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Obesity control and low protein diet preserve or even improve renal functions in Bardet-Biedl syndrome: A report of two cases

Erkan Dervisoglu^{1ABDEF}, Serkan Isgoren^{2BF}, Derya Kasgari^{3BF}, Hakan Demir^{2BD}, Ahmet Yilmaz^{1D}

¹ Department of Nephrology, School of Medicine, Kocaeli University, Kocaeli, Turkey

² Department of Nuclear Medicine, School of Medicine, Kocaeli University, Kocaeli, Turkey

³ Department of Internal Medicine, School of Medicine, Kocaeli University, Kocaeli, Turkey

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Summary

Background:

Bardet-Biedl syndrome (BBS) is a rare autosomal-recessive disorder characterized by abdominal obesity, mental retardation, dysmorphic extremities, retinal dystrophy, hypogonadism, and kidney structural abnormalities or functional impairment. It is now considered a significant cause of chronic and end-stage renal disease in children. To the best of our knowledge there have been no previous studies on the role of diet in the management of renal functions in patients with BBS.

Case Reports:

Two siblings, aged 32 and 27 years, with BBS are presented. On admission both patients were obese, with body mass indexes (BMI) of 40 and 39 kg/m². Their creatinine clearances (CrCl) were 41 and 24 mL/min. After 2 years of follow-up with a diet consisting of 0.6 g/kg/day protein and 1400 kcal/day energy, their BMI's were decreased to 29 and 27 kg/m², whereas their CrCl's were increased to 44 and 32 mL/min, respectively. ^{99m}Tc-MAG3 scintigraphy also revealed improved renal function.

Conclusions:

Since this syndrome most likely results in end-stage renal disease, follow-up of renal dysfunction is essential. Low protein diet and/or obesity control may slow the progression of renal failure in patients with BBS.

key words:

Bardet Biedl syndrome • chronic renal failure • low protein diet • obesity control

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Author's address:

Erkan Dervisoglu, Department of Nephrology, School of Medicine, Kocaeli University, 41380, Kocaeli, Turkey, e-mail: dervisoglu@yahoo.com

BACKGROUND

Bardet-Biedl syndrome (BBS) is a rare autosomal-recessive disorder characterized by abdominal obesity, mental retardation, dysmorphic extremities (syndactyly, brachydactyly or polydactyly), retinal dystrophy or pigmentary retinopathy, hypogonadism or hypogonitalism (limited to male patients), and kidney structural abnormalities or functional impairment [1]. Its reported prevalence is 1/100,000, with a predicted heterozygote frequency of 1/160. Beales et al. reported an increased risk of renal agenesis and renal cancer among heterozygous carriers of a BBS mutation, although this finding was not supported by a very recent study [2,3]. In the last 2 decades renal impairment has been recognized as an important feature of BBS [4,5]. It is now considered a significant cause of chronic and end-stage renal disease (ESRD) in children [6].

To the best of our knowledge there is no data about the role of diet on the management of renal functions in patients with BBS. We report 2 patients with BBS whose renal functions were improved by low protein diet and obesity control at 2-years follow-up.

CASE REPORTS

The first patient, a 32-year old female patient with a history of BBS, was referred to our unit for renal function impairment on June 2005. She was born to healthy consanguineous parents and diagnosed with BBS on the basis of obesity, polydactyly (hexadactyly of the right hand, in which a 6th digit was surgically excised), slight mental retardation, hypogonitalism (hypoplastic uterus and vaginal aplasia) and visual loss since age 5. She was obese on admission, with a body mass index (BMI) of 40 kg/m², and her blood pressure was 110/70 mmHg. Blood results were as follows: Hgb 14 g/dL, serum creatinine 1.5 mg/dL (ref. 0.7–1.3), and blood urea nitrogen 19 mg/dL (ref. 7–25). Urinary analysis showed a

specific gravity of 1.007, and was negative for protein. Renal ultrasound showed small kidneys with increased echogenicity. Her creatinine clearance (CrCl) was 41 mL/min. with a daily urinary protein excretion of 300 mg.

The second patient, the 27-year old sister of the previous patient, was referred to us at the same time for renal function impairment. She also was diagnosed with BBS on the basis of polydactyly (hexadactyly of both hands and feet, in which all extra digits were surgically excised), slight mental retardation, and visual loss since age 1. At age 11, she was also detected to have hypogonitalism (hypoplastic uterus). She too was obese on admission, with a BMI of 39 kg/m², and blood pressure 110/80 mmHg. Blood results were as follows: Hgb: 13.8 g/dL, serum creatinine 2.4 mg/dL, and blood urea nitrogen 35 mg/dL. Urinary analysis showed a specific gravity of 1005, and was negative for protein. Renal ultrasound showed small, slightly hyperechoic kidneys with parenchymal cysts of a maximal diameter of 13 mm. Her CrCl was 24 mL/min, with a daily urinary protein excretion of 198 mg.

In both patients ^{99m}Tc-MAG3 scans were performed to evaluate the severity of renal function loss. In patient 1, ^{99m}Tc-MAG3 scan revealed slightly decreased perfusion, extraction and excretion of the radioactive tracer (Figure 1A). In patient 2, ^{99m}Tc-MAG3 scans also showed poor perfusion, decreased and delayed radioactive tracer accumulation, as well as poor excretion (more severe than that of patient 1) (Figure 2A). Both patients were diagnosed with chronic kidney disease (CKD) based on glomerular filtration rate, and were put on a diet of daily protein intake of 0.6 g/kg and daily energy intake of 1400 kcal. Compliance to the diets was very good after a period of training, and they never missed an appointment.

At the end of the 2 years follow-up, on June 2007, the BMI of the first patient decreased to 29 kg/m², and daily protein

Figure 1. ^{99m}Tc-MAG3 renal scintigraphies of patient 1 at 2005 (A) and at 2007 (B).

Figure 2. ^{99m}Tc-MAG3 renal scintigraphies of patient 2 at 2005 (A) and at 2007 (B). Note that at the end of the 2-year follow-up both renal scintigraphies show an improvement of the peak time and a significant improvement in the transit and excretion of the radionuclide in both kidneys (especially in patient 2).

excretion decreased to 182 mg, and CrCl increased to 44 mL/min. The BMI of the second patient decreased to 27 kg/m², daily protein excretion decreased to 82 mg, and CrCl increased to 32 mL/min. The ^{99m}Tc-MAG3 scans were repeated to evaluate the status of renal functions. In patient 1, the scintigraphy revealed a mild improvement in the perfusion, extraction, and excretion capability of both kidneys (Figure 1B). In the second patient, the control scintigraphy revealed significant improvement in the perfusion, extraction, and excretion capability of both kidneys (Figure 2B).

DISCUSSION

Here, for the first time, the improvement of renal functions by low protein diet and obesity control is reported in 2 siblings with BBS. This is also the first imaging demonstration of the clinical response to low-protein diet and obesity control therapy in 2 cases with BBS, demonstrating the potential of ^{99m}Tc-MAG3 renal scintigraphy in the follow-up of this disease.

Renal structural and/or functional abnormalities not only constitute one of the principal manifestations of BBS; renal impairment is frequent and an important cause of death, which contributes to the substantially reduced survival [7]. The renal structural and functional abnormalities in BBS include: renal parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, dysplastic kidneys, unilateral agenesis, vesicoureteral reflux, hypertension, chronic renal insufficiency, end-stage renal disease, urinary concentration defects, and renal tubular acidosis [6,7]. Both patients presented here had atrophic kidneys with increased echogenicity, and 1 also had renal parenchymal cysts.

In the 2 cases presented, intervention resulted in improvement in renal function. In patients with CKD it is known that low protein diets are associated with slower progression of renal failure, or a delay in the necessity of renal replacement therapy [8]. Low protein diet manifests its effect by ameliorating proteinuria, decreasing workload on the remaining nephrons, reducing oxidant stress, and decreasing insulin resistance [9]. However, there is not sufficient data on the use of low protein diets in patients with BBS. At this point it may be argued that low protein diet is beneficial in patients with BBS, as it is in patients with non-BBS related CKD.

Obesity is a well known feature of BBS [1]. Several abnormalities that can lead to kidney injury have been identified in obese subjects, including insulin resistance, inappropriate

activation of the renin-angiotensin-aldosterone system, as well as increased oxidative stress, coagulability, and impaired fibrinolysis [10]. It has been demonstrated that a higher BMI is also a strong and potentially modifiable risk factor for ESRD [11]. We therefore recommend aggressive obesity control in patients with BBS as well as in non-BBS obese subjects. More clinical studies with additional patients and long-term follow-up are needed to more accurately determine the effect of obesity control on renal functions.

CONCLUSIONS

Since this syndrome most likely results in ESRD, follow-up of renal dysfunction is essential. Low protein diet and/or obesity control may slow the progression of renal failure in patients with BBS.

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