

## A 13-year-old female with Bardet- Biedl syndrome - A case report

<sup>1</sup> Dr. Syed Nesar Ahmed, <sup>2</sup> Dr. Md Abu Shahin, <sup>3</sup> Dr. Romal Chowdhury, <sup>4</sup> Dr. Md Nahiduzzamane Shazzad, <sup>5</sup> Dr. Md Rafiqul Alam, <sup>6</sup> MA Jalil Chowdhury

<sup>1</sup> Phase-A student, Department of Pulmonology, NIDCH, Dhaka, Bangladesh.

<sup>2</sup> Assistant professor, Department of Rheumatology, BSMMU, Kazi Nazrul Islam Ave, Dhaka, Bangladesh.

<sup>3</sup> Phase-A student, Department of Pulmonology, NIDCH, Dhaka, Bangladesh

<sup>4</sup> Medical officer, Department of Rheumatology, BSMMU, Kazi Nazrul Islam Ave, Dhaka, Bangladesh

<sup>5</sup> Associate Professor, Department of Medicine, BSMMU, Kazi Nazrul Islam Ave, Dhaka, Bangladesh

<sup>6</sup> Professor, Department of Medicine, BSMMU, Kazi Nazrul Islam Ave, Dhaka, Bangladesh

### Abstract

Bardet Biedl syndrome is a rare disease. A case report is presented here where a 13 years old girl presented with obesity, night blindness, learning difficulties and polydactyly. Obesity and night blindness started from since childhood. Her milestones of development were normal but having some learning difficulties. Her parents are healthy as well as her siblings. On examination she looks apathic, extreme obese, having polydactyly and retinitis pigmentosa and high B.P. On laboratory findings there is only dyslipidaemia. On the basis of clinical features she was diagnosed as a case of Bardet-Biedl syndrome.

**Keywords:** Bardet Biedl syndrome, Female child, Normal stature

### 1. Introduction

Bardet Biedl syndrome is a rare autosomal recessive condition with a wide spectrum of clinical features. Bardet-Biedl syndrome (BBS) is characterized by rod-cone dystrophy, truncal obesity, postaxial polydactyly, cognitive impairment, male hypogonadotrophic hypogonadism, complex female genitourinary malformations, and renal abnormalities [1]. The syndrome is named after Georges Bardet and Arthur Biedl [2]. Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder. BBS was first described by Bardet and Biedl in the 1920 [2]. The principal manifestations are rod-cone dystrophy (Retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. Other features like hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dental anomalies and developmental delay are not always present.

The diagnosis of Bardet-Biedl syndrome (BBS) is established by clinical findings. Beales *et al.* [1999] and Beales *et al.* have suggested that the presence of four primary features or three primary features plus two secondary features is diagnostic [3] (Table-1).

**Table 1:** Modified diagnostic criteria<sup>3</sup> (Four features are required to be present or Three primary plus two secondary features are required)

Primary Features
1. Rod-cone Dystrophy
2. Obesity
3. Polydactyly
4. Learning Disabilities
5. Hypogonadism in males
6. Renal Anomalies

Secondary Features
1. Speech disorder/Delay
2. Strabismus/cataracts/astigmatism
3. Brachydactyly/ syndactyly
4. Developmental delay
5. Nephrogenic diabetes insipidus
6. Ataxia/poor coordination/imbalance
7. Mild spasticity
8. Dental crowding/hypodontia/small roots
9. Left ventricular hypertrophy/congenital heart disease
10. Hepatic fibrosis

### 1.1 Case report

A 13-year-old female (Figure-1) was admitted in medicine unit of Bangabandhu Sheikh Mujib Medical University (BSMMU) with the complaints of progressive weight gain and night blindness since childhood. Her parents enrolled her in a school, but she eventually dropped out because of poor learning capability. Her milestones of development were normal. She is the fourth children from a non-consanguineous marriage. Her parents are healthy as well as her siblings. None of her maternal and paternal uncles has such type of problems.

On examination she had apathic, depress look, puffy face, found to be obese with weight 97 kg, height 152cm and a BMI of 41, B.P: 140/85 mmHg, polydactyly on both feet (Figure-2), MMSE score 22 out of 30, IQ 65, retinitis pigmentosa on funduscopy (Figure-3). Other systemic examinations including genital examinations reveals normal. Laboratory examination including complete blood count, OGTT, SGPT, S.Creatinine, S.TSH, FT4, S.prolactin, urinalysis, ultrasonography of whole abdomen were found to be normal except F.lipid profile- S.Cholesterol 224 mg/dl, S.TG- 236 mg/dl, HDL 36 mg/dl and LDL 139 mg/dl.

We ultimately diagnosed the patient as Bardet-Biedl syndrome (BBS) on clinical background.



Fig 1



Fig 2



Fig 3

## 2. Discussion

The syndrome was described by Bardet Biedl in the 1920. It was later erroneously coupled with another disorder described by Laurence and Moon and was consequently referred to as Laurence - Moon-Biedl syndrome. BBS is distinguished from the much rarer Laurence- Moon syndrome, in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness but without polydactyly<sup>[4, 5]</sup>.

The prevalence of BBS is 1:160000 in Europe and North America<sup>[6]</sup> although higher incidence has been reported in the isolated populations of Newfoundland [1:13000]<sup>[7]</sup> and Kuwait [1:17000]<sup>[7]</sup>.

Retinal dystrophy (100%) is the first major feature of the disorder. It is found occasionally in the first decade but present in almost all patients by the second decade<sup>[8]</sup>. The reported case noticed night blindness at the age of 5 years.

Obesity is the second major feature of BBS, with a frequency of 72-96 percent depending on measurement criteria. Obesity usually begins in childhood and the severity increases with age, with the majority of cases exhibiting symptoms within the first year of life<sup>[3]</sup>. Our reported case developed obesity at the age of 4 years.

Limb-abnormalities are the third major feature of BBS. Limb deformities have been reported at varying frequencies<sup>[3, 9]</sup>. Of these, post-axial polydactyly, polydactyly, and brachydactyly of both hands and feet are most common. Partial syndactyly, fifth finger clinodactyly and a prominent gap between the first and second toes are sometimes associated<sup>[3]</sup>. It is presented only in both feet of our reported case.

Mental retardation is a more disputed feature of BBS. Recently, objective IQ tests determined that only a minority of patients are mentally retarded. An IQ of 79 or below is found in 44 per cent of BBS patients. The decrease in IQ level correlates with the presence of visual handicap<sup>[3, 9]</sup>. Our reported case also have this feature.

Hypo-genitalism is reportedly more frequently in BBS males than females<sup>[3]</sup>. In BBS females, genital abnormalities encompass a wide range, including hypoplastic fallopian tubes, uterus, and ovaries, partial and complete vaginal atresia, absent vaginal orifice, and absent urethral orifice<sup>[10]</sup>.

<sup>11]</sup>. Bardet-Biedl syndrome males have small penis and testes (88%)<sup>[9]</sup>. Renal failure is the major cause of morbidity and early mortality in BBS. A wide range of renal abnormalities has been described (chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, vesico-ureterix reflux. These features are absent in our reported case.

In 1999, modified diagnostic criteria were defined after a study conducted in England in 109 BBS patients<sup>[3]</sup>. Patients who had 4 primary characteristics or 3 primary and 2 secondary criteria were identified as BBS(Table1).Our case had four primary criteria- Retinitis pigmentosa, Obesity, Polydactyly and Learning difficulties thus fulfilling the diagnostic criteria of Bardet-Biedl syndrome. BBS is an autosomal recessive disorder characterized by non-allelic heterogeneity. BBS is genetically, heterogeneous with four loci mapped to date. These are BBS1 (11q13)<sup>[12]</sup>, BBS2 (16q22)<sup>[13]</sup>, BBS3 (3p13)<sup>[14]</sup>, and BBS4 (15q21)<sup>[15]</sup>. We have recently shown that the BBS1 locus is involved in ~45% of affected white families. The BBS4 locus appears to be the next most common<sup>[16]</sup> but there are several families of Middle Eastern and Asian origin which do not show linkage to any known locus. Genotype-phenotype correlations between the various loci do not show obvious differences, with the possible exception of minor effects on growth<sup>[6]</sup>. The most plausible hypothesis regarding a shared function for BBS proteins is that they assist microtubule-related transport and cellular organization processes, in particular relating to ciliary/flagellar and centrosomal activities. This hypothesis is supported by several studies using different model organisms<sup>[17, 18, 19]</sup>. Some of the phenotypes exhibited by BBS proteins, including retinal degeneration, skeletal anomalies and renal cysts or malformations bear resemblance to human diseases associated with abnormal cilia function<sup>[20]</sup>.

Though a lot of progress has been made about this rare disease, there are still lots more things need to be known about its pathophysiology. Further large scale studies are required to understand the genetic complexity of Bardet-Biedl Syndrome. The disease is incurable, and therefore, persists as a chronic condition. However, timely symptomatic treatment ensures a good prognosis.

### 3. Conclusion

Further larger scale studies should be conducted in order to understand the exact

Pathogenesis of this syndrome. We presented here a rare syndrome which is more common in male with short stature but can be occurred in a female without short stature as like in our case. In the light of this case, the literature about BBS was reviewed.

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