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Bartter Syndrome in a Child with Solitary Functioning Kidney

Soliter Böbrekli Çocuk Olguda Bartter Sendromu

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ABSTRACT

Bartter Syndrome (BS) is a hereditary condition characterized by polyuria, renal salt wasting, and hypokalemic metabolic alkalosis with high serum renin and aldosterone levels. Patients with BS usually have symptoms in the first two years of life, but they might also be diagnosed at school age or later. Associations between congenital renal and urinary system anomalies and BS are extremely rare. Here we present a case of a 4-year-old girl having a solitary functioning kidney (SFK) due to right renal agenesis, who eventually diagnosed as BS in the light of clinical and laboratory findings. The patient applied to the pediatric nephrology department with the complaint of polyuria. Laboratory evaluation revealed hyponatremia, hypochloremia, hypokalemia with metabolic alkalosis, and high renin and aldosterone levels. Urine sodium, chloride, potassium excretions were increased. Sweat test was normal. CLCNKB mutation with the diagnosis of classic BS was negative. We assume that our patient might have another type of BS with a milder mutation. Urinary anomalies accompanying BS are very rarely reported and up to our knowledge the togetherness of renal agenesis and BS has not been defined in the literature yet.

Key Words: Bartter syndrome, Renal agenesis, Solitary functioning kidney

ÖZ

Bartter Sendromu (BS), poliüri, renal tuz kaybı, yüksek renin ve aldosteron düzeylerinin eşlik ettiği hipokalemik metabolik alkaloz ile karaterize kalıtsal bir hastalıktır. BS hastalarında semptomlar sıklıkla yaşamın ilk iki yılı içerisinde görülmekle birlikte okul çağından sonra da tanı konabilmektedir. Konjenital böbrek ve üriner sistem anomalileri ile BS birlikteliği çok nadirdir. Burada sağ renal ageneziye bağlı soliter böbreği olan ve daha sonra klinik ve laboratuvar bulguları ışığında BS tanısı alan 4 yaşında bir kız hasta sunulmuştur. Hasta, yaklaşık iki yıldır devam eden çok idrar yapma şikayetiyle çocuk nefroloji polikliniğine başvurmuştur. Laboratuvar incelemelerinde hiponatremi, hipokloremi, hipokalemi, metabolik alkaloz, renin ve aldosteron yüksekliği ile birlikte idrarda sodium, potasyum ve klor atılımında artış kaydedilmiştir. Ter testi normal olan hastadan klasik BS ön tanısıyla CLCNKB gen mutasyonu varlığı araştırılmış, mutasyon saptanmamıştır. Hastada diğer BS tiplerinin hafif bir formunun olabileceği düşünülmüştür. Renal agenezi ile BS birlikteliği literatürde daha önce bildirilmemiş olup diğer üriner anomaliler ve BS birlikteliği de çok nadirdir.

Anahtar Kelimeler: Bartter sendromu, Renal agenezi, Tek böbrek

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INTRODUCTION

Bartter Syndrome (BS) is a group of rare autosomal-recessive disorders caused by defective salt reabsorption in the thick ascending limb of the loop of Henle and is characterized by renal salt wasting, hypokalemia, metabolic alkalosis, hyperreninemic hyperaldosteronism with normal blood pressure and hyperplasia of the juxtaglomerular apparatus (1). BS is clinically classified as antenatal BS (aBS) and classic BS (cBS). Five subtypes of BS are defined based on the mutated gene which are SLC12A1 (BS type I), KCNJ1 (BS type II), CLCNKB (BS type III/cBS), BSND (BS type IV) and CASR (BS type V) (2,3).

Classic BS, which is also known as Type III BS, often presents in the first 2 years of life, but the patients might also be diagnosed at school age or later (2). Similar to the antenatal/neonatal types, patients with cBS also have polyuria, polydipsia, salt craving and a tendency to dehydration, but normal or just slightly increased urinary calcium excretion without the tendency to develop kidney stones and nephrocalcinosis (2-4).

Associations between congenital renal and urinary system anomalies and BS are extremely rare (5,6). BS has been reported once in association with congenital anomalies of the kidney and urinary tract (6). We present a case of clinically diagnosed BS which was accompanied by solitary functioning kidney (SFK). To the best of our knowledge, the association of BS and SFK due to renal agenesis has not been reported previously.

CASE

A 4-year-old girl applied to our pediatric nephrology department with the complaints of polydipsia, polyuria, salt craving and decreased weight gain prominent for the last two years. The patient also had the diagnosis of antenatally detected right renal agenesis. She was born after 38 weeks of gestation; her birth weight was 3100 g, and there was no history of polyhydramnios. She had healthy parents who did not have consanguinity, and the family history did not include any known renal diseases.

On admission, her body weight was 14 kg (10-25th percentile), and her length was 97 cm (10-25th percentile). Body temperature, heart rate, blood pressure, and respiratory rate were normal on physical examination. Facial appearance and other systemic findings were normal as well.

Urinary system ultrasound showed the absence of the right kidney. Nephrocalcinosis or any other anatomical anomalies were not detected in the left kidney. Dimercaptosuccinic acid (DMSA) scan performed at the age of 6 months, showed the absent renal uptake on the right side and homogenous uptake of the left kidney, and voiding cystourethrography was normal with no reflux.

Laboratory tests revealed hyponatremia (serum sodium: 129 mmol/L), hypokalemia (serum potassium: 2.3 mmol/L), and hypochloremia (82 mmol/L) with metabolic alkalosis (pH: 7.53, HCO3: 32). Complete blood count, blood urea nitrogen, serum creatinine, calcium, phosphorus, magnesium, uric acid and alkaline phosphatase levels were all in normal ranges. Urine analysis revealed a urine pH of 5 and specific gravity of 1012 on the dipstick. The results of renal tubular functioning tests were as follows; urine output 3.8 ml/kg/hour, fractional excretion of sodium (FeNa) 8.3% (normal <1–3%), FeCl 5.4% (normal <1–3%), FeK 45 % (normal <10–15%), FeMg 1.1% (< 1.5%), FeUA 22% (normal 5-13%), tubular reabsorption of phosphorus 88% (normal >85%), and the spot urine Ca/Cr ratio was found to be 0.19 (normal <0.21). Urinary protein excretion was 2.8 mg/m^2/hour (normal <4 mg/m^2 per hour), calcium excretion 3.2 mg/kg/24 hour (normal <4 mg/kg/24 hour) and glomerular filtration rate 95.5 ml/min/1.73m^2. The blood gas results of the patient were consistent with metabolic alkalosis (pH: 7.53, HCO3: 32 mmol/L). Aldosterone and renin activity levels were significantly elevated at 257 ng/dl and 56.7 ng/ml/h, respectively (Table I). Sweat test to exclude Cystic Fibrosis was normal. Clinical and laboratory features showed that our patient had BS. Only CLCNKB mutation was searched in the patient, however no mutation regarding this gene was detected.

With the apparent clinical diagnosis of BS, oral supplementation with sodium chloride (8 mmol/kg/day), potassium chloride (3 mmol/ kg/day) and treatment with indomethacin were administered. Metabolic alkalosis, serum sodium, potassium, and chloride levels gradually improved with medical treatment. At the last follow-up visit, she was 5 years old. It was learned that the family discontinued the medications and instead they change the diet of the patient with salty and potassium rich one.

Tablo I: Laboratory data of the patient.

Serum BUN (mg/dL)	10 (7-20)
Serum creatinine (mg/dL)	0.4 (0.3-0.8)
Serum sodium (mmol/L)	129 (135-148)
Serum potassium (mmol/L)	2.3 (3.5-5.1)
Serum chloride (mmol/L)	82 (101-109)
Blood gas pH	7.53
Serum bicarbonate (mmol/L)	32
Aldosterone (ng/dL)	257 (3.7-43.2)
Renin activity (ng/mL/h)	56.7 (1.2-2.4)
Fractional excretion of sodium (FeNa)	8.3% (normal <1-3%)
Fractional excretion of potassium (FeK)	45% (normal 10-15%)
Fractional excretion of chloride (FeCl)	5.4% (normal <1-3%)
Urine protein excretion	2.8 mg/m^2/hour (<4 mg/m^2/h)
Urine calcium excretion	3.2 mg/kg/day (<4 mg/kg/day)
CLCNKB mutation	Not detected

At the last follow-up, despite not continuing the medications but having a salt and potassium rich diet, the patient's serum sodium, potassium, and chloride levels were found to be at the lower limit of the normal ranges, and she did not have any clinical symptoms.

DISCUSSION

In BS, the type of the mutation is the most important thing to delineate the clinical symptoms and prognosis of the patient. Some of the patients with genetically diagnosed BS might have milder clinical course based on the mutation type (7-9). The diagnosis of our patient is based on the clinical and the laboratory findings, since we could only search the CLCNKB mutation which eventually evidenced as negative.

Associations between congenital renal and urinary system anomalies and BS are extremely rare (5,6). Tomimatsu et al. (5) reported the first case which was associated with an urological anomaly and neonatal BS in an infant. They described a newborn with unilateral multicystic dysplastic kidney (MCDK) and neonatal BS. They speculated that it may be possible that increased amniotic fluid pressure or fetal polyuria itself leads to the functional obstruction of the urinary tract and partly contributes to the pathogenesis of MCDK.

Westland et al. (6) reported the case of a girl with BS Type III and severe bilateral congenital anomalies of the kidney and the urinary tract (CAKUT) with an antenatal presentation. In that case, ultrasound demonstrated a MCDK with a duplex system on the right side, a large ureterocele in the bladder and a bilateral megaureter without vesicoureteral reflux. Genetic studies detected a homozygous alteration in CLCNKB, which is consistent with BS Type III (7,8,10). The authors pointed out that, although CLCNKB mutations generally have milder clinical findings, in this case it presented as antenatal BS with severe course, because it was associated with CAKUT.

Since there are not any proofs showing the association between urological anomalies and BS, it was also speculated that glomerular hyperfiltration in the solitary kidney may lead to an increased electrolyte load in the thick ascending limb of Henle's loop which might aggravate the symptoms of BS (5,11). In animal studies, glomerular hyperfiltration has been described in renal mass reduction (12). Furthermore, recent reports have suggested the presence of hyperfiltration in tubular disorders in children with a solitary kidney (11,13).

Our patient, unlike other two cases, had a solitary left kidney without a right MCKD. The clinical findings are consistent with BS Type III however we were not able to show a mutation in CLCNKB gene.

To the best of our knowledge, this is the third report in the literature demonstrating the association between urinary anomaly and BS, and is the first with concomitant unilateral renal agenesis and BS. We may speculate that, in our patient, SFK might have potentiated the clinical findings of BS. Nevertheless, it is hard to say that these two conditions are whether apart from each other or SFK might have additional effect on the clinical prognosis on BS.

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