Case Report

Bardet Biedl Syndrome in All Siblings – A Rare Case Report

Priyanka Gupta*, Monika Jain, Vatsala Vats, Ashish Kakkar

Department of Ophthalmology, Shri Guru Ram Rai Medical Collage, Dehradun, Uttrakhand, India.

Abstract

Bardet Biedl Syndrome (BBS) is autosomal recessive ciliopathy. Presenting features comprise mainly retinal dystrophy, central obesity, polydactyly, mental retardation and infertility. The patient is not socially acceptable for this disease. Symptomatic rehabilitation is the only way to provide quality of life to these patients. Limited cases have been reported with the involvement of two or more siblings. Three siblings reported to our OPD with diminution of vision and mental retardation. On evaluation, all siblings met the diagnostic criteria of BBS. A multidisciplinary approach was taken for their needful rehabilitation.

Keywords: Familial Bardet Biedl syndrome, Hypogonadism, Mental retardation, Moon-like facies, Polydactyly, Retinal dystrophies.

Introduction

Bardet-Biedl syndrome (BBS) is an autosomal recessive condition characterized by rod-cone dystrophy, postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction.[1] BBS gene expression varies both within and between families.[2] Several cases of BBS have been reported to date. Only a few cases had all the siblings affected by similar complaints. We here report a familial case of BBS affecting all the siblings within the same family.[3]

Case Report

Three children presented in our OPD with complaints of diminution of vision and mental retardation and associated features. They were two daughters and one son.

Sibling 1

A 28-year-old female with a complaint of diminished vision in both eyes day and night for seven years, which was progressive in nature. She had a history of operations in her hands and feet for extra digits. Her mental performance was much lower than others of the same age group. She had low hearing ability as well. She attained menarche at the age of 16 years with irregular menstrual cycles. Her best corrected visual acuity (BCVA) at the presentation was 3/60 in both eyes on Snellen's chart. Systemic examination revealed truncal obesity, operated polydactyly and brachydactyly involving both hands and feet. Dental malocclusion was also present. On slit lamp examination, the anterior segment was normal. Fundus examination revealed bilateral diffuse retinal dystrophy, arteriolar attenuation and retinal pigments (Figs 1a, b). The patient refused further examination, investigation and photographic documentation.

Sibling 2

A 22-year-old female presenting with similar complaints of reduced vision and hearing along with low mental ability. She had BCVA hand movement close to face OD and 1/60 OS. Anterior segment examination was normal. Fundus examination shows retinitis pigmentosa (RP) like features (Figs 2a, and b). On psychiatric assessment, IQ tests reveal mental age corresponding to 5.6 years (moderate intellectual disability). Systemic evaluation showed moon-like faces, truncal obesity, and operated polydactyly in hand and feet (Figs 3a, b, c, d). She has not attained her menarche yet (Sexual Maturity Rating stage 1). Her ENT evaluation revealed bilateral sensorineural hearing loss (SNHL).

Address for correspondence: Priyanka Gupta, Department of Ophthalmology, Shri Guru Ram Rai Medical Collage, Dehradun, Uttrakhand, India.
E-mail: priyankagupta8405@gmail.com

How to cite this article: Gupta P, Jain M, Vats V, Kakkar A. Bardet Biedl Syndrome in All Siblings – A Rare Case Report. UP Journal of Ophthalmology. 2024;12(2): 56-59.
Received: 18-09-2024, **Accepted:** 19-10-2024, **Published:** 29-11-2024

UP JOURNAL OF OPHTHALMOLOGY
An Official Journal of Uttar Pradesh State Ophthalmological Society, UPSOS (Northern Ophthalmological Society, NOS)
p-ISSN: 2319-2062 | DOI: 10.56692/upjo.2024120208

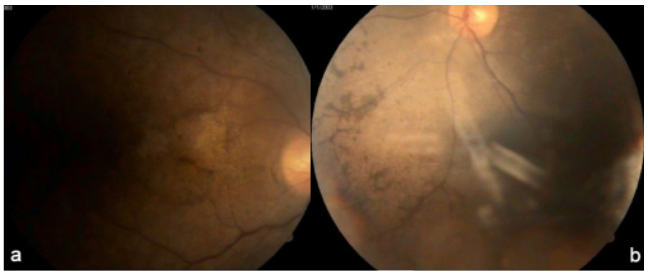

Fig. 1: colour fundus photographs of siblings 1 showing pigmentary retinal dystrophy (a)right,(b) left

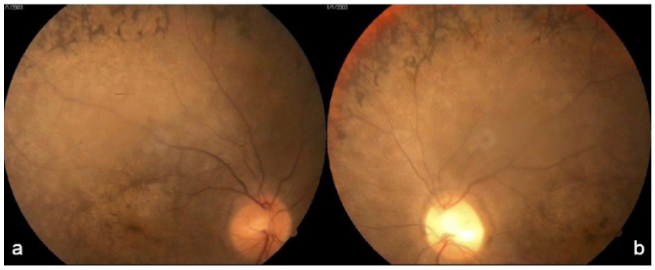

Fig. 2: colour fundus photographs of siblings 2 showing pigmentary retinal dystrophy (a)right,(b) left

Cardiac evaluation was found to be normal. Complete blood count (CBC), liver function tests (LFT) and renal function tests (RFT) were normal. Further renal, gynecological, and radiological evaluation could not be performed due to financial constraints.

Sibling 3

A 13 years old male with complaints of diminution of vision and low mental performance. Although enrolled in school, but was unable to perform well. He faced a lot of mental and social setbacks. BCVA was 2/60 in both eyes. Anterior segment examination was found normal. Fundus examination shows RP features (Figs 4a and b). IQ assessment reveals mental age corresponding to 6.16 years (mild intellectual disability). Systemic evaluation showed moon-like faces, polydactyly in hands and feet, and hypogonadism (Sexual Maturity Rating stage 2) Fig. 5 (a-d). ENT and cardiac evaluation were normal. CBC, RFT, and LFT were normal.

On interviewing, parents did not reveal consanguinity. The mother did not have significant antenatal and natal history. All children were delivered at home with an uneventful natal and postnatal period. No other children of other families or other blood relatives had similar complaints like mental retardation, diminution of vision, hearing loss and polydactyly.

All children was prescribed capsules of vitamin A 25,000 IU, once a day for three months. They were referred to a special school for rehabilitation. Visual disability certificates were issued to give them social and financial assistance. Parents were sent to a genetic counselor.

Discussion

BBS is a pleiotropic and multisystem disorder characterized by rod-cone dystrophy, polydactyly, learning difficulties,

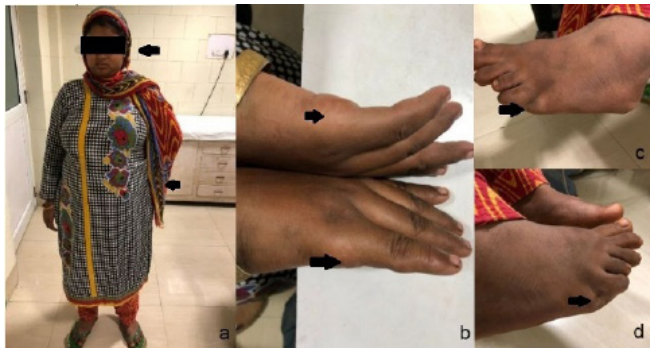

Fig. 3: Clinical photographs of sibling 2 depicting (a) moon like facies,(b)) operated polydactyly of hand,(c) operated polydactyly of left feet,(d. operated polydactyly of right feet

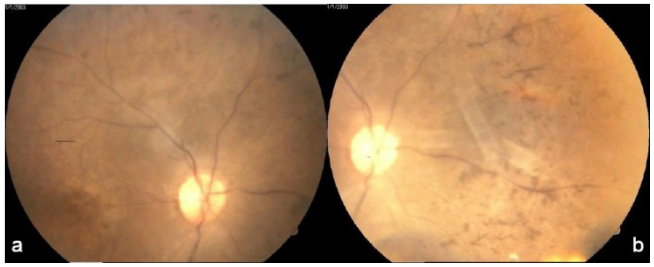

Fig. 4: colour fundus photographs of siblings 3 showing pigmentary retinal dystrophy (a) right, (b) left

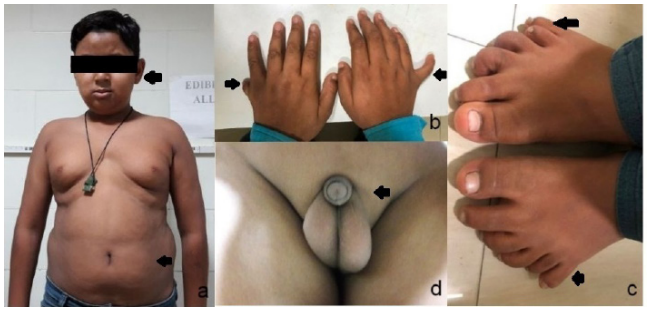

Fig. 5: Clinical photographs of sibling 3 depicting (a) moon like facies with truncal obesity,(b) polydactyly in hands,(c) polydactyly in feets,(d) hypogonadism with Microphallus

renal abnormalities, obesity and hypogonadism. Bardet-Biedl syndrome (BBS) is named after Georges Bardet and Arthur Biedl. The first known case was reported by Laurence and Moon in 1866. However, 'LMDL' nomenclature is no longer considered valid as instead of polydactyly and obesity, paraplegia was the predominant symptom. This disorder is genetically heterogeneous.[4] Until 1998, it was thought to be located in four genes: BBS1 (11q13)[4] BBS2 (16q22)[5], BBS3 (3p13),[6] and BBS4 (15q21).[7] But until now, a total of nineteen genes have been identified for BBS, which play specific roles in cilium biogenesis and function.[8] Triallelic inheritance is also a feature of this disease reported. All these genetic disorders lead to the malfunction of primary cilia, a key component of cellular communication. BBS is thus categorized as a ciliopathy. [9]

Usually, BBS can be diagnosed by the presence of at least four major features or the combination of three major and at least two minor features.[10]

Major (Primary) features

(Four features are required to be present)

- Rod-cone dystrophy
- Polydactyly
- Obesity
- Learning disabilities
- Hypogonadism in males
- Renal anomalies

(Three primary plus two secondary features are required)

Minor (Secondary) features

- Speech disorder/delay
- Strabismus/cataracts/astigmatism
- Brachydactyly/syndactyly
- Developmental delay
- Polyuria/polydipsia (nephrogenic diabetes insipidus)
- 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

To date, not more than twenty cases of BBS have been reported in India.[11] Involving all siblings within the same family is a rare presentation, with very few cases being reported so far in literature to the best of our knowledge.

The incidence of BBS varies among different populations and is increased in regions with a high level of consanguinity. For instance, in North America and Europe, the prevalence of BBS is estimated at around 1/160,000.[12] This frequency rises to 1/13,500 in Kuwait, most likely due to the high level of consanguinity and founder effects.[13] But there was no consanguinity in our case and still, all the siblings were involved within the family.

Rod-cone dystrophy (atypical retinitis pigmentosa) has been diagnosed in 93% of cases and is a major diagnostic criterion.[12] Early vision loss is not a feature of isolated typical retinitis pigmentosa. Early onset of visual deterioration and progression to rapid blindness is seen in BBS patients. This feature was present in all siblings of our case.

Hypogonadism isn't a frequent feature in females affected by BBS, as was found in both the above two female cases. Following the onset of menstruation, irregular cycles were reported for the majority of females.[10] Attainment of late menarche with irregular cycles in sibling one and no menarche in sibling two might be an indicator of gonad involvement. This is more difficult to determine in females than males and thorough radiological and endocrinological investigations are indicated, although in our series, these could not be carried out because of refusal by parents and financial constraints.

Hearing loss is a rare manifestation of BBS. Hearing loss has been reported in 21% of cases but has largely been resolved by puberty.[10] However, three patients had unexplained sensorineural hearing loss (SNHL), which is similar to our case.

The incidence of limb defects (69% of BBS cases), post-pubertal obesity (71% of BBS cases) and learning difficulties (62% of BBS cases) have been reported.[10] All these features were seen amongst all siblings in our case series.

Conclusion

BBS is a rare genetic disorder. We report a rare case of familial case of BBS affecting all siblings within the same family in North India. There is no effective treatment for this disease. Specific symptoms related to visual, vocal, and social rehabilitation are to be ensured. Disability and privileged certificates can be a great help to the subjects. Advising to avoid consanguinity can help to prevent such familial incidences. Genetic counseling, gene mapping, and pedigree charting are necessary in familial cases like ours but financial limitation is a consideration. Regular follow-up of patients of BBS should be ensured for early identification of any life modifying or threatening complications and appropriate management of the same. Renal failure is common morbidity and mortality in such cases and it is seen that there is a 25% chance of recurrence for a family with an affected child, especially a consanguineous couple.[10] Abnormal presentation may sometimes confuse the clinician, especially with Cushing syndrome and Usher syndrome.[14] A multidisciplinary approach is necessary to pick up BBS cases especially pediatricians should refer such cases to an ophthalmologist on first detection, and vice versa.

References

1. M'hamdi O, Ouertani I, Chaabouni-Bouhamed H. Update on the genetics of Bardet-Biedl syndrome. MolSyndromol. 2014;5:51–56.
2. Fattahi Z, Rostami P, Najmabadi A, Mohseni M, Kahrizi K, Akbari MR, et al. Mutation profile of BBS genes in Iranian patients with Bardet- Biedl syndrome: genetic characterization and report of nine novel mutations in five BBS genes. J Hum Genet. 2014;59:368–375. 3.
3. Ruth Riise, Sten Andréasson, Margareta K Borgström, Alan F Wright, Niels Tommerup,Thomas Rosenberg, Kristina Tornqvist. Intrafamilial variation of the phenotype in Bardet–Biedl syndrome. British Journal of Ophthalmology 1997;81:378–385
4. Leppert M, Baird L, Anderson KL, Otterud B, Lupski JR, Lewis RA. Bardet-Biedl syndrome is linked to DNA markers on chromosome 11q and is genetically heterogeneous. Nat Genet 1994;7:108-112.
5. Kwitek-Black AE, Carmi R, Duyk GM, Buetow KH, Elbedour K, Parvari R, Yandava CN, et al. Linkage ofBardet-Biedl syndrome to chromosome 16q and evidencefor non-allelic genetic heterogeneity. Nat Genet 1993;5:392-396.
6. Katsanis N, Richard AL, David WS, Phuong MT, Baird L, Beales PL,et al. Identification of a Bardet-Biedl syndrome locus on chromosome 3 and evaluation of an efficient approach to homozygositymapping. Hum Mol Genet 1994;3:1331-1335.
7. Carmi R, Tatiana R, Anne E, Kwitek B, Khalil E, Darryl N,

Edwin MS, et al. Use of a DNApooling 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, Thakker R, Flinter FA. Bardet-Biedlsyndrome: a molecular and phenotypic study of 18families. J Med Genet 1997;34:92-98.
9. Satir P, Pedersen LB, Christensen ST. The primary cilium at a glance. J Cell Sci 2010;123:499-503.
10. 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.
11. Kumar S, Mahajan BB, Mittal J. Bardet-Biedl syndrome: A rare case report from North India. Indian J Dermatol Venereol Leprol 2012;78:228
12. Klein D, Ammann F. The syndrome of Laurence-Moon-Bardet-Biedl and allied diseases in Switzerland: clinical, genetic and epidemiological studies. J Neurol Sci. 1969;9:479–513.
13. Farag TI, Teebi AS. High incidence of Bardet Biedl syndrome among the Bedouin. Clin Genet. 1989;36:463–464.
14. Mets MB, Young NM, Pass A, Lasky JB. Early diagnosis of Usher syndrome in children. Transactions of the American Ophthalmological Society. 2000;98: 237–245.