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Nephrolithiasis with Bardet-Biedl syndrome in a three-year-old girl: A case report

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Abstract Bardet-Biedl syndrome is a multisystemic developmental disorder diagnosed on the basis of the presence of obesity, retinal defects, polydactyly, hypogonadism, renal dysfunction, and learning disabilities. Renal disease is clinically heterogeneous, but is recognized as a cardinal feature and is a major cause of mortality in BBS. We here presented a three-year-old girl with renal stone and Bardet-Biedl syndrome.

Key Words Bardet-Biedl syndrome; nephrolithiasis; renal disease; child.

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INTRODUCTION

Bardet-Biedl syndrome (BBS, OMIM 209900) is a pleiotropic genetic disorder with significant interfamilial and intrafamilial variation and characterized by mental retardation, obesity, retinitis pigmentosa, postaxial polydactyl, short stature, developmental delay, endocrinopathies, speech deficits, hearing loss, hepatic fibrosis, and renal abnormalities [1].

In BBS, renal abnormalities are one of major causes of morbidity and mortality [2]. The renal abnormalities are variable, but the syndrome's classic manifests are cystic tubular disease and anatomical

malformations [3]. Nephrolithiasis with BBS have been reported in two cases so far. However, these patients have also another renal disease. Here, we differently presented a three-year-old girl with renal stone and BBS, without another renal disease.

CASE REPORT

A three-year-old girl was admitted to our clinic for episodes of flank pain. It was learned from medical history that she was the first offspring of consanguineous parents and her sister (five-month-old) has chronic renal failure associated with BBS. In physical examination, it was observed that her phenotype was complex, including short stature (83 cm, < 3 percentile), truncal obesity (body mass index: 22.1 kg/m^2, > 97 percentile), mental retardation, post-axial foot polydactyly. Furthermore, it was also noticed mental retardation and speech impairment. Laboratory tests revealed that complete blood count, blood gas, creatinine, liver enzymes and electrolyte were all normal (Table 1).

Laboratory data	Result
Serum	
Urea (mg/dl)	22.8
Creatinine (mg/dl)	0.50
Sodium (mmol/L)	140
Potassium (mmol/L)	4.5
Calcium (mg/dl)	10.2
Phosphor (mmol/L)	1.41
pH/HCO3	7.38/20.3
Urine	
Calcium/Cr (mg/mg)	0.18
Uric acid/Cr (mg/mg)	1.21
Oxalate/Cr (mg/mg)	0.02
Citrate/Cr (mg/mg)	0.89
Cysteine/Cr (mg/mg)	0.05

Table 1. Laboratory data of patient with Bardet-Biedl syndrome and renal stone

The urinalysis showed the following: pH 6.0, density 1015, protein (-), erythrocytes (-), leucocytes (+), and 5-10 leukocytes in urine microscopy in each area. However, urine culture was sterile. Ultrasonography revealed 5 and 3-mm diameter two stones in the left renal pelvis without dilatation of the pelvicaliceal system.

According to the clinical evidence, she met three primary criteria and three secondary criteria (Table 2). Her younger sister had also same phenotypic characteristics. All these findings thought use that the patient had coexistence of BBS and renal stone. For etiology of renal stone, urine calcium, uric

acid, oxalate, and cystine excretion were evaluated. All were detected in normal range. Potassium citrate therapy was added and her parents were advised to maintain a high fluid intake (1.5-2 L/m^2 per day). After six months follow-up, the USG showed that the size of the stones decreased as 2- and 3-mm diameter.

Primary features	Secondary features
Obesity	**Developmental delay**
Retinal dystrophy	**Behavioral problems**
Hypogenitalism	Neurological problems
Post-axial poydactyly	**Speech problems**
Renal abnormalities	Brachydactyly, syndactyly, clinodactyly
Learning disabilities	Eye anormalies
	Diabetes mellitus
	Hepatic fibrosis
	Congenital heart disease
	Anosmia
	Dental anomalies
	Hearing loss
	Polyuria/polydipsia
	Hirschsprung's syndrome

*In our patient, clinical findigs are shown in bold.

Table 2. Diagnostic criteria for Bardet-Biedl syndrome

DISCUSSION

BBS is a rare developmental disorder with a prevalence of 1/125,000 to 1/ 175,000 in Europe and North America. The syndrome exhibits clinical and genetic heterogeneity. The primary clinical features include rod-cone dystrophy, postaxial polydactyly, central obesity, male hypogonadism, cognitive impairment, renal dysfunction, and genitourinary malformations [4]. The secondary features include brachydactyly or syndactyly, eye abnormalities like strabismus, cataract and astigmatism, developmental delays, speech disorders or delays, ataxia, diabetes mellitus, craniofacial dysmorphism, nephrogenic diabetes insipidus, hepatic fibrosis and congenital heart disease [5]. Presence of four primary or three primary plus two secondary features is diagnostic for the syndrome [5]. Our patient had polydactyly, obesity, learning disabilities, speech, behavioral, and developmental problems (three primary and three secondary clinical features) (Table 2). However, flank pain related renal stone was the presenting clinical feature.

The one of the cardinal signs of the syndrome is kidney involvement. Kidney

involvement is immensely variable and often asymptomatic. Previous one study determined as 82% the frequency of occurrence of renal disease [6]. In this syndrome, renal abnormalities were reported anatomic anomalies, renal insufficiency, renal cysts, fetal lobulation, scarring, dysplasia, unilateral agenesis, ectopia, vesicoureteric reflux, calyceal clubbing or blunting [5]. Renal failure is an important cause of death in BBS [2,7]. Our patient's young sister had renal insufficiency, but she had only renal calculi.

In BBS, nephrolithiasis is quite rare, and have been reported two cases in literature so far. In one of these cases, renal stone occurred after four years from renal transplantation [8]. In the 22-year-old other case, renal stone consisted of in kidney with infundibular stenosis [9]. However, there was not any renal disease except stone in our patient.

BBS is genetically heterogeneous with 14 genes (BBS1- BBS14). BBS genes encode proteins localized to the primary cilia, basal body, or centrosome [10]. Evidences of a growing number of suggest that BBS proteins are important for cilia function [11]. Cilia defects alter various physiological functions and thus lead to several disorders including cysts, retinal degeneration, liver fibrosis, anosmia, ataxia, cardiac defects, and hydrocephalus [12]. Also, defects in renal cilia are thought to be the major cause of renal abnormalities [13]. However, the coexistence of ciliopathy with nephrolithiasis without another renal defect has not shown in this syndrome so far. Besides, it was not observed findings of renal tubular disorder, which may cause renal stone in our patient (Table 1). Therefore, the combination of nephrolithiasis and BBS may also be incidental in this case.

In BBS, phenotypic variability is observed within families [3]. For example, in one of the families, in which five patients were affected, one died during the neonatal period, two developed end stage renal disease at 14 and 15 years of age,

respectively, whereas one had duplication of the right collecting system as the only renal phenotype [14]. The intra familial differences have been explained with epistatic effects of modifier genes and/or the presence of a third BBS gene mutation [15,16]. Our patient and her sister have different renal phenotype can be an example for this situation.

In conclusion, BBS is a pleiotropic disorder with involvement of multiple organ systems and is also a model of oligogenic inheritance and epistasis. Here, we are reporting to be different renal phenotypic features within same family once again and the first case of BBS with renal stone without another a renal disease.

CONFLICT OF INTEREST

None declared.

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