Case Study of Bardet-Biedl Syndrome with Fetal Lobulation and Focal Segmental Glomerulosclerosis

Fetal Lobulation ve Focal Segmental Glomerulosclerosis ile Böbreği Tutan Bardet-Biedl Olgusu

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Abstract

Bardet-Biedl syndrome is a genetic autosomal recessive disease characterized by abdominal obesity, mental retardation, dysmorphic extremities, retinal dystrophy or pigmentary retinopathy, hypogonadism or hypogenitalism, and kidney involvement. Patients with renal involvement may present with both structural and functional abnormalities. Here, we present a 15-year-old male with Bardet-Biedl syndrome who has both fetal lobulation, a rare type of structural abnormality, and focal segmental glomerulosclerosis, having not been reported before. *Turk Jem 2008; 12: 32-4*

Key words: Bardet-Biedl syndrome, childhood, focal segmental glomerulosclerosis, kidney

Özet

Bardet-Biedl sendromu abdominal obezite, mental retardasyon, dismorfik ekstremiteler, retinal distrofi veya pigmenter retinopati, hipogonadizm veya hipogenitalizm ve böbrek tutulumu ile karakterize otozomal resesif genetik bir hastalıktır. Böbrek tutulumu %90–100 oranında ve daha çok yapısal anomaliler olarak bildirilmektedir. Bardet-Biedl sendromunda mortalitenin sıklıkla böbrekle ilgili komplikasyonlarla ilişkili olduğu bilinmektedir. Daha önceden bildirilmemiş olan fokal segmenter glomerulosklerozis gibi fonksiyonel bir böbrek tutulumunu göstererek, proteinüri ve ödemle başvuran bu hastalarda böbrek biopsisi yaparak patolojinin erkenden ortaya konulmasının ve etkin tedavisinin hastalığın prognozu açısından önemini vurgulamak amacı ile bu vakamızı sunmayı uygun bulduk. *Turk Jem 2008; 12: 32-4*

Anahtar kelimeler: Bardet-Biedl sendromu, çocukluk çağı, fokal segmental glomerulosklerozis, böbrek

Introduction

Bardet-Biedl syndrome (BBS) is a genetic autosomal-recessive disease formerly grouped with Laurence-Moon-Biedl syndrome but today considered a separate entity. BBS is characterized by abdominal obesity, mental retardation, dysmorphic extremities (syndactyly, brachydactyly, or polydactyly), retinal dystrophy or pigmentary retinopathy, hypogonadism or hypogenitalism (in males), and kidney involvement (1). The frequency of BBS is reported as 1:160,000, with renal involvement in 90% to 100% of these patients (2). Patients with renal involvement may present with both structural and functional abnormalities; however, structural abnormalities are more commonly seen (3).

In this article, we present a 15-year-old male with BBS who has both fetal lobulation, with a reported rate of 12%, and focal segmental glomerulosclerosis, having not been reported before.

Case report

A 15-year-old male was hospitalized with headache, impairment of visual acuity, oliguria, and periorbital edema. His birth weight was 2500 g, and his parents were first-degree relatives. The patient's overeating began at the age of 1 year, and he was always heavier than children in his age group. He began walking at 2 years of age, and his visual impairment was recognized at 3 years of age. His parents reported that he had an older brother who had 6 toes on each foot and who died as a result of renal insufficiency at 3 years of age.

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On physical examination it was noted that the patient had mental-motor retardation and abdominal obesity. His body weight was 89 kg (>97th percentile), his height was 168 cm (50th percentile), and his body mass index was 36.4 (>97th percentile). His blood pressure was 160/100 mmHg (>99th percentile), and his heart rate was 96 beats/min. Strabismus was present, and fundoscopic examination revealed retinitis pigmentosa. He was found to be prepubertal on genital examination, with small testes (3 cm3) and micropenis. The patient also had 6 fingers on each hand and 6 toes on each foot.

The patient's laboratory test results are shown in Table 1. In addition, serum protein electrophoresis revealed the following levels: albumin, 47.9%; a1, 2.8%; a2, 14.2%; b, 9.2%; and g, 25.9%. Urine protein electrophoresis revealed the following levels: albumin, 83.5%; a1, 3.6%; a2, 1.8%; b, 6.6%; and g, 4.5%. The right kidney measured 12 cm x 6.8 cm, and the left kidney measured 13.5 cm x 5.7 cm; each was large, had a lobulated appearance, and exhibited hyperechoic parenchyma on urinary Doppler ultrasonography.

Because of all of these findings, it was thought that the patient had BBS and nephrotic syndrome. Thus a renal biopsy was performed. Of the nine glomerules obtained on biopsy, one glomerule had total sclerosis and three glomerules had focal capsular adhesion. An increase in mesangial matrix and cellularity and partial glomerular basement membrane thickening were noted (Figures 1a and 1b). Deposition of IgM and C3 (+) was seen on immunofluorescent examination. A significant loss of podocytes was detected on electron microscopic examination.

Table 1. Laboratory test results

Test	Value
Complete blood count	Normal
Fasting serum glucose	86 mg/dL
Insulin	49.5 mIU/mL
HOMA-IR index*	10.5
Blood urea nitrogen	10 mg/dL
Creatinine	0.87 mg/dL
Uric acid	8.2 mg/dL
Total protein	5.3 g/dL
Albumin	2.2 g/dL
Total cholesterol	238 mg/dL
Triglycerides	294 mg/dL
Urine density	1015
pH	6
Protein	+++
Hematuria	Not present
Protein excretion in 24-h urine	75 mg/m^2/h

*The homeostasis model assessment–insulin resistance (HOMA-IR) index is calculated as follows: fasting insulin concentration (mU/mL) x fasting glucose concentration (mmol/L)/22.5. The normal value is < 4.5.

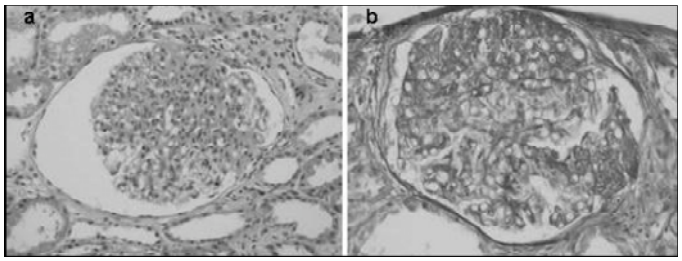

Figure 1. a. Increased mesangial matrix and adhesion of glomerular tuft to Bowman's capsule (HE, x200). **b.** Segmental sclerosis involving the periphery in one glomerulus (PAS, x200).

The patient was restricted to a 1500-kcal low-sodium diet and given metphormin. An angiotensin-converting enzyme inhibitor (ramipril 6 mg/m^2/d) and an angiotensin receptor blocker (losartan 0.75 mg/kg/d) were started as antihypertensives. After these therapies brought the patient's serum glucose levels and blood pressure under control, oral prednisolone was begun according to the classic protocol for treatment of nephrotic syndrome at a dosage of 2 mg/kg/d for focal segmental glomerulosclerosis. The patient is still on these treatments and is being followed by a pediatric nephrologist and an endocrinologist. The patient's blood pressure is within normal limits and proteinuria is not present.

Discussion

The BBS is a significant genetic cause of chronic and end-stage renal failure in children. Despite being a relatively rare recessive condition, BBS has come to prominence during the past few years owing to revelations of primary cilia dysfunction underlying pathogenesis. The study of this multi-system disorder, which includes obesity, cognitive impairment, genitourinary tract malformations and limb deformities, is beginning to reveal insights into several aspects of mammalian development and organogenesis. Involvement of BBS proteins in disparate pathways such as the noncanonical Wnt and Sonic Hedgehog pathways is highlighting their interplay in disease pathogenesis. The precise role of BBS proteins in renal pathogenesis is unclear. It is possible that BBS proteins are involved in the transport of proteins such as the polycystin ion channels and polaris to the distal end of the cilium, where they function as components of the sensory apparatus (4).

However, only 40-45% of major findings of Bardet-Biedl syndrome can be observed at the same time in any particular patient (5). In our case; polydactyly, obesity, learning disabilities, hypogonadism, renal abnormalities and eye involvement were present and detected at the age of 15.

As it has an adverse prognosis with an early onset of blindness, associated findings of the metabolic syndrome and increased vascular risk, and severe renal impairment, BBS, which should be promptly identified by the ophthalmologist, endocrinologist and nephrologists, is a rather rare and severe syndrome and often mis- or undiagnosed (6).

Renal failure is the major cause of morbidity and early mortality in BBS patients (7). A wide range of renal abnormalities has been described, with one study (8) showing 100% of subjects affected. These were the same patients as described by Green et al. (3) and the high frequency may perhaps represent a sampling bias since they were ascertained through a nephrology department. Characteristic cystic tubular disease, lower urinary tract malformations, chronic glomerulonephritis and defects of tubular concentrating ability are among the commonest causes of renal impairment (8). Beales et al. (2) reported structural abnormalities of kidneys as renal parenchymal cysts/communicating calyceal cysts (10%), calyceal clubbing and blunting (10%), fetal lobulation (12%), scarring (12%), dysplastic kidneys (5%), unilateral agenesis (4%), renal calculi (2%), vesicoureteric reflux with pyelonephritis (9%),

bladder obstruction (4%), hydronephrosis (4%), horseshoe kidney (2%), and ectopic kidney (2%). Matsukura et al. (9) reported acute poststreptococcic glomerulonephritis in a 12 years old Bardet-Biedl patient. The presence of diverse data about the ratio of renal involvement and components may be related to inadequate nephrologic evaluations in these patients. Urinary US can be sufficient for detection of many structural renal abnormalities, but performing advanced techniques such as IVP, CT, MR urography, renal scintigraphy, renal biopsy and other necessary examinations for functional abnormalities can influence the ratio and quality of renal involvement.

In this particular case, FSGS has been detected with renal biopsy in addition to detection of fetal lobulation in US. We wanted to present this case as he had all of the primary criteria of Bardet-Biedl syndrome during childhood period with both structural and functional abnormalities of kidneys, having not been reported before.

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