A Rare Disease with Rarer Presentation: A Case of Bardet-Biedl Syndrome Presented as End Stage Renal Disease Due to Glomerulonephritis

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Abstract

Background: Bardet-Biedl Syndrome (BBS) is an autosomal recessive disease resulting from non-motile ciliopathyand presents with obesity, retinal abnormality, polydactyly, mental retardation, and genital abnormality. Renal involvement is not a frequent feature. The purpose of the study to reminding readers of this issue and emphasize the necessity for further research on how to deal within the best way.

Case Presentation: A 17-year-old patient was admitted on 20th August 2023 at the Department of Nephrology, Chittagong Medical College Hospital, Chattogram with the features of BBS. According to clinical features and supportive investigation, he was diagnosed with Acute Kidney Injury (AKI) on Chronic Kidney Disease (CKD). The cause of CKD was probably due to Glomerulonephritis (GN). Renal replacement by hemodialysis was started along with other supportive medications.

Conclusion: Bardet-Biedl syndrome is a non-curable disease, which may present with end stage of renal disease.

Key words: Bardet-Biedl Syndrome, End stage renal disease, Glomerulonephritis.

Introduction

In 1920, French physician Georges Louis Bardet made the first reference to BBS. In 1922 Hungarian-Austrian pathologist Artur Biedl also described the disease and later the disease was named after their surname.[1,2] There is variation in the prevalence of BBS. Patients with BBS typically have an incidence of 1 in 140,000 to 1 in 160,000 over much of North America and Europe. The syndrome is more prevalent in the Bedouin community of Kuwait (1:13500 babies) and on the Canadian island of Newfoundland (1: 17000 infants).[3,4] It is a non-motile ciliopathy and an autosomal recessive genetic condition.[5] The majority of the twenty-two genes that have been identified are the cause of ciliary dysfunction.[6] Retinal dystrophy is the most prevalent characteristic of BBS patients and by the time they reach their third decade of life, nearly all of them have legal blindness. The second most prevalent characteristic among BBS patients is obesity, which typically starts very early around 2-3 years of age. Commonly observed limb malformations include polydactyly, brachydactyly, a noticeable space between toes, syndactyly and clinodactyly in the fifth finger.[5,7] BBS patients experience learning challenges and intellectual incapacity; this decline in IQ is always linked to visual impairments.[8] Males are mostly affected and they have genital anomalies, primarily hypogonadism, as well as micropenis, cryptorchidism and short scrotum.[9] First reports of BBS involvement in the kidneys were made in 1980.[9,10] Less than 1% of BBS patients have aberrant urine sedimentation.[11] It is seen usually in the second decade of life. The most common forms of renal involvement include ultrastructural alterations in the glomerular basement membrane, chronic interstitial nephritis and Membrano-proliferative Glomerulonephritis (MPGN).[12] Patients may present with different histological patterns of renal involvement, such as unilateral renal agenesis, renal cysts, lobulation, scarring, dysplastic kidneys and vesicoureteral reflux.[5] The purpose of the study to disseminated our knowledge and experience of clinical characteristics, presentation and treatment about this issue for the readers as future references.

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Case Presentation

A male, aged 17 years was admitted on 20th August 2023 at the Nephrology Inpatient Department of

Chittagong Medical College Hospital with complaints of severe anorexia and vomiting, scanty micturition for 4 months and multiple abscesses on different parts of the body with altered level of consciousness for 2 days.

Acute Kidney Injury (AKI) from sepsis on Chronic Kidney Disease (CKD) and uremic encephalopathy were found after an initial examination. His prior medical history includes central obesity and extra digits on both hands and feet. His mother said that he had missed developmental milestones, started to walk and speak at 4 and 5 years old, respectively. Later, he was enrolled in school, but his learning disabilities and subpar performance prevented him from keeping up with his year mates. He used to have a very good appetite but he was severely anorexic over the last 4 months and lost at least 10 kilograms (kgs) of weight. He is the first child of his parents who had a consanguineous marriage. His birth was uneventful via normal vaginal delivery. To his parents' knowledge to particular disease runs in their family. He has two sisters both of them are in good health. During admission, his vital signs showed that his blood pressure was 90/60 mmHg, his oxygen saturation was 92% on room air, his GCS was 11/15 (E3V3M5) and he was confused. He had bilateral moderate pitting pedal edema and was critically anemic. Auscultation of the chest revealed bilateral basal crepitation. His height was 4'3" and his weight was 45 kg. He had upper and lower limb postaxial polydactyly (Figures 1 & 2). His Body Mass Index (BMI) was 26.82 kg/m2. According to the Wechsler Intelligence Scale for Children, he had an IQ of 60. He had tinea corporis and many abscesses on his left arm, abdomen and right thigh. Other systematic analyses yielded no noteworthy results.

Table I Investigation results

Test	Result	Reference
Hemoglobin	5.5 g/dL	13.5–17.5 g/dL in male
Serum creatinine	16.2 mg/dL	0.6–1.2 mg/dL
Estimated glomerular filtration rate (eGFR)	4.22 mL/min/1.73m^2	90 to 120 mL/min/1.73m^2
Blood urea	170 mg/dL	7–18 mg/dL
S. Sodium	133 mEq/L	135–145 mEq/L
S. Potassium	4.2 mEq/L	3.5–5.0 mEq/L
HCO3	23 mEq/L	22–28 mEq/L
S. Calcium	7.1 mg/dL	8.4–10.2 mg/dL
Inorganic phosphate	6.4 mg/dL	3.0–4.5 mg/dL
Urine analysis	Albumin ++,	
	red blood cell 8-12/hpf	
	no cast	
S. testosterone	2.3 nmol/l	10–35 nmol/L
		during puberty in male
HBsAg	Negative	
Anti HCV	Negative	
S. TSH	1.26 IU/ml	0.5–5.5 IU/mL
RBS	4.6 mmoL/L	<7.8 mmoL/L
Electrocardiogram (ECG)	Sinus tachycardia	
Echocardiogram	ASD secundum with	
	left to right shunt	
USG of whole abdomen	Both kidneys are small	
	with increased echogenicity	
	and lost CMD (Right kidney	
	6 cm, left kidney 3.8 cm	
	along with cortical scarring) Cystitis.	

Investigations were suggestive of normocytic normochromic anemia, severe renal impairment and dyslipidemia. Ultrasonography of the whole abdomen revealed both kidneys are small with increased echogenicity and lost CMD (Corticomedullary Differentiation) (Right kidney 6 cm, left kidney 3.8 cm along with cortical scarring) and cystitis. Retinitis pigmentosa was found in color fundus photography. His hormone analysis showed low testosterone which is most likely due to secondary hypogonadism We couldn't do comprehensive genome sequencing, as it was not currently available at our hospital.

Based on the clinical features and investigations, we diagnosed the patient as a case of BBS with End-Stage Renal Disease (ESRD) due to GN. According to Forsythe and Bealesscore to diagnose BBS he had five primary features as well as three secondary features.[13] Moreover, the patient had anemia, raised serum creatinine, uremia, small-size kidney, hematuria and sub-nephrotic proteinuria which were the features of ESRD due to GN. Renal Replacement Therapy (RRT) was initiated urgentlyin our nephrology department along with Intravenous antibiotics and regular dressing was done. He responded well after initiation of treatment and his GCS and overall clinical parameters improved. We advised him to continue hemodialysis at least twice weekly. Further genetic counseling and patient education about this condition were alsoexplained to the guardians. The patient was askedfor regular

follow up at our Nephrology department for early diagnosis and prompt treatment of the disease complications as much as possible.

Figure 1 upper limb postaxial polydactyly

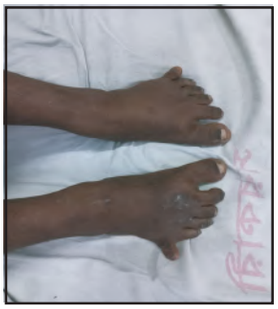

Figure 2 Lower limb postaxial polydactyly

Discussion

GN in BBS is an uncommon manifestation and ESRD can occur due to GN, structural abnormality in the kidney and other tubulo-interstitial disease especially abnormality in concentrating ability of the kidney.[14,15] This patient presented with uremic encephalopathy due to acute kidney injury and he had no previous diagnosis of BBS. Laboratory findings showed hematuria and sub nephrotic range proteinuria, which was most likely to be due to chronic glomerulonephritis. However, ultrasonography suggested this case as CKD. A Renal biopsy could not be done due to small size kidney. Ophthalmological assessment of the patient showed retinitis pigmentosa, and he had gross visual disturbance which occurs in BBS due to rod-cone dystrophy.[5] Although our patient had classic clinical features of BBS, he didn't seek medical advice till now and remained undiagnosed.[13]As a result, multiple complications arose due to this delay. Consanguineous marriage between parents is considered as a risk factor for BBS and it was present in this patient.[16] Genetic testing is required to confirm the diagnosis of BBS but could not be done as it is not readily available in Bangladesh. ESRD in BBS was reported previously but it was an uncommon phenomenon.[17,18] No definitive treatment is identified for BBS and only a supportive approach is followed while treating such patients.[5] ESRD patients can be treated by any modalities of renal replacement therapy like hemodialysis, peritoneal dialysis and kidney transplanatation.[19]

Limitations

Renal biopsy could not be done to identify specific GN. Genetic testing could not be performed.

Conclusion

BBS is a non-curable genetic disease, which may present with ESRD. This patient presented with features of BBS and ESRD. ESRD was probably due to GN. As there is no specific management, supportive management like hemodialysis was started.

Recommendation

Early diagnosis of BBS should be done. Frequent followups and supportive management of kidney disease are needed to reduce progression to ESRD.

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Contribution of authors

TR-Conception, data collection, critical review & final approval.

SH-Design, drafting, citing references & final approval.

MNH-Critical review, citing references & final approval.

Disclosure

All the authors declared no conflict of interest.

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