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Case Report

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An Unusual Urological Manifestation of Williams-Beuren Syndrome: Posterior Urethral Valve

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Keywords
Posterior urethral valve · Williams-Beuren syndrome · Hydronephrosis · Vesicoureteral reflux

Abstract
Williams-Beuren syndrome (WBS) is a genetic, well-defined, rare, neurodevelopmental disorder characterized by intellectual disability, congenital heart defects, abnormal facial features, and growth, endocrine, and genitourinary abnormalities. The genitourinary abnormalities in WBS frequently include congenital structural renal defects, vesicoureteral reflux, nephrocalcinosis, proteinuria, and chronic renal insufficiency. Treatment of patients with posterior urethral valve (PUV) remains a clinical challenge, requiring long-term management from early infancy into adulthood in order to avoid progressive renal insufficiency. To my knowledge, this is the first worldwide case of WBS with PUV in a 12-year-old boy. Due to the delayed detection of the defect, chronic renal disease occurred as a risk for him. This case demonstrates the importance of early diagnosis of genitourinary anomalies such as PUV to prevent chronic renal disease in boys and especially in patients with WBS.

Introduction

Williams-Beuren syndrome (WBS) is a multisystem chromosomal disease caused by the deletion of the chromosome 7q11.23 region that involves the elastin gene. Commonly associated features include growth failure; infantile hypercalcemia; typical cognitive and behavioral profile; and cardiovascular, skeletal, renal, and genitourinary anomalies [1].

The incidence of renal and urinary tract anomalies varies from 3 to 86% in WBS [2]. Nephrocalcinosis, proteinuria, stenosis of the renal artery, and congenital renal structural defects are examples of genitourinary and renal involvement [3]. In the literature, various congenital genitourinary abnormalities, such as abdominal wall defects, external genitalia anomalies, and structural abnormalities of the urinary tract, have been reported in several studies and seem to be more common in WBS patients than in the normal population [4]. On the other hand, lower urinary tract symptoms are not unusual in children and adolescents with WBS, as described in previous articles [5, 6].

Posterior urethral valve (PUV) is the most common cause of congenital obstruction of the urethra. Although the

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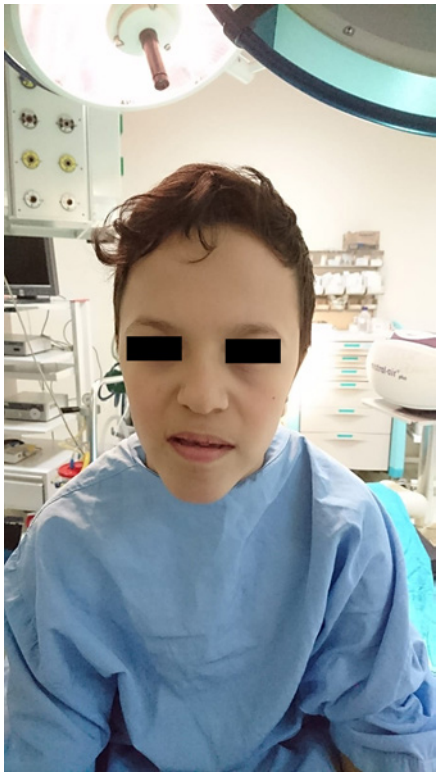

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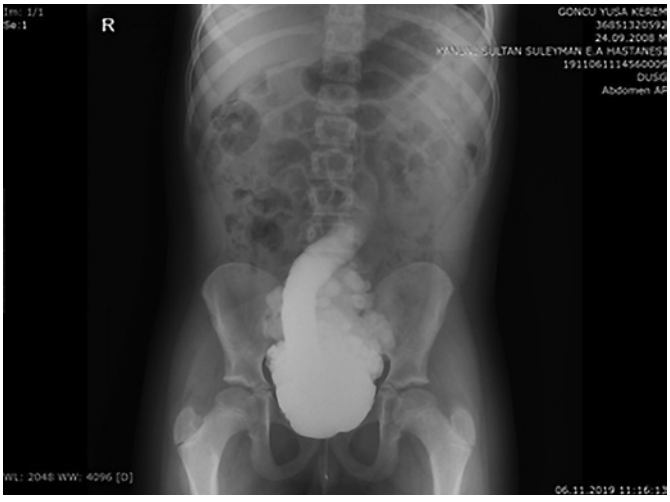

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Fig. 1. Phenotype of the patient.
Fig. 2. Bladder in VCUG. VCUG, voiding cystourethrography.

majority of cases are diagnosed during prenatal evaluation, in a group of patients the diagnosis may delay to older ages. Currently, it is true that early diagnosis of the disease is critically important for preventing the loss of renal function and supporting healthy improvement of the urinary system [7].

The literature of PubMed was searched with the words "Williams-Beuren syndrome," "urological manifestation," "posterior urethral valve," and "genitourinary findings." However, no coexistence of the defects could be found. Here, I describe the case of 12-year-old boy who presented with WBS and PUV, which has not been reported previously according to my knowledge.

Case Presentation

A 12-year-old boy was diagnosed with WBS when he was 8 months old. In FISH analysis, his karyotype was detected as 46XY (7q11.23), supporting the diagnosis of WBS. He was born by normal vaginal delivery and had an uneventful antenatal period. Although prenatal ultrasonography (USG) revealed grade 2 hydronephrosis, there was no pelvicalyceal dilatation in postnatal urinary USG. There had been no information about the bladder. The patient's medical history revealed that he had been under treatment with levothyroxine for a while for congenital hypothyroidism, but it was not needed any more. Furthermore, he had angiography history when he was 1 year old for the diagnosis of right ventricle hypertrophy, peripheral pulmonary stenosis, and supravalvular aortic stenosis. Any operation or medication was not suggested to the patient as a result of hemodynamic stabilization.

The patient was admitted to the pediatric urology department because of intermittent urination. His face was characteristic of WBS (shown in Fig. 1). On general physical examination, his weight for age was less than the 3rd centile and height for age was found to be less than the 10th centile. He had had a past history of intermittent urination, as noted by his mother, for 7 years. He was admitted several times to different centers with this symptom and was evaluated with abdominal USG. Compared with the left kidney, the right kidney was found to be slightly smaller in size. He had undergone cystoscopy once, but any pathology had not been detected previously.

The hematological evaluation and electrolytes were within normal levels. Blood urea nitrogen was 11.68 mg/dL, while serum Cr was 0.9 mg/dL. The glomerular filtration rate was 42 mL/min/1.73 m^2. Urinalysis revealed

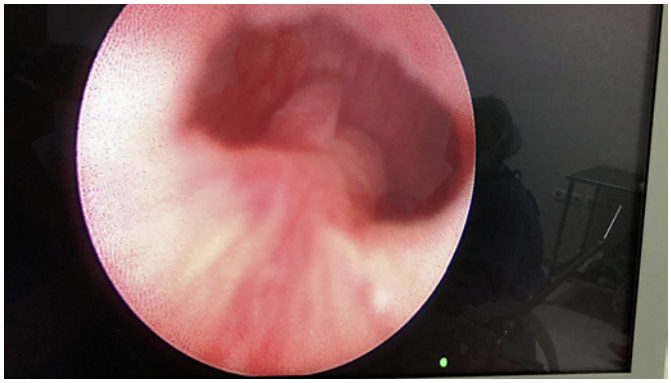

Fig. 3. Posterior urethral valve in cystoscopy.

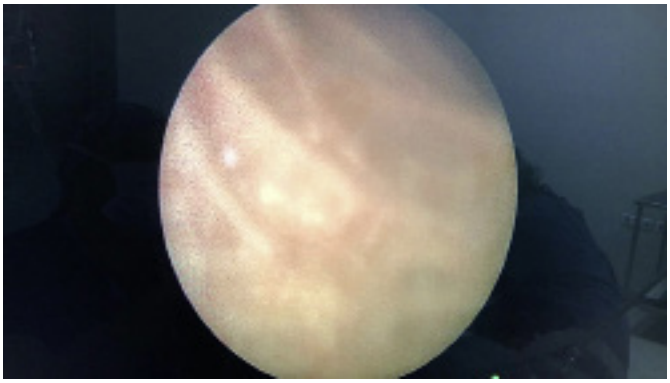

Fig. 4. Trabeculation of bladder.

protein 2+ and RBC 8–10/HPF. Urine culture was negative. On examination, high blood pressure (140/90), that is, ≥95th percentile, was detected. The pediatric nephrologist suggested antihypertensive drug therapy for chronic renal disease attributed to the high blood pressure and decreased glomerular filtration rate.

In the clinic, in order to highlight the etiology of intermittent urination, first abdominal USG was performed. The technique revealed bilateral hydronephrosis and an irregular thickened urinary bladder (wall thickening of 7 mm). Following this, *voiding* cystourethrography (VCUG) showed bilateral high-grade vesicoureteral reflux and a trabeculated bladder (shown in Fig. 2). Cooperated effective voiding study and evaluation were impossible regarding the mental status of the child. As a result, urodynamic studies could not be conducted. Due to neurogenic bladder findings, spinal MR was needed, and it revealed normal spinal neurologic anatomy. By cystoscopic evaluation, PUV was visualized (shown in Fig. 3). Also, trabeculated bladder was detected (shown in Fig. 4). Transurethral fulguration of valves was done at the 5–7 o'clock position. The postoperative period remained uneventful and mixion improved moderately. After PUV fulguration, tolterodine was initiated as an anticholinergic drug. In USG, bilateral hydronephrosis was regressed. The parents were advised to follow a strict urination protocol. He will be evaluated at the next follow-up visit in the pediatric urology clinic.

Discussion

PUV is a congenital urinary defect and may be associated with several congenital syndromes: Down syndrome, Klinefelter syndrome, prune belly syndrome, etc. [8, 9]. However, the medical literature does not consist of any report of PUV presentation with WBS simultaneously. Consequently, this is an original case where WBS coexisted with PUV.

The majority of cases with PUV are diagnosed in infancy and early childhood, especially during evaluation of male newborns for prenatal hydronephrosis [10]. On the other hand, the terms *delay in diagnosis* and *delayed presentation* should be used correctly to determine the clinical state of the patient. As in this case, delayed diagnosis of cases with PUV has been reported in several studies. While a few reports identify delayed presentation as a risk factor for poor renal function, others suggest that late presenting valves have good prognosis in terms of better recovery of lower urinary tract symptoms in the absence of hydroureteronephrosis. Eventually, there is a controversy about the prognosis of children with late presenting PUVs [11, 12]. The initial symptoms of delayed presentation of obstruction are age-dependent and nonspecific, and differ from those of early diagnosed PUVs [12]. In this case, because of the absence of PUV based on the previous cystoscopy finding in a different clinic, the case was diagnosed as non-neurogenic neurogenic bladder and followed up. As a result, the patient's definitive diagnosis was delayed. When the patient was referred to pediatric nephrology, he was evaluated as chronic renal disease and started on antihypertensive medication for hypertension.

Although a proposed standard procedure for the diagnosis of urethral obstruction does not exist, worldwide, a normal-appearing posterior urethra in VCUG is widely accepted to exclude PUV in children [12]. The patient could not be diagnosed with congenital PUV defect until he was 12 years old, so the renal parenchyma had become thinner with years due to reflux. The diagnosis and treat-

ment were done simultaneously during cystourethroscopy, after the detection of suspected PUV in VCUG and bilateral hydronephrosis in USG.

The prevalence of structural abnormalities of the urinary tract in WBS patients, detected with renal sonography, ranges from 10 to 35% [3, 4]. The reported congenital structural renal defects include renal agenesis, duplicated dystopic renal cyst, vesicoureteral reflux, nephrocalcinosis, and stenosis of the renal artery [3, 4]. In a study by Sammour et al. [3], renal abnormalities were detected by USG in 17.8% of the patients. Hydronephrosis was the major finding in 5 (6.3%) patients, followed by kidney duplication in 3 (3.8%). In the largest reported series, 23 (17.7%) of 130 patients had abnormal renal findings. The most common abnormality was kidney duplication in 9 (6.9%) patients, followed by unilateral renal agenesis in 5 (3.8%) patients and hydronephrosis in 1 (0.8%) patient [4].

Clinical manifestations of genetic disorders may be quite variable. Currently, PUV is not known as a manifestation in cases with WBS. I described this defect in this case in order to contribute to the information on previously known clinical manifestations of WBS and to draw attention to the importance of follow-up of antenatal hydronephrosis, especially in boys and especially in children in whom intellectual disability could occur. Therefore, detailed clinical and radiological evaluation of the abdomen and genitourinary system of patients with WBS and referral to a pediatric urologist and nephrologist are particularly recommended.

Statement of Ethics

Informed consent for publishing photos and details of the case was given by the family of the patient.

Conflict of Interest Statement

The author declares no conflict of interest.

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