

A case report of Bardet-Biedl syndrome

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Abstract

The Bardet-Biedl syndrome (BBS) is a rare ciliopathic human autosomal-recessive disorder, affecting multiple organ systems. Kidney abnormalities are a major cause of morbidity and mortality in Bardet-Biedl syndrome.

Background

The Bardet–Biedl syndrome (BBS) is a ciliopathic human genetic disorder that produces many effects and affects many body systems. It is characterized principally by obesity, retinitis pigmentosa, polydactyly, hypogonadism, and renal failure in some cases. Bardet–Biedl syndrome is a pleiotropic disorder with variable expressivity. The main clinical features are rod–cone dystrophy, with childhood-onset visual loss preceded by night blindness, postaxial polydactyly, truncal obesity that manifests during infancy and remains problematic throughout adulthood, specific learning difficulties in some but not all individuals, male hypogonadism and complex female genitourinary malformations, and renal dysfunction, a major cause of morbidity and mortality.

The secondary features of Bardet-Biedl syndrome are:

- Speech disorder / delay.
- Strabismus / cataracts / astigmatism.
- Brachydactyly / syndactyly of both the hands and feet is common, as is partial syndactyl (most usually between the second and third toes).
- Developmental delay: Many children with BBS are delayed in reaching major developmental milestones including gross motor skills, fine motor skills, and psychosocial skills (interactive play / ability to recognize social cues). However these delays are treatable with therapy.
- Polyuria / polydipsia (nephrogenic diabetes insipidus).
- Ataxia / poor coordination / imbalance.
- Mild hypertonia (especially lower limbs).
- Diabetes mellitus.
- Dental crowding / hypodontia / small dental roots; high-arched palate.
- Cardiovascular anomalies.
- Hepatic involvement.
- Anosmia.
- Auditory deficiencies.
- Hirschsprung disease.

The syndrome is named after Georges Bardet and Arthur Biedl.^[4] As of 2012, 14^[6] (or 15)^[7] different BBS genes have been identified. polydactyly and obesity, which are the key elements of the Bardet–Biedl syndrome.

Clinical Features

The major clinical features are:

- Eyes: Pigmentary retinopathy, poor visual acuity, low vision, and / or blindness caused by an impaired photoreceptor transport mechanism in the retina.^[8]
- Nose: Loss of or reduced sense of smell. (anosmia). Some patients claim extra-sensitive sense of smell.^[9]
- Hand and foot: Polydactyly (extra digits) or syndactyly (webbing of fingers and toes).
- Cardiovascular system: Hypertrophy of interventricular septum and left ventricle and dilated cardiomyopathy.
- Gastrointestinal system: Fibrosis.
- Urogenital system: Hypogonadism, renal failure, urogenital sinuses, ectopic urethra, uterus duplex, septate vagina, and hypoplasia of the uterus, ovaries, and fallopian tubes.
- Growth and development: Developmental Delay, especially of fine and gross motor skills.
- Behavior: a wide variety of socialization and social interaction problems have been identified with BBS.
- Defective thermosensation or mechanosensation. New finding reported in October 2007: "hitherto unrecognized, but essential, role for mammalian basal body proteins in the acquisition of mechano- and thermosensory stimuli [highlight potential] clinical features of ciliopathies in humans."^[10]
- Additional features: Obesity, possibly related to a decreased sensory function that would normally indicate satiation. Hyperphagia in some patients.^[11]

Genes involved include:

- BBsome: BBS1, BBS2, ARL6/BBS3, BBS4, BBS5, BBS7, TTC8/BBS8, BBS10, TRIM32/BBS11 BBS12, CCDC28B, CEP290, TMEM67, MKS1, MKKS^[6]
- chaperone: BBS6

Recent findings in genetic research have suggested that a large number of genetic disorders, both genetic syndromes and genetic diseases, that were not previously identified in the medical literature as related, may be, in fact, highly related in the gene typical root cause of the widely varying, phenotypically observed disorders. BBS is one such syndrome that has now been identified to be caused by defects in the cellular ciliary structure. Thus, BBS is a ciliopathy. Other known ciliopathies include primary ciliary dyskinesia, polycystic kidney and liver disease, nephronophthisis, Alstrom syndrome, Meckel-Gruber syndrome and some forms of retinal degeneration.^[16]

Case presentation

We present the case female patient of about one and half year of age, figure(1, A), presented to Al-Sallam teaching hospital in Mosul, to the maxillofacial surgery department complaining of multiple masses in the tongue, figure(1,B). From history the patient was complaining from complete bilateral blindness, and renal system congenital deformity. During examination the patient has mild central obesity, extra digits (postaxial polysyndactyly) in hands and feet, with total number of twenty four finger and toe. Figure (2). With regard to intra-oral examination the tongue masses are confined to the anterior two thirds of the tongue on both right and left lateral borders, ranging from 3mm to 5mm in diameter, with normal looking overlying mucosa and fibrotic texture.



A



B

Figure (1) A- The patient, B- tongue mass.



Figure (2): Six fingers and toes

Histopathological examination done for the tongue masses following excisional biopsy under general anesthesia of one of the tongue masses, revealed a polypoidal type of mass with fibrous tissues in the center and normal orthokeratinized overlying oral mucosa.

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. BBS is an autosomal recessive disorder characterized by non-allelic heterogeneity. BBS is genetically heterogeneous, with four loci mapped to date.

Conclusions

Close follow-up for renal involvement in patients with BBS and ALMS from an early age is highly recommended to prevent ESRD and also so renal replacement therapy can be started immediately.

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