Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublisher.com

Paediatrics

Bardet-Biedl Syndrome- A Case Report

Dr. Suraiya Begum[1*], Dr. Md. Benzamin[2], Dr. Muhammad Rezaul Karim[3], Dr. Abul Bashar Md Osman Hayder Mazumder[4]
[1]Associate Professor, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh
[2]Resident, Department of Paediatric Gastroenterology Bangabandhu Sheikh Mujib Medical University, Bangladesh
[3]Resident, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh
[4]Resident, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh

Case Report

***Corresponding author**
Dr. Suraiya Begum

Article History
Received: 14.07.2018
Accepted: 28.07.2018
Published: 30.07.2018

DOI:
10.21276/sjams.2018.6.7.51

Abstract: Bardet-Biedl syndrome (BBS) is a rare ciliopathic autosomal recessive genetic disorder. It presents with varied clinical manifestations like retinitis pigmentosa, polydactyly, central obesity, mental retardation and renal dysfunction. Other rare manifestations include diabetes mellitus, heart disease, hepatic fibrosis and neurological manifestations. Most of these symptoms may not be present at birth but appear and progressively worsen during the first and second decades of life. We, here, have presented a 4-year-old girl with features of Bardet-Biedl syndrome.
Key-wards: Bardet-Biedl syndrome, Retinitis pigmentosa, Polydactyly, Obesity, Diabetes mellitu,
Abbreviations: BBS- Bardet-Biedl syndrome.

INTRODUCTION

Bardet-Biedl syndrome (BBS) is a rare genetic disorder with severe multi-organ impairment. Its frequency in Europe and North America is 1: 100,000 [1]. The incidence is much higher in some populations with a high level of consanguinity or those that are geographically isolated. Disease incidence of 1 in 3700 in the Faroe Islands and 1 in 17,000 live births in Kuwait [2]. Male to female ratio is approximately 1.3: 1 [3]. In Bangladesh, the actual prevalence rate is unknown. Mutations in at least 21 BBS genes have been identified as causative factors [4].

CASE REPORT

A 4-year-old girl, 3rd issue of consanguineous parents, admitted on October 2016 in the paediatric ward of Bangabandhu Sheikh Mujib Medical University with the complaints of excessive weight gain since 1 year of age and no micturition control yet.

On query, mother also gave history of polyphagia, polyuria, polydipsia, and poor vision. There was no history of constipation, palpitations, hearing impairment, breathing difficulty, dental problem, and limb weakness. She was delivered by caesarean section at term due to maternal gestational diabetes mellitus, birth weight was 5 kg. Postnatal history was not significant except for the anomaly of polydactyly in her three limbs. She had no history of developmental delay.

On examination, she had rounded face with double chin, gynecomastia and pendulous abdomen. (Figure 1) Her BP was120/90 mm of hg (Both systolic and diastolic pressure lies above 99th centile). Her weight was 32 kg (above 97th centile), height was 106 cm (in between 75-90th centile) and body mass index was 28.5kg/m2 (above 97th centile). Bedside urine for albumin and sugar was negative. Musculoskeletal system examination revealed postaxial polydactyly in three limbs and short, broad, stubby fingers and toes (Figure 2). She had high arch palate. On eye examination, visual acuity was 6/60 in both eyes. Anterior segment was normal, fundus showed choroidoretinal mild pigmentary changes in both eyes. Psychological evaluation by IBAS showed total score was 25% of 4 year's Assessment. Cardiovasuclar system examination showed no abnormality. Investigations including CBC, urine analysis, ALT, X-ray chest, ECG and echocardiography were normal. Ultrasonography of whole abdomen revealed mild hepatomegaly with fatty change and both kidneys were normal. Hearing assessment was normal. Biochemistry revealed normal creatinine and ALT, raised TG (215 mg/dl; N-32-100mg/dl), and oral glucose tolerance test showed fasting blood sugar was 5.00 mmol/L (N-4-6mmol/l) and 2 hours after glucose intake was

11.3mmol/L (N- <7.8mmol/l). Her serum cortisol level, and thyroid function was normal. We diagnosed the case as Bardet Biedl syndrome as our patient had 3 primary and 3 secondary features. As there is no specific curative therapy available for this syndrome. The girl was managed symptomatically. Genetic counseling was done. The patient was discharged with diabetic diet, antihypertensive drug and regular physical activity, and capillary blood glucose monitoring was advised.

Four primary feature or three primary features and two secondary features are required for a clinical diagnosis of Bardet-Biedl syndrome [1].

Table-1: Diagnostic features of Bardet-Biedl Syndrome

Primary feature	Our case	Secondary feature	Our case
Rod-cone dystrophy (93%)	+	Speech disorder/delay (54-81%)	-
Polydactyly (63-81%)	+	Strabismus/cataracts/astigmatism	-
Obesity (72-92%)	+	Brachydactyly/syndactyly (6-100%/8-95%)	+
Learning disabilities (61%)		Developmental delay (50-91%)	-
Genital anamolies (59-98%)		Ataxia/poor coordination /imbalance (40-86%)	-
Renal anomalies (53%)		Spinal problem	-
		Mild spasticity (especially lower limbs)	-
		Diabetes mellitus (6-48%)	+
		Dental crowding/ hypodontia/ Small roorts/high arched plate (51%)	+
		Congenital heart disease (7%)	-
		Hepatic fibrosis	-
		Anosmia/hyposmia (60%)	

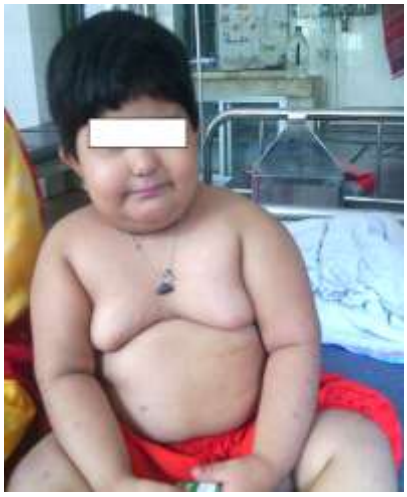

Fig-1: Shows rounded face with double chin, gynecomastia and pendulous abdomen

Fig-2: Shows poly-dactyly of both upper limbs and right lower limb

DISCUSSION

Bardet-Biedl syndrome was named after Georges Louis Bardet, a French physician and Artur Biedl, a Hungarian Pathologist and endocrinologist. It is a genetically determined heterogeneous autosomal recessive condition. At present, there are already 21 known BBS genes *(BBS1–BBS20* and *NPHP1)* and their number is likely to increase due to the invention of exome sequencing and analysis of previously unstudied populations [4]. Among them, BBS1 and BBS10 are the two main genes involved in BBS and each of this gene mutation is present in more than 20% of the cases [5]. The detailed biochemical mechanism that leads to BBS is still unclear. It is caused by defects in the cellular ciliary structure and hence it is a ciliopathy [5]. The first known case was reported by Laurence and Moon in 1886 and there was a controversy in medical literature with the condition described by Laurence and Moon, referred as Laurence-Moon syndrome (LMS). After 22 years, prospective cohort study of Newfoundland families with BBS, Moore et al concluded that BBS and LMS are different spectrum of same entity [6]. BBS is distinguished from the much rarer LMS, in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly [7].

The primary and secondary features of BBS are given in Table I. The diagnosis of BBS can be made if four primary, or three primary and two secondary features are observed [3]. Our patient had retinitis pigmentosa and decreased visual acuity. Retinitis pigmentosa is one of the hallmarks of this disorder and found occasionally in the first decade but usually present in almost all patients by second decade. Decreased visual acuity can result from macular involvement of the disease. The patient was obese with hepatomegaly which was may be due to fatty change of liver. He had dyslipidemia associated with obesity. Obesity present in 75% of patients usually begins in the childhood and the severity increases with age [3]. Cause of obesity is unknown but appears to be the effect of a combination of hyperphagia and altered disposal of calories [3]. Learning disability is a primary feature of BBS, which is probably due to moderate mental retardation and decreased visual acuity, our patient has both mental retardation and decreased visual acuity. Limb deformities have been reported at varying frequencies. Of these, polydactyly, and brachydactyly of both hands and feet are most common [3]. Hypo-genitalism is reportedly more frequently present in BBS males than females [1]. A wide range of renal abnormalities such as chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, and vesico-ureterix reflux has been described but our patient had no renal abnormalities. Renal failure is the major cause of morbidity and early mortality in BBS and 25% die by the age of 44 years [9]. Renal function was found to be normal in our patient. Diabetes mellitus is diagnosed in 32-45% of cases with BBS and it is usually Type 2 but occasionally Type 1 [9]. Our patient had diabetes mellitus and was controlled by dietary measure and physical activity; diabetes mellitus was also observed by Haque M [10]. Hussain et al. reported a case of BBS in our country in a twelve year old boy having all the cardinal features such as obesity, mental deficiency, polydactyly, syndactyly, retinopathy, genital hypoplasia and renal anomalies [11]. Our patient had three primary features such as polydactyly, retinitis pigmentosa, obesity and three secondary features such as diabetes mellitus, brachydactyly, and high arch palate. Some authors also mention hypertension, liver abnormalities, bronchial asthma, otitis, rhinitis, craniofacial dysmorphism [1,12]. Our patient had hypertension treated with antihypertensive drug.

Diagnosis of Bardet-Biedl syndrome is mainly based on characteristic clinical features. Investigations are done to assess the features that may help in the diagnosis. Genotyping of Bardet-Biedl syndrome may not always be required to make the diagnosis as it is not available at all places specially developing countries like Bangladesh. Multidisciplinary approach is needed for management of Bardet-Biedl syndrome. Regular monitoring of renal function, liver function, blood glucose, lipid and endocrine profile is necessary. Attention should be given to blood pressure control and weight management along with regular ophthalmological examination. Visual aids, special schools and educational programs to overcome learning disabilities are important. Speech therapy, behavioral therapy and hormone replacement therapy are required in many cases. Surgical removal of accessory digits may be necessary for cosmetic purpose.

CONCLUSION

Many progresses have been made about this disease. Further studies are needed to understand the pathophysiology and genetic complexity of the disease. Though the disease is incurable, careful evaluation and symptomatic management may provide good prognosis.

ACKNOWLEDGEMENT

We gratefully acknowledge the work of the ophthalmology and neurology department, BSMMU.

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