

## A case report: Bardet-Biedle syndrome

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### Abstract

Bardet-Biedle syndrome is an autosomal recessive disorder named after George Bardet & Arthur Biedle. Bardet-Biedle syndrome is characterized by rods-cones dystrophy, truncal obesity, postaxial polydactyly, cognitive impairment, male hypogonadism, and renal abnormalities. The purpose of this article is to provide detailed review of Bardet-Biedle syndrome.

**Keywords:** Bardet-Biedle Syndrome, Retinitis Pigmentosa, Rods-cones dystrophy.

### Introduction

Bardet-Biedle syndrome (BBS) is a rare autosomal recessive disorder that affects many parts of body. Incidence of Bardet-Biedle has been estimated to be 1 in 1,00,000 live birth. Ratio of male and female is 1.3:1. At the conception each sibling of an affected individual has 25% chance of being affected, 50% chance of being carrier and 25% unaffected. There are fourteen genes to be associated with Bardet-Biedle syndrome. The gene product encoded by these BBS gene called BBS protein and are located in basal body and cilia of cells.

Genes are – BBS<sub>1</sub>, BBS<sub>2</sub>, ARL6/BBS<sub>3</sub>, BBS<sub>4</sub>, BBS<sub>5</sub>, MKLS/BB<sub>6</sub>, BBS<sub>7</sub>, TCC8/BBS<sub>8</sub>, B1/BBS<sub>9</sub>, BBS<sub>10</sub>, TRIM32/BBS<sub>11</sub>, BBS<sub>12</sub>, MKS1/BBS<sub>13</sub>, LEP290/BBS<sub>14</sub>. Mutation in more than one BBS locus may result in clinical phenotype of Bardet-Biedle syndrome.

### Case Report

A 30 years old male came to our eye OPD with complains of diminished vision during day and complete loss of vision during night since 10 years. Patient was mentally retarded since birth, also he had learning disabilities. On physical examination he had truncal obesity, extra digits in all limbs and also difficulty in walking. There was no family history of any congenital malformation. On ocular examination both eyes externally normal, vision in right and left eyes were hand movement. On ophthalmoscopy: Both eyes disc were pale, waxy, blood vessels attenuated, bony corpuscles like pigmentary changes were present. Diagnosis of Bardet-Biedle syndrome is established by clinical finding. Beales et al (2001) has suggested that the presence of four primary features or three primary features plus two secondary features is diagnostic.



Fig. 1: Showing postaxial polydactyly



Fig. 2: Showing postaxial polydactyly, central obesity

### Discussion

Bardet-Biedle syndrome is rare genetic anomalies. It is very difficult to diagnose, especially in the young

patient, because many of symptoms are not yet obvious and may vary considerably from one patient to another.

**Primary Features:** Rod-cone dystrophy (79%): Atypical pigmentary retinal dystrophy with early macular involvement is characteristic fundus abnormalities in Bardet-Biedle syndrome (retinitis pigmentosa). In retinitis pigmentosa visual acuity, dark adaptation and peripheral visual field are affected.

Postaxial polydactyly (21%): It may involve either all four limbs or hands or feet alone.

Truncal obesity (72%).

Learning disability.

Hypogonadism in male or genital abnormalities in female.

Renal abnormalities: Renal malformation and abnormal renal function leading to end stage renal disease. It can be major cause of death.

**Secondary features:** Speech delay: It is often delayed until age of 4 years.

Developmental delay: Gross motor skill, fine motor skill.

Eye abnormalities: Strabismus, cataract, astigmatism.

Brachyductyly/Synductyly.

Diabetes mellitus.

Orodental abnormalities.

Cardiovascular anomalies.



**Fig. 3: Showing Carries teeth & periodontitis**



**Fig. 4: Fundus showing Retinitis pigmentosa**

## Treatment

Because there is no known cure of BBS, so physician and surgeon can concentrate according to organs involvement.

## Retinitis Pigmentosa

Antioxidant may be useful in treating patient with Retinitis pigmentosa but no clear, prospective evidence in favour of vitamin supplementation yet exists.

A recent comprehensive epidemiologic study concluded that very high dose of vitamin A palmitate 15,000 U/d slow the progress of retinitis pigmentosa by about 2% per year.

Beta-carotene doses of 25,000 IU have been recommended.

Vitamin E 800 IU/d has been recommended.

Decosahexaenoic acid (DHA), Acetazolamide, Calcium channel blockers are in clinical trial.

Lutein and Zeaxanthin are macular pigments that the body cannot make but instead come from dietary sources. Lutein is thought to protect the macula from oxidative damage and oral supplementation has been shown to increase the macular pigment. Dose—20 mg/d.

## Recent advancement in the treatment of retinitis pigmentosa

**Stem Cell transplantation:** A stem cell is a multipotent cell with capacity to self-renew and to produce daughter cells and capable of differentiating into multiple mature cells. These are derived from inner cell mass of the developing blastocyte and are capable of indefinite cell renewal and proliferative in culture. They are also pluripotent, meaning that they can generate all cell types of the body.

In the context of Retinitis pigmentosa embryonic stem cells in vitro have yielded both glial and neuronal cell types. Thus embryonic stem cells have been differentiated into retinal precursor cells that express marker of retinal development including Pax16, Lhx2, Rx/Rax and Six3/6. Stem cells injected either intravitreally or subretinally.

## Different types of stem cell

Embryonic: Pluripotent

Sources: Inner cells mass, embryonic gonad

Fetal: Multipotent

Source: Umbilical cord, placenta, Amniotic fluid

Adult: Multipotent/Unipotent

Source: Bone marrow, Skin endothelium

## Technique of preparation of stem cell injection

From the bone marrow aspirate stem cell separated by ficoll density separation method. The harvested mononuclear cells are evaluated for:

Viability test

Cell morphology

CD<sub>34</sub> + count

Total cell count

The dose of stem cells usually used are 2-4 million BMSC in 0.1 ml. The dose may be increased or decreased depending on the results.

#### Concentration of ESC

$5 \times 10^5$  BMSC/0.5  $\mu$ l of normal saline

Volume injected 0.1 ml

Prognosis is very poor.

#### Differential Diagnosis

- 1. Muckusick-Kaufman syndrome:** Characterized by postaxial polydactyly, congenital heart disease and hydrometrocolpos in female and genital malformation in male. There is no hydrometrocolpos in BBS.
- 2. Alstrom syndrome:** Characterized by Rod-Cone dystrophy, obesity, sensory-neural hearing deafness, developmental delay and progressive hepatic and renal dysfunction. Due to presence of sensoryneural deafness BBS is excluded.
- 3. Joubert syndrome:** Include irregular breathing in infancy, developmental delay, intellectual disability. Additional features retinal dystrophy, cystic kidney disease. In BBS there is no irregular breathing in infancy.
- 4. Senior-Loken syndrome:** Include retinitis pigmentosa, renal disease, developmental delay, ataxia, occipital encephalocele. BBS is excluded due to presence of ataxia, occipital encephalocele.
- 5. Leber congenital amaurosis:** Severe retinal dsyrophy, visual prognosis is poor characterized by nystagmus, sluggish or near absent papillary response, photophobia, keratoconus. A characteristic finding is Franceschetti's oculo-digital sign comprising eye poking, pressing and rubbing.

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