ratio males–females 18:1).

According to recent studies [14, 15] rare association of chromosome abnormalities can be determinate in a prune-belly patient:

- Trisomy 13;
- Trisomy 18;
- Turner syndrome with fetal ascites (pathogenetic mechanism thought to involve abdominal distention by ascites rather than by urinary obstruction);
- Ring X-chromosome lacking XIST;
- Cat-eye syndrome;
- Rarely with trisomy 21;
- Mosaic unbalanced chromosome constitution of chromosome 16;
- Presence of a small additional chromosome fragment;
- Interstitial deletion of chromosome 1 [del(1)(q25q32)].

Major pathological disorders, crossing in symptomatic triad, can complement other pathological changes localized to the musculoskeletal system, heart, lung, etc. because of pathological embryogenesis [7, 10].

Etiopathogenesis for this dysplastic syndrome has not yet been fully elucidated. Theories had been issued but cannot explain the complexity and severity of malformations pathological changes.

Several theories have attempted, in time, to explain the production of pathological lesions in the dysplastic syndrome:

- Intrauterine urethral obstruction;
- Circulatory disturbances during abdominal muscle and reno-urinary apparatus development (Obrinsky);



- Abnormalities of the autonomic nervous system (Swenson), unconfirmed by electron microscopy;
- Hormonal theory, the role of estrogen in generating changes in the reno-urinary apparatus;
- Embryopathy theory states the presence of suffering of the embryo between weeks 6 and 12 of intrauterine life, during which time it occurs from mesoblast the development of somites and side blades;
- Embryopathy theory, which states supports the aggression of a factor X, during embryogenesis in the 6–12 weeks of intrauterine life, when mesoblast is developing;
- Hereditary theory emphasizes the role of chromosomal abnormalities in X-linked transmission (Lattimer).

### Pathology

Macroscopic pathological changes are visible at birth and consist of:

1. Abnormalities of the abdominal muscles, characterized by aplasia in all abdominal muscles so that the abdominal wall is formed, fascia, fat and skin plicae (full form).

In the incomplete form, are interested muscles such as longitudinal abdominal muscles or oblique or transverse with compliance with upper abdomen.

Microscopically, the muscles are aplastic or hypoplastic with normal local innervation.

2. Urinary abnormalities are extremely important for diagnosis but also of the patient vital prognosis.

Morphological lesions are:

- Uretero-hydronephrosis;
- Mega bladder;
- URACA permeable;
- Abnormalities of bladder neck;
- Urethral stenosis;

Microscopic highlights:

- Kidney dysplasia with significant fibrosis;
- Glomerulo-tubular unit can look embryo-cystic;
- Renal parenchyma can be reduced to a thin blade;
- At the core system, uretero-vesico-urethral, you can view the absence of muscle fibers, areas of fibrosis and calcification.

3. Cryptorchidism, present in 90% of cases with normal or atrophied testicles.

4. Other malformations associated to triad: congenital clubfoot (equina), congenital hip dysplasia, diverse congenital heart lung malformation, ear anomalies, eye abnormalities, megadolicocolon, cranio-facial abnormalities.

Pulmonary injury (lung hypoplasia, atelectasis, cystic adenomatous degeneration, etc.) is increasingly present; therefore, some authors support the combination of pulmonary lesions presence in the classical diagnostic triad for prune-belly syndrome [1–5].

### Case particularities

Our observation shows that the prune-belly syndrome is a complex and rare dysplasia with poor prognosis.

Diagnostic is often based on morphological lesions that make up the main clinical presentation.

Aplasia or hypoplasia of the righteous abdominal alongside renal-urinary anomaly and cryptorchidism

outlines the diagnostic triad of prune-belly syndrome. The association of other malformations is rule and they can be located musculoskeletal, cardiac, otic or others.

As shown, the etiopathogenesis of this malformation is not clarified and genetic testing seeks to clarify some unknown aspects of embryogenesis-affected segments.

Morphopathological changes at our case-child are complex and proved at gross examination, both *in vivo* and *in vitro*; the character and the specificity of these changes were highlighted by objective clinical exam right from birth, complex methods with radio-imaging investigations, and finally even from the necroptic exam, both macroscopically and microscopically.

We considered it appropriate to present a case, often with complex and multi-malformative dysplasia, both for the scientific value but rather for the medical practice impact.

The severity of morphological lesions and deep functional disturbances that may occur, represent life endanger conditions for the patient. Our case has scientific value by its rarity and complexity of posed malformations. It has practical value by the fact that substrate lesion is highly polymorphic, which predisposes to complications (trentant UTI, acute and chronic renal failure, hypotension, hypertension, etc.) and unpredictable developments. For medical practice is a complex case requiring complex therapeutic, etiology, pathogenesis, reconstruction surgery and intensive care procedures.

### Conclusions

Urogenital dysplasia in children are rare conditions, but with significant morphopathological lesions, endangering patients' lives and development.

Symptomatic triad: aplasia (hypoplasia), cryptorchidism and reno-urinary apparatus abnormalities, support the diagnosis of prune-belly syndrome.

Prune-belly syndrome, in addition to symptomatic triad associates malformations of the lung, heart, locomotor apparatus, eye and ear, eventually outgoing for compromising the biological and functional condition of sick the organism.

Anatomopathological examination shows severe malformations presented and viewing by microscopic examination states the presence of degenerative processes in damaged organs (muscle hypotrophy, fibrosis, calcifications, cysts, etc.).

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