Bardet Biedl Syndrome- A Case Report

M Azizul Haque¹, L S Sharmin², Q Tarikul Islam³, A R M Saifuddin Ekram⁴

Abstract

Bardet Biedl syndrome is a rare autosomal recessive condition with a wide spectrum of clinical features. The accepted major criteria for diagnosis include retinal dystrophy, obesity, polydactyly, male hypogonadism, mental retardation and renal dysfunction. We have presented a 16 year old male patient exhibiting characteristic features of Bardet Biedl syndrome (BBS) and then the literature is reviewed.

Introduction

Bardet Biedl syndrome (BBS) is a rare autosomal recessive disorder. BBS was first described by Bardet and Biedl in the 1920s.¹ The principal manifestations are rod-cone dystrophy (Retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. Other features not always present include hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dental anomalies and developmental delay.²³

There is widespread controversy whether Bardet Biedl syndrome and Laurence-Moon syndrome are separate entities or whether they are simply phenotypic variation of the same disorder. We are presenting here a case of BBS which is rarely encountered in clinical practice.

Case Summary

Md. S, a 16 year old male patient attended Medicine Outpatient Department of Rajshahi Medical College Hospital with the complaints of poor genital development and night blindness. His parents enrolled him in a school, but he eventually dropped out because of poor learning capability. He learned to walk at the age of two and half years. He learned to speak at 3 years of age and had difficulty in finding words. He is the second children from a non-consanguineous marriage. His parents are healthy, as are his other brothers and sisters. One of his maternal uncles has an illness similar to him. On examination he was found to be obese with a BMI of 31.2. Other findings were polydactyly of all four limbs, micropenis with normal testis, astigmatism in left eye, horizontal nystagmus in both eyes, gait ataxia, and retinitis pigmentosa on fundoscopy. There was no clinical evidence of spastic paraparesis. Laboratory examination including complete blood count, urinalysis, ultrasonography of whole abdomen, renal function tests, thyroid function tests were found to be normal.

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Table-1: Modified diagnostic criteria\(^3\) and clinical manifestation in case.

<table>
<thead>
<tr>
<th>Primary Features</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rod-cone Dystrophy</td>
<td>+</td>
</tr>
<tr>
<td>Polydactyly</td>
<td>+</td>
</tr>
<tr>
<td>Obesity</td>
<td>+</td>
</tr>
<tr>
<td>Learning Disabilities</td>
<td>+</td>
</tr>
<tr>
<td>Hypogonadism in males</td>
<td>+</td>
</tr>
<tr>
<td>Renal Anomalies</td>
<td>-</td>
</tr>
<tr>
<td>Secondary Features</td>
<td></td>
</tr>
<tr>
<td>Speech disorder/Delay</td>
<td>+</td>
</tr>
<tr>
<td>Strabismus/cataracts/astigmatism</td>
<td>+</td>
</tr>
<tr>
<td>Brachydactyly/syndactyly</td>
<td>-</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>+</td>
</tr>
<tr>
<td>Nephrogenic diabetes insipidus</td>
<td>-</td>
</tr>
<tr>
<td>Ataxia/poor coordination/imbalance</td>
<td>+</td>
</tr>
<tr>
<td>Mild spasticity</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>-</td>
</tr>
<tr>
<td>Dental crowding/hypodontia/small roots</td>
<td>-</td>
</tr>
<tr>
<td>Left ventricular hypertrophy/congenital</td>
<td>-</td>
</tr>
<tr>
<td>Hepatic fibrosis</td>
<td>-</td>
</tr>
</tbody>
</table>

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.\(^4,5\)

The prevalence of BBS is 1:160000 in Europe and North America\(^6\) although higher incidence has been reported in the isolated populations of Newfoundland [1:13000]\(^2\) and Kuwait [1:17000]\(^7\). 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.\(^8\) 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.\(^3\) Limb-abnormalities are the third major feature of BBS. Limb deformities have been reported at varying frequencies\(^3,9\). 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.\(^3\) 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.\(^3,9\) Hypo-genitalism is reportedly more frequently in BBS males than females.\(^3\) 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.\(^10,11\) Bardet-Biedl syndrome males have small penis and testes (88%).\(^9\) 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. Mild to moderate mental retardation and learning difficulties are additional features of the syndrome.\(^2,3\) In 1999, modified diagnostic criteria were defined after a study conducted in England in 109 BBS patients.\(^3\) Patients who had 4 primary characteristics or 3
primary and 2 secondary criteria were identified as BBS (Table 1). Our case had five major and four of the minor criteria 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), BBS2 (16q22), BBS3 (3p13), and BBS4 (15q21). 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 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. 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. 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.

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.

References


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