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Laurence - Moon - Bardet - Biedl Syndrome - A Case Report

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Abstract: ***Laurence - Moon - Bardet - Biedl syndrome (LMBBS), a rare autosomal recessive defect, mostly occurs in children born from consanguineous marriages. The features of this syndrome are obesity, hypogonadism, rod and cone dystrophy likely retinitis pigmentosa, polydactyly, nystagmus, intellectual disability, polydipsia/polyuria and clumsiness. In this case report, we present a case of 14 - years - old male child came with complaint of rapid weight gain in last 2 months and pain in abdomen since last 5 days. On examination, he was found to have diminution of vision and had multiple itchy hyperpigmented macules over trunk and abdomen, hexadactyly, central obesity and polydipsia. Fundus examination revealed rod - cone dystrophy in the form of retinitis pigmentosa and absent pubic, axillary and facial hair indicating hypogonadism. The patient was diagnosed with LMBBS.***

Keywords: obesity, hypogonadism, retinitis pigmentosa, endocrine, polydactyly

1. Introduction

Laurence - Moon - Bardet - Biedl Syndrome (LMBBS) is a ciliopathic, pleiotropic autosomal recessive defect mostly occurs in children born from consanguineous marriages [1]. The symptoms become manifest between first two decade of life, diminution of vision being the first one. The estimated incidence rate is 1 in 1, 60, 000 in northern European population and 1 in 13, 500 in some Arab population [2]. The clinical diagnosis of LMBBS is done with presence of four primary features or three primary and two secondary features. The primary feature includes Cone - rod dystrophy, polydactyly, obesity, learning disabilities, hypogonadism in males and renal anomalies whereas the secondary features include speech disorders, brachydactyly, developmental delay, polyuria/polydipsia, ataxia, poor coordination/ clumsiness, diabetes mellitus, left ventricular hypertrophy, hepatic fibrosis, spasticity and hearing loss. Few features like short stature, crowding of teeth, hypermobile or lax joints and early osteoarthritis are also reported [3].

Fundus examination reveals major changes such as constricted arterioles, disc pallor and peripheral pigment changes such as pigment atrophy and bone specular pigmentation plus areas of white deposits.

At an early stage, degenerative changes are observed in maculae of patients with persistent decrease in central vision thus making them blind by the age of 30 years [4]. More than half of the total cases reveal that women are more commonly affected than men. Moreover, functional and morphological abnormalities are observed in up to 90% of affected patients. The renal abnormalities occur with range of activities, often causing substantial morbidity and the autopsy reveal it to be the chief cause of mortality [5].

2. Case Presentation

A 14 - years - old male child came to outpatient department with complaint of rapid weight gain for 2 months and abdominal pain for 5 days. The diminution of vision especially at night started few years back but patient's father did not seek any medical advice.

The clinical evaluation showed a young male child of average height, having central obesity with BMI of 35 kg/m^2. Multiple hyperpigmented macules were observed over trunk. He was having painful gynaecomastia, absence of axillary, facial and pubic hair (Image 1, 2, 3). Patient had hexadactyly in both feet (Image 4). Ophthalmic examination revealed patient has diminution of vision, especially at nightand patient was able to count fingers at 1 meter i. e., vision was 1/60. Fundus examination revealed bilateral retinitis pigmentosa, disc pallor, arterial attenuation and few bony spicules seen in periphery (Image 5, 6).

Suspecting hypogonadism patient's serum testosterone levels were done and the value found to be 1.887 ng/ml (Range: 3 to 9 ng/ml). MRI brain with contrast study revealed hypoplastic pituitary (Image 7). Father gave history regarding scholastic performance and was having good grades till eighth standard. Patient was having increased thirst and average 24 - hour urine output volume was 2400ml.

Cone - rod dystrophy, central obesity, hexadactyly, polyuria/ polydipsia, delayed puberty and hypoplastic pituitary led to the diagnosis of Laurence - Moon - Bardet - Biedl Syndrome. Patient was planned for androgen replacement therapy and was given Injection Testosterone 100mg/ml, one third dose per month and three doses to be given.

There is no definitive treatment for this syndrome and thus patient's father has been counselled regarding the course of

the disease, dietary modification, testosterone, vitamin A supplements etc.

3. Discussion

In 1866, Laurence and Moon explained a case of a 7 - years - old female with rod - cone dystrophy, hypogonadism, mental retardation, polydactyly and obesity. In 1920, Bardet described a 4 - years - old female patient presented with rod - cone dystrophy, obesity, polydactyly and mental retardation. Two years after Bardet's report, Biedl highlighted the scenario of clinical signs which includes skull abnormalities, anal atresia, mental deficiency and gastrointestinal disorders [6]. Since these discoveries' presence of above manifestation as union, often in normal mother and father (Consanguineous marriage) has been called Laurence - Moon - Bardet - Biedl syndrome.

Consanguinity is commonly practiced in various middle eastern countries, such as Kuwait, Saudi Arabia, Iran, Pakistan and in Southeast Asia such as India. It has been a chief contributing factor to disease frequency. Families in these countries have approx.0.1% homozygous genes of the total genome. In Pakistan, more than half of all marriages are consanguineous in nature, with 80% of them among first cousins, thereby increasing the possibility of homozygous mutations [7].

The reason behind this study is scarcity of data available on LMBBS in India. Our patient being male, and majority of patient reported to be females further adds to this fact.

Confusion still exists between Laurence - Moon Syndrome (LMS) and Bardet - Biedl Syndrome (BBS). Pigmentary retinal degeneration, mental retardation and hypogonadism are common in both, whereas spastic paraplegia is predominant in LMS, and polydactyly and obesity are seen in BBS. Because of some common features, some of the researchers believe BBS to be a part of LMS [8]. BBS is a rare ciliopathic disorder that affects 12 genes (BBS1 to BBS12) which form proteins essential in the functioning of the cilia, thereby causing structural and functional anomalies [9]. Two defective genes, one from each carrier parent, yield an offspring affected by LMBBS; thus, the probability, in this case, was 25%. Therefore, genetic counselling is beneficial for both patients and their families [10].

The treatments available for LMBBS are mainly toward managing the manifestations of the illness. Physical therapy aimed toward improving strength helps. Exercise can reduce the symptoms of spasticity. A dedicated regimen of nutritious, well - balanced meals and regular exercise is recommended, as there is an increased incidence of diabetes and abnormal cholesterol levels in patients with LMS. A low protein diet also slows the progression of renal diseases in BBS [11]. The poor functional capacity of the anterior pituitary gland, resulting in slow metabolism, poor growth, and impaired fertility, can be managed with hormone replacement therapies. Levothyroxine can aid in increasing the body metabolism, resulting in reduced lethargy, hair loss, and obesity. Growth hormone supplementation reduces the psychosocial burden of short stature, whereas testosterone supplementation can be given in patients with markedly low levels to prevent underdeveloped genitalia. Accessory digits are generally non - functional and can be removed for cosmetic purposes. Typically, retinal dystrophy is the first symptom that arises before the age of 10 years but affects almost all patients below the age of 20 years [12].

As patient exhibited diminution of vision long back which went unnoticed and lead to late diagnosis of LMBBS when significant damage has occurred. Ideally patient in puberty is referred to

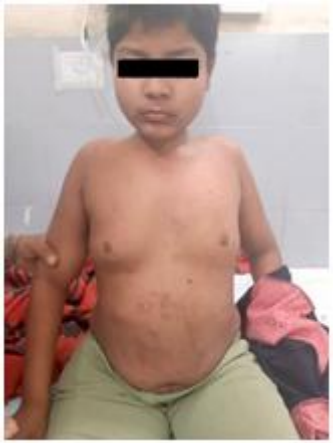

Image 1: Central Obesity, Gynecomastia, Hyperpigmented Macules

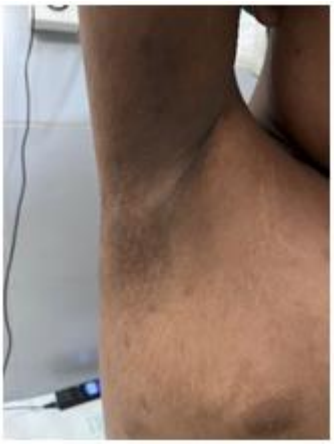

Image 2: Absence of Axillary Hair

Image 3: Absent Pubic Hair

Image 4: Hexadactyly counsellor to cope up from this stressful period

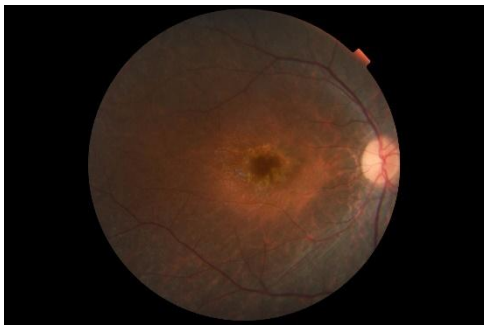

Image 5: Right Eye Retinitis Pigmentosa (Disc Pallor, Bony Spicules, Cone - rod Dystrophy)

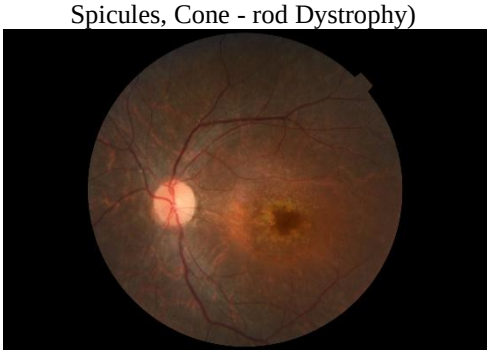

Image 6: Left Eye Retinitis Pigmentosa (Cone - rod Dystrophy)

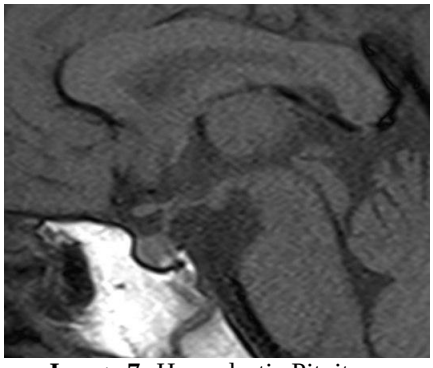

Image 7: Hypoplastic Pituitary

4. Conclusion

LMBBS carry significant disability and morbidity and early diagnosis helps the medical professionals to manage this condition aggressively to delay the progression. As this syndrome being rarehas multisystem involvements, might cause difficulty to diagnose. Timely diagnosis and better management would help the child to adjust to the society more easily. Counselling regarding marriages outside the family is to be done and should be encouraged.

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Declaration of consent: An informed consent was taken from parents of patient.

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