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BARDET BIEDL SYNDROME-A RARE CASE REPORT

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ABSTRACT Laurence Moon Bardet Beidl Syndrome is a rare ciliopathic and pleiotrophic human autosomal recessive genetic disorder, which involves & affects multiple organ system. Consanguinity is commonly found amongst parents of this condition. The characteristic features of the disorder are progressive rod cone dystrophy, atypical retinitis Pigmentosa, myopia, central obesity, mental retardation, Anisometropia, Astigmatism, Postaxial Polydactyly, Hypogonadism in males, renal involvement. It affects males and females equally. The treatment of Laurence Moon Bardet Beidl Syndrome is usually directed towards the specific symptoms that are apparent in each individual. We present a case report of 16 year old male patient presenting in pediatric department with progressive loss of vision, headache, obesity,weakness & polydactyly. The history of consanguinity is absent in this index case.

KEYWORDS : Lawrence Moon Bardet Biedel Syndrome, Obesity, Polydactyly, Hypogonadism, Retinitis Pigmentosa.

INTRODUCTION

Laurence Moon Bardet Biedl Syndrome which is a rare ciliopathic human autosomal-recessive disorder with a spectrum of ocular associations such as progressive visual impairment due to rod cone dystrophy, (Atypical retinitis Pigmentosa), Myopia, Astigmatism, Anisometropia, Strabismus, keratoconus, optic atrophy, Nystagmus. Other features are central obesity, hearing difficulties, hypogonadism in males, renal involvement, mental retardation & postaxial polydactyly.[3] The Patients generally have onset of symptoms within the first 10 years of life and among them the first complaint is usually poor night vision. The frequency of the syndrome is estimated to be 1:1,60,000.

Bardet-Biedl syndrome (BBS) affects many parts of the body. Signs and symptoms can vary among affected individuals, even within the same family. The major features include:[6,7,8]

- Progressive vision loss due to deterioration of the retina. This usually begins in mid-childhood with problems with night vision, followed by the development of blind spots in peripheral vision. Blind spots become bigger with time and eventually merge to produce tunnel vision. Most individuals also develop blurred central vision and become legally blind by adolescence or early adulthood (over 90% of cases).
- Extra finger next to the pinky (postaxial polydactyly)
- Kidney problems (polycystic kidneys)
- Obesity that develops around 2-3 years of age
- Abnormalities of the genitalia and infertility due to hypogonadism
- Learning disorders

BBS may also be associated with other features, including:[6,7,8]

- Diabetes
- High blood pressure
- Heart defects
- Bowel disease (Hirschsprung disease)
- Neurological problems resulting in gait and
- coordinationimpairment
- Speech and language problems
- Behavioral disorders
- Distinctive facial appearance
- Dental abnormalities

CASE REPORT

This 16 years old male patient presented to the Pediatric Department with complaints of progressive loss of vision since 5 years, weakness since 3 months, unable to see since 1 month, headache since 20 days loss of appetite since 15 days and fever since 15 days. The patient was born out of non-consanguinous marriage with normal attainment of developmental milestones. His parents and siblings were apparently normal. There was history of female sibling death right after birth born in a twin delivery. There was history of two sentences closely with leaving no space in between.

On examination, his weight was 67 kg with a height of 160 cm. Patient was severely pale, obese and hypertensive - BP 170/100 taken in left arm in sitting posture by auscultatory method, BMI of 26.17. Heart rate was 86/minute Voice was high pitched and breathy. Hypogonadism, micropenis with bilateral gynaecomastia was present in the patient with testicular volume of 3.2ml and 4.2ml, and micropenis. There were no beard hairs, no moustache with few curled hairs on pubic and axillary areas. There was postaxial polydatyly with hexadactyly of 3 limbs and postaxial heptadactyly with syndactyly in right hand. There was no syndactyly in left hand or both feet. Patient was having vision loss with only light perception present. Ophthalmologic examination revealed presence of bilateral retinitis pigmentosa, horizontal nystagmus. The patient was not mentally retarded.

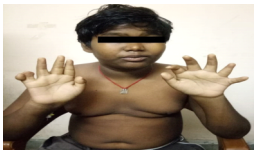

Fig 1: Child With Obesity, Gynaecomastia & Polydactyly.

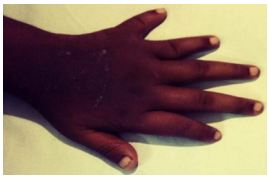

Fig 2: Child With Postaxial Hexadactyly Of Left Hand.

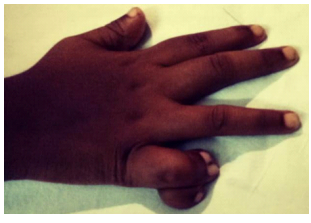

Fig 3: Child With Postaxial Heptadactyly Of Right Hand.

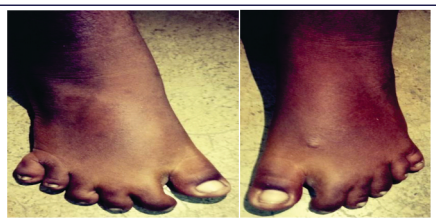

Fig 4: Child With Postaxial Hexdactyly Of Right & Left Foot.

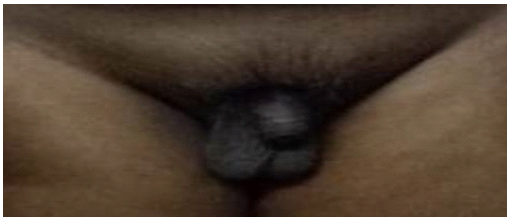

Fig 5: Bardet Biedel With Hypogonadism And Micropenis

INVESTIGATION

CBC Hb 3.8g/dl, PCV 11.7 %, RBC Count 0.96 million/mm^3, MCV 123 fl, MCH 39.6pg, MCHC 32.2 g/dl, Platelet count0.85 lakh/mm^3, TLC 3900 mm^3, Neutrophils 60%, Lymphocytes 36%, Eosinophils 2%, Mpnocytes 2%, Basophils 0%.

PBS Pancytopenia, Megaloblastic blood picture

LFT Total Bilirubin 1.9 mg/dl, Direct Bilirubin 0.9mg/dl, Indirect Bilirubin 1mg/dl,Total Protein 5.6g/dl, Albumin 3.3 g/dl, Globulin 2.3g/dl, A:G ratio 1.4, SGOT 39U/l, SGPT 23 U/L, SAP 44U/L.

RFT Urea 69 mg/dl, Creatinine 1mg/dl

LIPID PROFILE LDL/HDL Cholesterol ratio 3.6, Non HDL Cholesterol 56.7mg/dl, LDL Cholesterol 29.9 mg/dl, VLDL Cholesterol 26.8 mg/dl

HORMONAL ASSAY LH 0.15 mIU/ml, FSH 1.01 mIU/ml, T3 0.49 ng/ml, T4 9.63 µg/dl, TSH 0.41 µIU/ml, Vit B12 <83 pg/ml, Prolactin 7.48ng/ml, Testosterone 24.4 ng/dl

Routine Examination of Urine Within Normal Limits.

Urine culture No Growth.

USG Scrotum Right Testis 28*19*14 mm with volume 4.2 cm^3, Left Testis 31*19*12 mm with volume 3.2 cm^3

CECT Abdomen Ascending colon wall thickening, maximum diameter 11 mm at hepatic flexure region, Right sided nephrolithiasis, Left sided renal concretions, multiple lymph nodes in right iliac fossa and retroperitoneum suggestive of Koch abdomen.

ECHOCARDIOGRAPHY - Normal Limits.

The patient was treated with packed red cell transfusion, antihypertensives and injection of vitamin B12. A low calorie and low protein diet help in obesity control and may also slow the progression of renal failure in patients with BBS. The patient was advised diet control as per Nutritionist recommendations and physical exercises. The patient was planned to give testosterone supplementation in next follow-up visit as per Endocrinological consultation.

DISCUSSION

In 1886 Laurence and Moon explained first case of Laurence–Moon syndrome (LMS). After two years of Bardet's report, Biedl studied two cases and highlighted the complete scenario of clinical signs which includes skull abnormalities, anal Atresia, mental deficiency and gastrointestinal conflicts. Since these discoveries, presence of symptoms such asobesity, hypogonadism, retinal pigment defects, psychological hindrance and Polydactylism in several conditions as combinations, frequently in children with normal parents (cousin marriages) had been termed as Laurence-Moon-Bardet-Biedl Syndrome (LMBBS). Laurence-Moon-Biedl-Bardet syndrome (LMBBS) is no longer considered as a valid term as patients of Laurence and Moon had paraplegia but no polydactyly and obesity, which are the key elements of the BBS. Hence, Laurence-Moon syndrome is usually considered a separate entity.

The detailed biochemical mechanism that leads to BBS is still unclear. Twelve genes (BBS1 to BBS12) that are responsible for the disease have been cloned. The BBS proteins are components of the centrosome and affect the ciliary transport; hence, the disease falls under the spectrum of "ciliopathies." [4]

Eleven genes are known to be associated with this syndrome and those are BBS1, BBS2, ARL6/ BBS3, BBS4, BBS5, MKKS/BBS6, BBS7, TTC8/BBS8, B1/BBS9, BBS10, TR1M32/BBS11.This syndrome is transmitted as an Autosomal recessive trait from the parents. The diagnosis of LMBBS is established by clinical criteria.

Modified Diagnostic Criteria For Bardet-biedl Syndrome[5]

Primary features	Secondary feature
Rod cone dystrophy	Speech disorder/delay
Rod cone dystrophy	Strabismus/cataracts/astigmatism
Obesity	Brachydactyly/Syndactyly
Learning disabilities	Developmental delay
Hypogonadism in males	Polyuria/Polydipsia (Nephrogenic Diabetes Insipidus
Renal anomalies	Ataxia/poor coordination/imbalance
	Mild spasticity
	Diabetes mellitus
	Dental crowding/Hypodontia/Small roots/High arched palate
	Left ventricular hypertrophy/Congenital Heart disease
	Hepatic fibrosis

The present case of Bardet Biedel Syndrome was having many classic features like obesity, postaxial polydactyly, retinitis pigmentosa with progressive loss of vision, hypertension, learning problems, hypogonadism.

The Treatment of Laurence-Moon-Biedl-Biedl syndrome is directed toward the specific symptoms that are present in each individual. Treatment may require the coordinated efforts of a team of pediatricians, orthopedic surgeons, pathologists, audiologist, ophthalmologists, nephrologists, and other healthcare professionals. Individuals with this syndrome needs to undergo a regular ophthalmologic examinations as well as periodic assessments to determine the presence of any complications potentially associated with this disorder such as kidney dysfunction, diabetes mellitus, liver function and high blood pressure.

There is no cure for Bardet-Biedl syndrome. Treatment generally focuses on the specific signs and symptoms in each individual:

- While there is no therapy for the progressive vision loss, early evaluation by a specialist can help to provide vision aids and mobility training. Additionally, education of affected children should include planning for future blindness.
- Management of obesity may include education, diet, exercise, and behavioral therapies beginning at an early age. Complications of obesity such as abnormally high cholesterol and diabetes mellitus are usually treated as they are in the general population.
- Management of intellectual disability includes early intervention, special education and speech therapy as needed. Many affected adults are able to develop independent living skills.
- Although kidney transplants have been successful, the immunosuppressants used after a transplant may contribute to obesity. Affected individuals may also need surgery for polydactyly (extra fingers and/or toes) or genital abnormalities.
- As children approach puberty, hormone levels should be monitored to determine if hormone replacement therapy is necessary. Additionally, it should not be assumed that affected individuals are infertile - so contraception advice should be offered.

CONCLUSION

Diagnosis of this syndrome is missed because of its rarity. Pediatricians and other specialties need to have adequate information on Bardet Biedel Syndrome for accurate diagnosis due to its conflicting prognosis.

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