

## Case Report

### Bardet biedl syndrome- A case report

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#### Abstract

Bardet biedl syndrome (BBS) is a rare, genetic disorder with involvement of multiple systems and wide spectrum of clinical features. It is also known as Laurence-Moon syndrome (LMS). Characteristic features of this disorder are cone-rod dystrophy, postaxial polydactyly, truncal obesity, kidney abnormalities and learning difficulties. It may also be associated with diminished size and decreased function of the testes in males (hypogonadism) and complex genitourinary abnormalities in females. Bardet-Biedl syndrome is inherited mostly as an autosomal recessive trait. It affects males and females equally. This syndrome is usually diagnosed in childhood based upon thorough clinical evaluation and detection of characteristic findings (e.g., visual problems due to retinal dystrophy, obesity, polydactyly). Genetic testing may assist in diagnosing the disorder in selected cases (e.g., individuals with certain BBS1 and BBS10 gene mutations). The treatment of Bardet-Biedl syndrome is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of specialists. We present a case of 10yrs female patient with Bardet Biedl syndrome presenting in medicine department with vague abdominal pain, learning difficulties, obesity, decreased night vision and polydactyly. On investigations she had type IV Choledochal cyst & left mild hydronephrosis.

**Key words:** Bardet biedl, obesity, polydactyly

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#### Introduction

Bardet biedl syndrome is a rare genetic disorder with involvement of multiple systems and wide spectrum of clinical features. Principal manifestations of this disorder are rod-cone dystrophy (sometimes called atypical retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction.<sup>[1]</sup> Other features not always present include hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dental anomalies and developmental delay.<sup>[1,2]</sup> 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>[3]</sup> Recent research has demonstrated that some individuals with the clinical findings of Laurence-Moon syndrome have had mutations in genes linked to Bardet-Biedl syndrome. This discovery has led some researchers to suggest that little evidence exists to continue to classify these two disorders as distinct entities.

#### Case report

A 10 yrs old female patient presented to medicine department with vague abdominal pain. On careful history and examination she was found to be having learning difficulties, obesity, decreased night vision and polydactyly. Laboratory examination including complete blood count, urinalysis, renal function tests, thyroid function tests were found to be normal. Ophthalmological examination showed retinitis pigmentosa.

Ultrasound abdomen showed multiple cystic lesions involving intra & extrahepatic biliary channels corresponding to Choledochal cysts and left mild hydronephrosis. MRCP showed type IV Choledochal cyst. Her BMI was 28kg/m<sup>2</sup>. Limb examination showed post-axial polydactyly in all four limbs. Her intelligence quotient (IQ) was 75. However, she was not able to learn adequately and was poor performer in school. No genital abnormalities were found in the patient. She had developmental delay. Clinically she was diagnosed to be Bardet-Biedl syndrome as per modified diagnostic criteria. Hepatobiliary finding of Choledochal cyst in our case was co-incidental. There was no evidence of hepatic fibrosis in this case. Genetic tests were not done due to non-availability of the test in our institute and poor socio-economic status of the patient. The patient was treated symptomatically by a team of specialists.

#### **Discussion**

Bardet-Biedl syndrome is named after Georges Bardet and Arthur Biedl. It is usually diagnosed in childhood based upon thorough clinical evaluation and detection of characteristic findings (e.g., visual problems due to retinal dystrophy, obesity, polydactyly). In 1999, modified diagnostic criteria were defined after a study conducted in England in 109 BBS patients.<sup>[2]</sup> Patients who had 4 primary characteristics or 3 primary and 2 secondary criteria were identified as BBS (Table 1).

Genetic testing may assist in diagnosing the disorder in selected cases (e.g., individuals with certain BBS1 and BBS10 gene mutations. Investigators have determined 12 separate genes known to cause Bardet-Biedl syndrome (BBS1-BBS12).<sup>[4-9]</sup> The most common defective gene associated with Bardet-Biedl syndrome is the BBS1 gene located on the long arm (q) of chromosome 11 (11q13). Researchers have determined that

approximately 20-30 percent of individuals with Bardet-Biedl syndrome do not have a mutation of one of the 12 identified genes indicating that more, as-yet unidentified, genes may cause Bardet-Biedl syndrome. The gene products encoded by these *BBS* genes, called BBS proteins, are located in the basal body and cilia of the cell.<sup>[10]</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>[11, 12, 13]</sup> 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>[14]</sup> For clinical surveillance, initial investigation and follow up of BBS patients the recommended scheme is given in table 2.

The treatment of Bardet-Biedl syndrome is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of Pediatricians, orthopedic surgeons, cardiologists, dental specialists, speech pathologists, audiologists, ophthalmologists, nephrologists, and other healthcare professionals. Individuals with Bardet-Biedl syndrome should undergo regular ophthalmologic examinations as well as periodic assessments to determine the presence of complications potentially associated with the disorder such as kidney dysfunction, diabetes mellitus, liver function and high blood pressure. Early intervention is important in ensuring that children with Bardet-Biedl syndrome reach their highest potential. Genetic counselling may be of benefit for affected individuals and their families.

**Summary**

Bardet–Biedl syndrome is a rare, genetic disorder with variable expressivity and a wide range of clinical variability. Main clinical features are cone-rod dystrophy, postaxial polydactyly, truncal obesity, kidney abnormalities and learning difficulties. Few more congenital anomalies such as Choledochal cyst, as in our case, can be found

which are not reported in the literature. Diagnosis is based on modified diagnostic criteria with 4 primary or 3 primary and 2 secondary features, along with genetic testing in selected cases. The treatment of Bardet-Biedl syndrome is directed toward the specific symptoms and may require the coordinated efforts of a team of specialists.

**Table 1: Modified diagnostic criteria for Bardet-Biedl syndrome <sup>[2]</sup>**

<i>Primary features</i>	<i>Secondary features</i>
Rod-cone dystrophy	Speech disorder/delay
Polydactyly	Strabismus/cataracts/astigmatism
Obesity	Brachydactyly/syndactyly
Learning disabilities	Developmental delay
Hypogonadism in males	Polyuria/polydipsia (nephrogenic diabetes insipidus)
Renal anomalies	Ataxia/poor coordination/imbalance
	Mild spasticity (especially lower limbs)
	Diabetes mellitus
	Dental crowding/ hypodontia/small roots/high arched palate
	Left ventricular hypertrophy/congenital heart disease
	Hepatic fibrosis

**Table 2: Initial investigation and follow up recommendations for a person with Bardet-Biedl syndrome <sup>[2]</sup>**

*Baseline*

- Electroretinogram (ERG)/visually evoked responses (VER)
- Renal ultrasound
- Intravenous pyelogram (IVP) or DMSA/DPTA scan
- ECG & echocardiogram
- Prader-Willi syndrome exclusion by molecular testing

*Consider*

- CT/MRI brain scan/renal
- Electroencephalogram (EEG)
- Statementing of educational needs
- Registration of blindness
- Speech assessment & therapy

*Six monthly*

- Urine analysis (dipstick)

*Annually*

Blood pressure

Urea & creatinine levels



Figure 1: 10yrs old female diagnosed with Bardet Biedl Syndrome. All four limbs showed postaxial polydactyly.



Figure 2: 10yrs old female diagnosed with Bardet Biedl Syndrome. There is characteristic facial feature and truncal obesity.

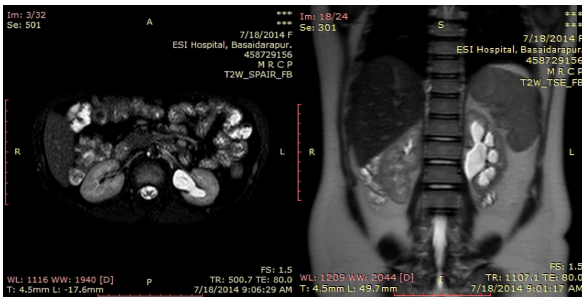


Figure 3: 10yrs old female diagnosed with Bardet Biedl Syndrome. There is left mild hydronephrosis and caliceal blunting, however, no evidence of fetal lobulation.

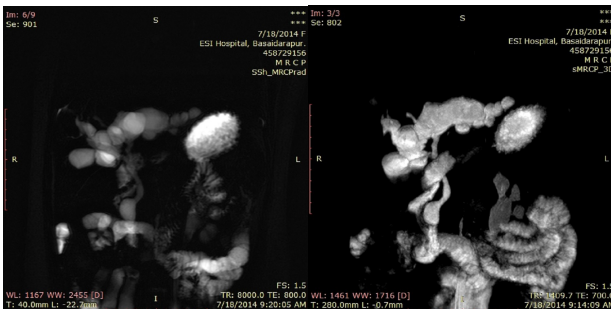


Figure 4: 10yrs old female diagnosed with Bardet Biedl Syndrome. Thick slab & 3D projection view MRCP images show type IV Choledochal cyst.

**References:**

1. Green JS, Parfrey PS, Harnett JD, et al. The cardinal manifestations of Bardet-Biedl syndrome, a form of Laurence-Moon-Biedl syndrome. *N Engl J Med* 1989;321:1002-9.
2. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *J Med Genet* 1999; 36:437-446.
3. Laurence JZ, Moon RC. Four cases of "retinitis pigmentosa" occurring in the same family, and accompanied by general imperfections of development. *Ophthalmol Rev* 1866;2:32-41.
4. Leppert M, Baird L, Anderson KL, et al. Bardet-Biedl syndrome is linked to DNA markers on chromosome 11q and is genetically heterogeneous. *Nat Genet* 1994;7:108-12.
5. Kwitek-Black AE, Carmi R, Duyk GM, et al. Linkage of Bardet-Biedl syndrome to chromosome 16q and evidence for non-allelic genetic heterogeneity. *Nat Genet* 1993;5:392-6.
6. Sheffield VC, Carmi R, Kwitek-Black A, et al. Identification of a Bardet-Biedl syndrome locus on chromosome 3 and evaluation of an efficient approach to homozygosity mapping. *Hum Mol Genet* 1994;3:1331-5.
7. Carmi R, Rokhlina T, Kwitek-Black AE, et al. Use of a DNA pooling strategy to identify a human obesity syndrome locus on chromosome 15. *Hum Mol Genet* 1995;4:9-13.
8. Beales PL, Warner AM, Hitman GA, et al. Bardet-Biedl syndrome: a molecular and phenotypic study of 18 families. *J Med Genet* 1997;34:92-8.
9. Bruford EA, Riise R, Teague PW, et al. Linkage mapping in 29 Bardet-Biedl syndrome families confirms loci in chromosomal regions 11q13, 15q22.3-q23, and 16q21. *Genomics* 1997;41:93-9.
10. Ansley SJ, Badano JL, Blacque OE, Hill J, Hoskins BE, Leitch CC, Kim JC, Ross AJ, Eichers ER, Teslovich TM, Mah AK, Johnsen RC, Cavender JC, Lewis RA, Leroux MR, Beales PL, Katsanis N (October 2003). "Basal body dysfunction is a likely cause of pleiotropic Bardet-Biedl syndrome". *Nature* 425 (6958):628-33.
11. Ansley SJ, Badano JL, Blacque OE, Hill J, Hoskins BE, Leitch CC, et al. Basal body dysfunction is a likely cause of pleiotropic Bardet-Biedl syndrome. *Nature* 2003; 425:628-633.
12. Li JB, Gerdes JM, Haycraft CJ, Fan Y, Teslovich TM, May-Simera H, et al. Comparative genomics identifies a flagellar and basal body proteome that includes the BBS5 human disease gene. *Cell* 2004; 117:541-552.
13. Blacque OE, Reardon MJ, Li C, McCarthy J, Mahjoub MR, Ansley S, et al. Loss of *C. Elegans* BBS-7 and BBS-8 protein function results in cilia defects and compromised intraflagellar transport. *Genes Dev* 2004; 18:1630-1642.
14. Pazour GJ, Rosenbaum JL. Intraflagellar transport and cilia-dependent diseases. *Trends Cell Biol* 2000;12:551-555.