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A Rare Genetic Disorder – Bardet Biedl Syndrome

KEYWORDS: BBS, Retinal Dystrophy, Polydactyly , Obesity, Hypogonadism

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ABSTRACT *A 24 years old male patient was admitted to the infectious ward for gastroenteritis from which he recovered in a day. Patient also hadpolydactyly, poor vision, cognitive impairment, learning difficulties,clumsy gait & pedal oedema. After investigating and thorough examination, a diagnosis of Bardet Biedl Syndrome (BBS) was made.*

Introduction:
BardetBiedl Syndrome (BBS) is a rare autosomal recessive disorder characterised by retinal dystrophy, obesity, polydactyly, developmental delay,renal dysfunction & hypogonadism. The diagnosis can be confirmed by gene sequencing study in almost 80% of the cases. BBS gene encodes protein which is required for cilia & basal body generation. We diagnosed BardetBiedl Syndrome in a twenty four years old man on the basis of clinical findings.

Case Detail:
A 24 years male patient was admitted to the infectious ward for gastroenteritis from which he recovered in a day. His mother told that his milestones had been delayed, he had cognitive impairment and he was a school drop-out. There was no history of birth injury. He has one male sibling who is normal.

Examination revealed that he had 1) truncal obesity 2) high arched palate 3) pedal oedema 4) knee joint swelling 5) flat foot (Fig1) and 6) four palmar creases(Fig 3),7) polydactyly including three extra fingers on ulnar border of right hand(Fig 3), one extra finger on ulnar side of left hand and one extra finger on radial side of right foot. 8)His external genital development was poor with a small sized penis and testes(Fig 2)9)Patient had impaired vision with only light perception. He was pale.

Investigations included complete blood count, Kidney function test with serum electrolytes, chest X-ray, X-rays of knee joints, hands and feet, ECG, blood sugar level, 2D Echo, fundus examination, ultra sonography of abdomen and pelvis and stool examination.

Patient's haemoglobin was 6.1 gm% and he was given two units of packed cells. Ultrasound revea led multiple well defined cystic lesions in the upper pole of both kidneys, largest of the size 2.3 by 1.2 cm sized with bladder wall cystitis. BUN was 44mg% and serum creatinine 2 mg%. X-ray of both hands revealed soft tissue growth in left hand with bony growth on ulnar margin with soft tissue swelling over right hand suggestive of polydactyly. 2D Echo study revealed mildly dilated right atrium and right ventricle with moderate pulmonary hypertension and preserved systolic function. Fundus examination revealed hyperaemic patches over macula and macular dystrophy. Stool examination was normal.

Figure -1

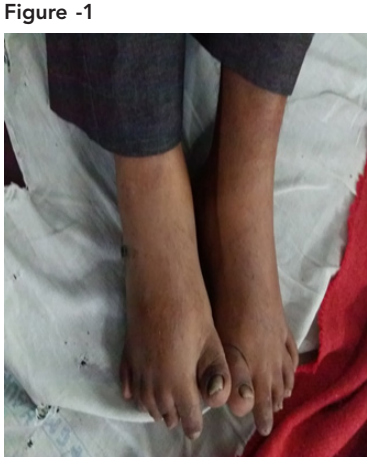

Figure -2

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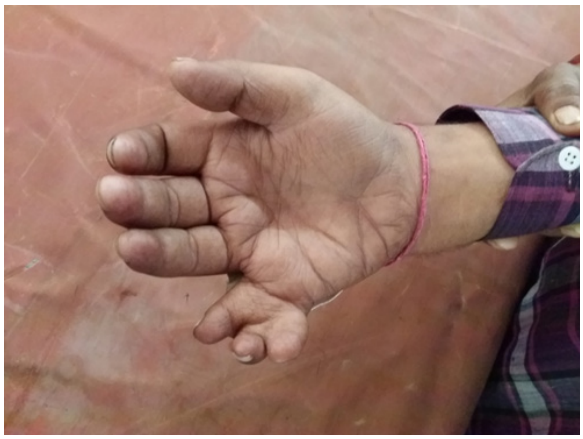
Figure -3



Discussion:
This syndrome is named after Georges Bardet and Arthur Biedl.[1]

Laurence Moon Syndrome has similar features like obesity, hypogonadism, mental retardation, polydactyly, retinitis pigmentosa. But the obesity is severe due to recessive mutation in leptin or its receptor[6]

Major clinical features of BBS

Eyes:
Pigmentary retinopathy, poor visual acuity, low vision, and/or blindness caused by an impaired photoreceptor transport mechanism in the retina[2] Our patient had macular degeneration and hyperaemic patches on retina.

Nose:
Loss of or reduced sense of smell. (anosmia). Some patients claim extra-sensitive sense of smell[3]. Our patient did not have these features.

Hand and foot:
Polydactyly (extra digits) or syndactyly(webbing of fingers and toes) or brachydactyly(small digits). Our patient had polydactyly.

Cardiovascular system:
Hypertrophy of interventricular septum and left ventricle and dilated cardiomyopathy. Our patient had dilated right atrium and right ventricle with moderate pulmonary hypertension.

Urogenital system:
Hypogonadism, renal failure, urogenital sinuses, ectopic urethra, uterus duplex vagina, and hypoplasia of the uterus, ovaries, and fallopian tubes. Our patient had multiple well defined cystic lesions in the upper pole of both kidneys, largest of the size 2.3by 1.2 cm sized with bladder wall cystitis.Kidney function tests were also abnormal. His external genital development was poor with a small sized penis and testes as shown in fig. 2.

Growth and development:
Developmental delay, especially of fine and gross motor skills. Our patient had delayed milestones with cognitive impairment.

Behaviour:
A wide variety of socialization and social interaction problems have been identified with BBS. Our patient was relatively normal regarding his social interaction.

Defective thermo sensation or mechanosensation.
This is a recently reported finding.This patient did not have sensory involvement.

Gastrointestinal system:
Fibrosis of G. I. tract. This was not present in our patient.

Additional features:
Obesity, possibly related to a decreased sensory function that would normally indicate satiation, hyperphagia in some patients[4] Our patient was moderately obese with weight 76kg, height 152cm, BMI 32.9 and a waist- hip ratio of 1.12.

The detailed biochemical mechanism that leads to BBS is still unclear.The gene products encoded by these *BBS* genes, called BBS proteins, are located in the basal body and cilia of the cell[5]which are involved in a process called intraflagellar transport (IFT), a bi-directional transportation activity within the cilia along the long axis of the ciliary shaft that is essential for ciliogenesis and the maintenance of cilia. .

Since abnormalities of cilia are known to be related to a wide range of disease symptoms including those commonly seen in BBS patients, it is now widely accepted that mutated BBS genes affect normal ciliary functions, which, in turn causes BBS.

A theory that photoreceptor cells are nourished by the IFT of retinal cilia now offers a potential explanation for the retinal dystrophy common in BBS patients after their early years of life.

Genes involved include:
BBsome: BBS1, BBS2, ARL6/BBS3, BBS4, BBS5, BBS7, TTC8/BBS8, BBS10, TRIM32/BBS11 BBS12, CCDC28B, CEP290, TMEM67, MKS1.

Summary..The reported case has majority of the features of BBS.

1)BBS has Autosomal Recessive Inheritance
2)The important clinical features are obesity, hypogonadism, mental retardation, polydactyly and retinal lesions. Our patient had these features.
3) Diagnosis is based on clinical findings.

Laurence Moon Syndrome has features as obesity, hypogonadism, mental retardation, polydactyly, retinitis pigmentosa. Spastic paraparesis is often present. Some consider these two diseases as similar. But the obesity Laurence – Moon-Biedl Syndrome is severe due to recessive mutation in leptin or its receptor.[6] In our patient obesity was milder and diagnosis of Bardet Biedl Syndrome was made on clinical basis, which may be confirmed after genetic study that was not possible for us.

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