LAURENCE-MOON-BARDET-BIEDL SYNDROME: A CASE REPORT

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INTRODUCTION

Laurence-Moon-Bardet-Biedl Syndrome (LMBBS) is a rare autosomal recessive innate disorder, ensuing as a result of consanguineous marriage. It characteristically manifests as a congenital ciliopathy with a saga of widely distinct primary and secondary clinical features. Patients with LMBBS experience rapid decline in the functionality of the brain, eyes, kidneys, hands, and feet. The cardinal features typical of the syndrome include mental retardation, atypical retinitis pigmentosa, hypogonadism, polydactyly, obesity, and renal impairment.

Nonetheless, it may also present with certain secondary characteristics including speech disorders, gait disturbances, developmental delay in achieving milestones, diabetes insipidus, syndactyly, dental crowding or hypodontia, and congenital heart disease. Renal impairment is also a frequent clinical manifestation. Such patients are confused, along with impeded memory, poor judgment skills, and uncoordinated, and clumsy motor movements. While renal impairment remains the major cause of mortality since end-stage renal disease is a frequent complication in such patients; overall, LMBBS is a rare syndrome of multi-organ involvement with various degrees of complications and an uneven life span [1].

CASE PRESENTATION

A 13 years old female patient presented to the general medicine outpatient department (OPD) with the chief complaints of obesity, learning difficulty, polyuria, polydipsia, and gradual loss of vision since childhood followed by night blindness. Detailed history revealed that she was the fifth child of consanguineous marriage, born full term at home in a village. Bilateral polydactyly and syndactyly were observed since birth, however, she started to gain weight in infancy. The patient demonstrated delayed milestones compared to her siblings evidenced by the fact that she took her first step at the age of 4 years. Moreover, the patient is neither able to read or write properly nor could she retain the things she has learned the past day. The patient further elaborated on her ailment that she is unable to see during the night and has near to complete vision during the day. Probing into the family history revealed that one of her brother age 8 years also has the same clinical features while the remaining eight siblings were normal.

On general physical examination, she had marked obesity with a BMI of 38 kg/m2 and a moon-like face (fig 1). Polysyndactyly was noted in both hands along with polydactyl of the right foot (fig 2,). There was a lack of pubic and axillary hair. Central Nervous Examination revealed a wide-based stance while walking and an inability to recall even the simplest information like where does she live? Abdominal examination revealed a soft, distended, non-tender abdomen with grayish striae. Respiratory and cardiovascular examinations were unremarkable. Ultrasound of the abdomen and pelvis showed grade 2 fatty liver and mildly increased left renal echogenicity. Eye examination revealed color vision defect on Ishihara color chart and reduced visual acuity of 6/24 in both eyes. The Hiding Heidi Test showed a 25% decreased vision perception. Laboratory investigations revealed normal full blood count, C-reactive protein (CRP), renal function test, liver function test, lipid profile, and thyroid function test. However, her follicular stimulation hormone (FSH) and luteinizing hormone (LH) were below the normal level. As this patient met the criteria for the diagnosis of LMBBS, the diagnosis of LMBBS was made, a multidisciplinary team (MDT) was taken on board and the treatment was focused on managing symptoms. Ophthalmic support, hormone therapy, and speech and occupational therapy were recommended. The patient was sent out on multivitamins and supplements and the parents were counseled regarding the nature, course, and poor prognosis of the disease.

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DISCUSSION

LMBBS is a heterogeneous disorder with familial occurrence manifesting various clinical features that results in a complex association of problems affecting several body parts. It was named after the four scientists who initially described the symptoms. Although LMBBS is considered a single entity, it comprises two distinct syndromes i.e. Laurence Moon Syndrome (LMS) and Bardet Beidl Syndrome (BBS). Both are genetically inherited in an autosomal recessive pattern. However, LMS has an atypical pigmented retinopathy along with hypogonadism, neurological defects, and mental retardation but no polydactyly or obesity which are the cornerstones of the BBS. Nonetheless, the symptoms of LMBBS are obvious, yet it remains an underdiagnosed condition. It predominantly affects females and has the occurrence of 1:140000 to 1:160000 in North America and Europe respectively, while greater

The occurrence was reported in Kuwait and Newfoundland, having 1:13500 to 1:17500 respectively[2]. The patient described in this case report is a typical representation of LMBBS. Genetic testing to date has revealed 19 culprit genes associated with the disease, all of which encode protein cilia. LMS is caused by changes in PNLP6 genes whereas BBS results from mutations in at least 14 different BBS genes. About one-quarter of all cases of Bardet-Biedl syndrome

results from mutations in the BBS1 gene. Another 20 percent of cases are caused by mutations in the BBS10 gene. The other BBS genes each account for only a small percentage of all cases of this condition [3]. Both parents need to carry one copy of the mutated gene for the child to develop LMBBS. The first prime feature of LMBBS is retinal dystrophy and vision loss which often ensues due to impaired photoreceptors in retinal tissue involving macula leading initially to night blindness, followed by complete blindness over course of time. It is usually observed in the first decade of life in few people and observed by all in the second decade.

Another important feature of LMBBS, obesity, begins in childhood and progresses as the patient ages with a frequency of 72-96 % as determined by the measurement criteria. The average body mass index (BMI) reported in female patients is 31.5 kg/m2, while in male patients is 36.6kg/m2 [4,5]. Skeletal abnormalities particularly polydactyly and syndactyly are another main feature of this syndrome with polydactyly usually occurring in 69% of LMBBS patients [6]. people with LMBBS often have decreased levels of sex hormones estrogen and testosterone mainly due to the small size of the pituitary gland. As a result of a weak signal to produce estrogen and testosterone, the reproductive organs of both men and women suffering from LMBBS may be underdeveloped resulting in reduced fertility or sometimes even infertility. Mental sub normality is a borderline manifestation of this syndrome. It is debatable but most patients have lower IQ with learning disabilities attributed to weak cognitive capacity. The patient under discussion presented with all five aforementioned symptoms. A study carried out by Beales et al. on 109 BBS patients devised a modified diagnostic criterion[7]. According to the criteria, an individual must have at least four primary features or three primary and two secondary features to be identified as BBS patient. [Table 1]

Another main feature associated with LMBBS is a renal impairment which is a leading cause of mortality. Impaired urinary concentration capacity, recurrent urinary tract infections, and hypertension are early presentations. There are several renal abnormalities detected including dysplastic kidneys, parenchymal cyst, calyceal clubbing, and chronic renal failure. Typical radiographic pictures are seen in these patients.

LMBBS requires a multidisciplinary approach and an early diagnosis to ensure the quality of life. Counseling regarding hereditary nature, the risk of the disease, and creating awareness regarding consanguineous marriage can reduce the prevalence of the disease. Furthermore, early detection of the disease can significantly reduce the advancement of manifestations. Treatment options at a later stage mostly comprise supportive treatment. Spectacles and visual aids have been advised to improve visual quality; physical exercise and a low-calorie diet are the mainstream treatment to reduce obesity. Moreover, hormonal therapy can improve hypogonadism to some extent. Additionally, in order to slow down the cognitive impairment, educational evaluation should be performed and analyzed by a clinical psychologist who can also counter the mood symptoms if produced as a consequence of this disease [8].

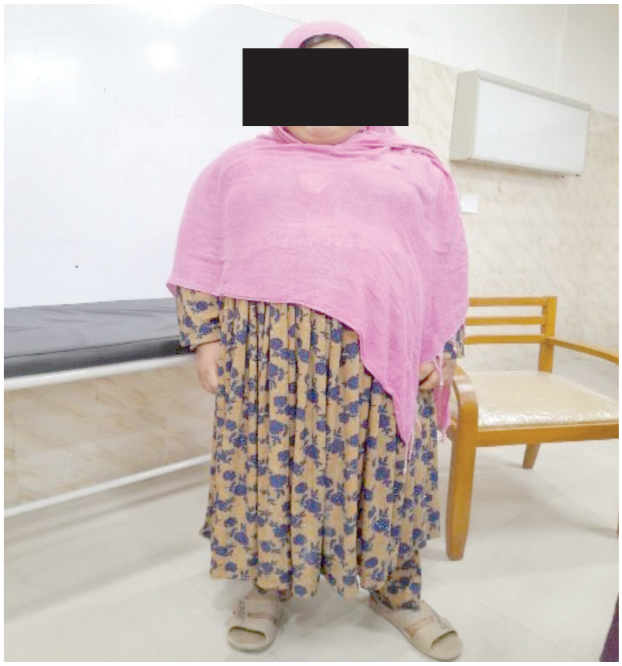

Fig 1: Karyotyping revealed a genotype of 46 XY.

Fig 2: Polysyndactyly.

CONCLUSION

LMBBS, a rare genetic disorder, imposes considerable morbidity and mortality. As there is no definite treatment to date, early diagnosis is essential to manage the complications related to this condition like retinitis pigmentosa, morbid obesity, and metabolic syndrome. A multidisciplinary evaluation approach involving physicians, ophthalmologists, endocrinologists, pediatricians, and radiologists can significantly alter the course of the disease, enabling the affected individuals to integrate better into the community. Consanguineous marriages being an effective contributor to LMBBS need particular attention. In this scenario, marriages outside of the family should be encouraged to limit the incidence. As the disease carries a lot of morbidities, genetic study and genetic counseling are mandatory for patients with suspicion of LMBBS.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Munib N:	Did literature search, article formatting, and compilation
Haider I:	Conceived the idea, final review
Elahi S:	Article formatting, and compilation

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.