Bardet–Biedl Syndrome: A Rare Cause of Chronic Kidney Disease

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Abstract Bardet-Biedl syndrome (BBS) is a rare autosomal recessive condition characterized by retinitis pigmentosa, postaxial polydactyly, central obesity, and renal involvement. Renal failure is the commonest cause of death. We report a case of BBS with chronic kidney disease (CKD) at younger age (17 year) from India. This diagnosis should be considered in patients with renal disease and the characteristic phenotype of retinitis pigmentosa, postaxial polydactyly and central obesity. These patients should undergo regular monitoring of renal function test to early diagnosis and treatment of CKD to prevent morbidity and mortality. Renal transplantation is a viable option of renal

replacement therapy in these patients. These findings are valuable for comparing phenotype of BBS patients with CKD from various national and international centers.

Keywords Bardet-Biedl syndrome · Chronic kidney disease · Retinitis pigmentosa · Polydactyly · Central obesity

Introduction

Bardet-Biedl syndrome (BBS) is an autosomal recessive condition characterized by rod-cone dystrophy (retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal involvement. It has prevalence of 1 in 1,40,000–1 in 1,60,000 worldwide [1]. Renal involvement in the form of various structural and functional abnormalities is common and renal insufficiency is noted in ~5–25 %, with progression to end-stage renal disease (ESRD) in 4–10 %. ESRD in BBS patients is the final stage of the disease, increasing mortality in youth. Renal insufficiency is noted in ~5–25 %, with progression to ESRD in 4–10 %. ESRD is the most common cause of death in BBS [1]. Only few reports have been described from India regarding ESRD/chronic kidney disease (CKD) in BBS [2–5]. Herein, we report a case of BBS with CKD in a 17 year female from India.

Case Report

A 17 year old female presented for evaluation of altered renal function test at our institute. She was born to non-consanguineous parents in 1995 with low birth weight. Her parents noticed progressive decline in vision since

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childhood, presently she developed retinitis pigmentosa with impaired vision since 4 years (WHO category 3 visual impairment). She had no major illness in childhood but had polyuria and polydipsia. She had delayed milestones. She is not a known diabetic/hypertensive. Attained menarche at the age of 13 years and had irregular menstrual history. Scholastic performance was average and educated till tenth standard.

On Examination, she has central obesity (Fig. 1), pallor, polydactyly (upper and lower limb) (Figs. 2, 3). She had no dental anomalies or high arched palate, cardio respiratory and abdominal examination does not reveal any abnormalities. Her vital sign were normal, blood pressure, 110/70 mmHg; weight 69 kg; height 145 cm; and body mass index, 32.8 cm/kg.

Laboratory investigations revealed hemoglobin, 10.6 gm/l; total white cell count, $13.6 \times 10^3/\mu\text{l}$ (differential count: 70 % neutrophils, 25 % lymphocytes, 2 % monocytes, and 2 % eosinophils); platelet count, $317 \times 10^5/\mu\text{l}$; pack cell volume, 33.5 %; serum total protein, 7 gm/dl; serum albumin, 4 gm/dl; serum urea, 41 mg/dl; creatinine, 3.37 mg/dl [Modification of Diet in Renal Disease

Fig. 1 Showing truncal obesity

Fig. 2 Showing polydactyly in lower limb

Fig. 3 Showing polydactyly in upper limb

Fig. 4 Showing visual impairment

(MDRD) Study glomerular filtration rate (GFR) value based on 4 variables (age, race, gender, plasma creatinine), 18 ml/min/1.73 m²; sodium 142 meq/l; potassium 4.2 meq/l; calcium, 10 mg/dl; phosphorus, 6.7 mg/dl; and uric acid (8 mg/dl). Urine examination showed +1 albumin; specific gravity 1.003 and fasting blood glucose, lipid profile, liver profile were normal. The tests for antinuclear antibody (ANA), anti-double-stranded deoxyribonucleic acid, anti-neutrophil cytoplasmic antibody (c-ANCA/p-ANCA), were all negative and complement components (C3 and C4) were normal. Enzyme-linked immunosorbent assays test for human immunodeficiency virus, hepatitis B surface antigen and hepatitis C virus were negative. Fundus examination revealed rod-cone dystrophy (Retinitis Pigmentosa), Fundus image and tomogram done for impaired vision is shown in Figs. 4 and 5.

The ultrasonography of abdomen revealed bilateral contracted kidneys and ovaries are/uterus was normal. Cardiac evaluation echocardiography/electrocardiogram was normal. Hearing evaluation was normal. She is known case of hypothyroid and on tablet levothyroxine sodium, 125 microgram. Her thyroid function tests were normal

Fig. 5 Showing fundus image and tomogram of retinitis pigmentosa

[TSH, 3.5 (normal range, 0.27–4.2 mIU/l); T4, 136 (normal range, 66–181 nmol/l); T3, 1.8 (normal range, 1.3–3.1 nmol/l) (COBAS chemiluminescence)]. MRI brain and pituitary was normal. Urine examinations for mucopolysaccharides were negative. Chromosomal study from whole blood revealed 46 XX karyotype. With all the above clinical and laboratory finding it was diagnosed as BBS with CKD. Blood group of patient was A negative. She is under preparation for renal transplantation with her 35 year mother as donor with blood group O.

Discussion

On the basis of a review of 109 cases, Beales et al. [1] suggested following the diagnostic criteria for BBS; Major features included retinal dystrophy (>90 %), post axial polydactyly (21 %), truncal obesity (72 %), hypogonadism (more frequent in males), renal anomalies, chronic renal failure (30–60 %), hypertension (50–66 %). Minor features included learning disabilities, speech delay, developmental delay, behavioural abnormalities, Eye abnormalities, brachydactyly/syndactyly, ataxia, mild hypertonism, diabetes mellitus, orodental abnormalities, cardio vascular anomaly, anosmia. Four major or three major and 2 minor criteria are required for diagnosis.

So far, very few cases have been reported from India, of which only 3 had CKD. Somwanshi et al. [4] reported four cases with the typical phenotypic features of BBS in 1988. Pal et al. and Maheshwari et al. [5, 6] reported five case reports and all had normal renal function. Gupta et al. [3] reported the first case of BBS from India with renal insufficiency (creatinine 3.0 mg/dl) in a 20-year-old female who had bilateral hypoplastic kidneys on ultrasound and also had multiple fractures, possibly related to renal osteodystrophy. Hooda et al. [7] reported the first case from India who has

undergone successful preemptive living-related renal transplantation with 38 year old mother as the donor in BBS with stage III CKD in a 12-year-old male child presented with obesity, polydactyly, retinitis pigmentosa and hypogonadism. Investigations showed blood urea nitrogen 43 mg/dl, creatinine 4.3 mg/dl with normal echocardiography, Ultrasound showed small kidneys (right 6.3 cm, left 6.7 cm) with loss of cortico-medullary differentiation, mild cortical irregularity diethylene triamine pentaacetic acid (DTPA) scan showed bilateral impaired renal function (GFR right kidney 16.1 ml/min, left kidney 15.8 ml/min, and total GFR 31.9 ml/min). He was started on conservative management and underwent amputation of extra digits of hands. He progressed to ESRD in 1 year [creatinine, 11 mg/dl and calculated GFR of 5.68 ml/min]. Fourteen months post-transplantation, he was asymptomatic with creatinine of 1.1 mg/dl, and DTPA scan GFR of graft kidney of 56.3 ml/min. His maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil, and prednisolone. Ersoy et al. reported a 20-year-old patient in whom primary central nervous system lymphoma was diagnosed 20 months after renal transplantation. Although a few patients with BBS have been described to develop malignant disease, there was no previous association with lymphoma [8]. Pal et al. [5] has reported an 18-year-old female with pigmentary retinopathy, hypogonadism, dwarfism, polydactyly, obesity, and mental retardation, but without renal involvement. Prakash [9] reported cysts in the left kidney with normal renal functions, in a 30-year-old patient. Gupta et al. [3] reported of BBS in a 20-year-old female with serum creatinine of 3 mg/dl and ultrasonography finding of bilateral hypoplastic kidneys and multiple fractures, possibly related to renal osteodystrophy. Jethani et al. [10] reported BBS in a seven-year-old boy presented with impaired vision and multiple systemic anomalies including facial asymmetry, ventricular septal defect, polydactyly and

hypospadias with mental retardation. The diagnosis of the BBS is often delayed until about 9 years of age when visual problems first appear [11]. BBS was reported in an 11 year boy presented with complaint of excessive weight gain along with central obesity, postaxial polydactyly, mental retardation [IQ, 55], retinitis pigmentosa, hypogonadism, functional renal impairment [proteinuria] and nonalcoholic steatohepatitis. He was prescribed glasses, advised for fat and refined carbohydrate-restricted diet and exercise with careful monitoring for hypogonadism [12]. Dilated cardiomyopathy was incidentally diagnosed during surgical treatment for lower limb fracture in BBS patient [13]. Rath et al. [14] described the first case from India with ESRD who was treated with continuous ambulatory peritoneal dialysis (CAPD). Sowjanya et al. [2] reported a 16 year old female with ESRD. Prakash [9] reported another 30-year-old patient with BBS who had cysts in the left kidney with normal renal function. ESRD in BBS patients has been reported at age range of 4–57 years [2–5, 15–19].

Management of BBS is supportive and includes training and rehabilitation for blind and mentally retarded patients, hearing aids for deafness, and diet and exercise for obesity. Organizations such as the Foundation Fighting Blindness and the Laurence-Moon-Bardet-Biedl Society provide emotional and social support and help in all-round development. Early and regular screening for hypertension, diabetes, and renal involvement is required.

The management of renal failure in BBS does not differ from that due to any other cause and all three modalities of long-term renal replacement therapy (RRT), i.e., hemodialysis, CAPD, and renal transplantation can be offered to these individuals. Still, it represents a very rare indication for kidney transplantation [7, 8, 15]. Renal transplantation is a viable option of renal replacement therapy in these patients. Genetic counseling is advised for affected individuals. With regard to genotype-phenotype correlation, patients with a mutation in the BBS6, BBS10, or BBS12 gene (10 of 33 patients) had more severe renal disease [8]. Still, it represents a very rare indication for renal transplantation [8, 15, 16]. Such renal transplant patients are known to be at increased risk for the development of severe obesity, malignancies and cardiovascular complications after transplantation [17].

Conclusion

We report a case of BBS with CKD in a 17 year female from India. This diagnosis should be considered in patients with renal disease and the characteristic phenotype of retinitis pigmentosa, postaxial polydactyly and central obesity. Renal involvement is common and renal failure is most common cause of death in BBS. These patients should

undergo regular monitoring of renal function test to early diagnosis and treatment of CKD to prevent morbidity and mortality. Renal transplantation is a viable option of RRT in these patients. These findings are valuable for comparing phenotype of BBS patients with CKD from various national and international centers.

Disclosure Informed written permission and ethical clearance taken from patient to publish case data and photograph.

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