

# Bardet Biedl Syndrome

S. Basnet, A. K. Sharma

Department of Paediatrics, Tribhuvan University, Institute of Medicine, Maharajgunj, Kathmandu

## Abstract

Bardet Biedl syndrome is a rare autosomal recessive condition characterized by central obesity, retinitis pigmentosa and postaxial polydactyly.

## Introduction

Bardet Biedl syndrome (BBS) is an autosomal recessive condition characterized by rod-cone dystrophy (retinitis pigmentosa), post axial polydactyly, central obesity, hypogonadism and mental retardation.<sup>3</sup> Other features, not always present, include hepatic fibrosis, diabetes mellitus, reproductive abnormalities, endocrinological disturbances, short stature, developmental delay, and speech deficits.<sup>4</sup> BBS occurs throughout the world but is exceedingly rare in most population (1:100000). However it is reported to occur at much higher frequency in inbred population. We report a Nepalese girl with BBS.

## Case report

A 13 yrs old girl born of a non-consanguineous marriage presented for evaluation of excessive weight gain since early childhood. There was no history of vomiting, headache, dizziness, vertigo, photophobia., excessive sleepiness, constipation or pigmentation of skin. She was born full term by LSCS for breech presentation with a weight of 3.7 kg. She had postaxial polydactyly at birth in all four limbs and underwent surgical removal of extradigits of both hands at 22 days of life. Early developmental milestones were achieved at usual ages. She had poor school performance since early school. She was studying in class 6 at time of this presentation and her academic performance was below average. At 7 years of age, she noticed poor vision especially at night for which glasses were prescribed but her problem persisted. She had not attained menarche until the present encounter. Her elder brother has similar problem and weighs 120 kg.

On examination, her weight was 74 kg (> 95<sup>th</sup> percentile), height was 153 cm (75<sup>th</sup> percentile) and BMI was 31.62 (95<sup>th</sup> percentile =25.2) with a head circumference of 56 cm.

Her mid parental height was 156cm. Her BP was 120/70 mmHg, and her sexual maturity rating was premenarchal (Tanner- stage I) despite her height being close to mid-parental height. No dysmorphic features were identified except for post axial polydactyly in both lower limbs. She was mentally retarded with IQ of 70 . Examination of eye under slit lamp showed presence pigmentary changes in the retina typical of retinitis pigmentosa. Systemic examination was otherwise unremarkable. Ultrasound of the abdomen showed bilateral renal cysts. Her blood sugar, renal function tests and CT head were normal.



**Fig. 1:** Bardet Biedl syndrome girl with her elder brother



**Fig. 2:** Postaxial polydactyly in both lower limbs

## Discussion

Bardet Biedl syndrome (BBS) is an autosomal recessive condition characterized by rod-cone dystrophy (retinitis pigmentosa), post axial polydactyly, central obesity, hypogonadism and mental retardation. Apart from obesity our patient had retinitis pigmentosa, postaxial polydactyly, central obesity and mild mental retardation which are four primary features of BBS. Her repeated hospital visits in past had not been conclusive for the diagnosis probably secondary to absence of retinal pigmentary changes during those evaluations. Although retinal pigmentation is seen in all (100%) patients, few patients develop those changes in the first decade.

Laurence Moon described four cases of retinitis pigmentosa accompanied by obesity, hypogonadism and spastic paraplegia in 1866. Bardet and Biedl separately described patient with obesity, retinitis pigmentosa, polydactyly, mental retardation and hypogonadism. The combination of these symptoms is known variously as Laurence-Moon-Bardet-Biedl syndrome, Laurence-Moon -Biedl syndrome, Laurence- Biedl syndrome. In 1970, Ammann recognized the presence of two distinct autosomal recessive disorders, which he termed Laurence-Moon syndrome and Bardet-Biedl syndrome.

Due to significant overlapping in clinical presentation of these two syndromes, a new diagnostic criterion has been proposed for diagnosis of BBS.<sup>5</sup> (table 1)

### Primary features

Retinitis pigmentosa  
Postaxial polydactyly  
Central obesity  
Learning disabilities  
Hypogonadism in male

### Secondary features

Speech disorder/delay  
Strabismus/cataract/astigmatism  
Brachycephaly/syndactyly  
Developmental delay  
Polyuria/polydipsia (neurogenic diabetes insipidus)  
Ataxia/ poor coordination/imbalance  
Mild spasticity (especially in lower limbs)  
Diabetes Mellitus  
Dental crowding/hypodontia/Small roots/  
high arched palate  
Left ventricular hypertrophy/ congenital heart disease  
Hepatic fibrosis

4 primary or 3 primary and 2 secondary features are required for diagnosis

### (Table 1. Diagnostic criteria for Bardet Biedl syndrome)

BBS is genetically heterogeneous, with 11 loci mapped to date. BBS1 gene (11q13) accounts for 20-30% of the cases.<sup>6</sup> Though eleven genes associated with BBS have been identified, their sequences have not illuminated the molecular and cellular etiology of the disease. 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 evidence that some of the phenotypes exhibited by BBS proteins, including retinal degeneration, skeletal anomalies and renal cysts/malformations bear resemblance to human diseases associated with abnormal cilia function.<sup>7</sup>

Retinal dystrophy (100%) is the first major feature of this disorder. It is found occasionally in the first decade but present in almost all patients by the second decade. The appearance of the fundus does not predict vision and the defect has been described as an atypical pigmentary retinal dystrophy of the photoreceptors with early macular involvement.<sup>2,8</sup>

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>

Limb-abnormalities are the third major feature of BBS. Of these, post-axial polydactyly, and brachydactyly of both hands and feet are most common. Our patient had polydactyly in all four limbs. Partial syndactyly, fifth finger clinodactyly, and a prominent gap between the first and second toes are sometimes associated.<sup>2,3</sup>

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>2,3,9</sup>

Our patient also had renal cyst. Renal failure is the major cause of morbidity and early mortality in BBS subjects. Associated structural renal abnormalities include renal cyst, renal scarring, fetal lobulation, vesicoureteric reflux, unilateral agenesis, ectopia, calyceal clubbing and blunting.<sup>10,11</sup> Chronic glomerulonephritis, and defects of tubular concentrating ability are among the commonest causes of renal impairment.<sup>12</sup>

Management of BBS is supportive which includes training and rehabilitation for blindness and mental retardation, diet and exercise for obesity. Early and regular screening for diabetes, hypertension and renal disease are required.

## Conclusion

Genetic syndromes should be considered in an obese child with mental retardation. Eye evaluation for retinal pigmentation should be a part of examination in patient with positive family history.

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