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Laurence -Moon-Bardet- Biedl syndrome with Diabetes Mellitus

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Abstract:

A 13 year old boy presented with obesity, reduced vision, mental retardation, hypogonadism, delayed development and learning difficulty. On examination, he had polydactyly, moon face, bilateral gynaecomastia, small penis and testis. Retinitis pigmentosa was found on fundoscopy. With these typical features, he was diagnosed as a case of Laurence-Moon-Bardet-Beidle syndrome. It is a rare autosomal recessive disorder with mutation in 6 loci identified so far. It is commonly found in communities with high inter-family marriage. Clinical features appear early in childhood and diagnosis is usually done by puberty. Prominent features include rod-cone dystrophy leading to blindness, postaxial polydactyly, central obesity, learning disability, hypogonadism in males, renal dysfunction with increased risk for renal cell carcinoma.

***Keyword**: Laurence-Moon-Bardet-Biedl syndrome, Obesity, Polydactyly, Retinitis pigmentosa*

Introduction:

Laurence-Moon-Bardet-Biedl syndrome (LMBBS) is a rare, genetically heterogeneous, autosomal recessive disorder[1]. The five cardinal features include polydactyly or syndactyly, pigmentary retinopathy, obesity, mental retardation and hypogonadism. Other systemic features include brachycephaly, short stature, congenital heart block, deafness, neurological disorders and kidney disorders. Though features start to appear early in childhood, diagnosis is often delayed till after puberty[2].

We report here a classical case of Laurence-Moon-Bardet-Biedl syndrome of 13-year- old boy. We also present a brief review of the diagnosis and management of this rare and interesting syndrome.

Case Report:

A 13 year old boy presented with gradually worsening loss of vision for the last 2 years and obesity since childhood despite dietary restriction. He was mentally retarded, had history of delayed development and learning difficulty. None of his relatives had similar condition and there was no history of consanguinity among his parents. On examination, he had short stature (height 1.30 m) with gross obesity (weight 69kg, BMI 40.82 kg/m2), moon face, hexadactyly in all 4 limbs(Fig.-1&2), bilateral gynaecomastia, small penis and testes. His visual acuity was reduced. Fundoscopy revealed bilateral retinitis pigmentosa (Fig.-3). Other features were normal.

His CBC, S creatinine, Urea was within normal limit. FBS was 12.8 mmol/l & 2 hours after 75 gm glucose was 20.4 mmol/l. ECG, Echocardiography, X- Ray chest and USG of abdomen was normal. S.Cholestrol was 194 mg/dl, HDL27 mg/dl, LDL99mg/dl and Triglyceride was 363 mg/dl. S. Testosterone was 1.7ng/ml (normal 2.88-8.64ng/ml). LH was 12 U/L (N:1.0-9.0U/L) and FSH was 14 U/L (N:1.0-10.0U/L). TSH was 2.5mU/L (N:0.2-4.5mU/L) and FT_4 was 15pmol/L (N: 9-21pmol/L). Growth hormone assay was 4µg/l (N: 0.5-6 µg/l).

Fig.-1: *Hexadactyly in both hands.*

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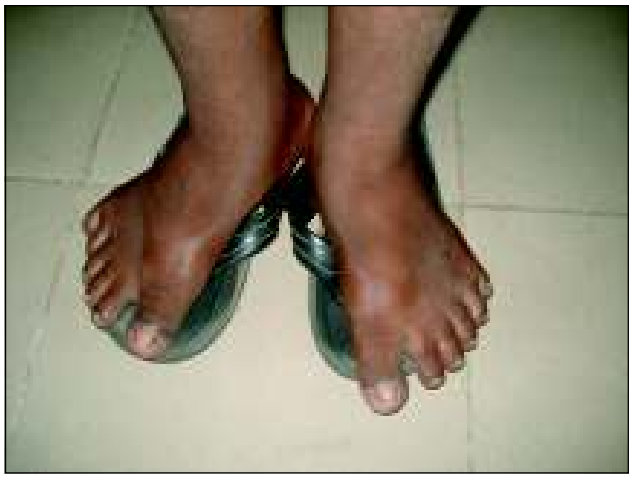

Fig.-2: *Hexadactyly in both feet*

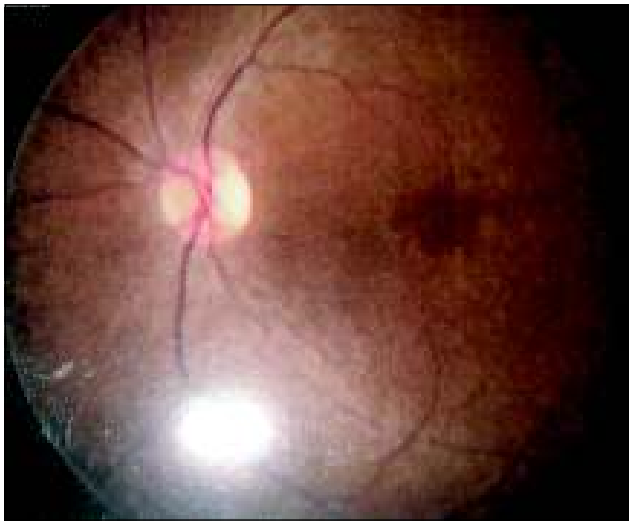

Fig.-3: *shows retinitis pigmentosa.*

This patient has all the five cardinal features of LMBBS. In addition he also had Diabetes Mellitus. Finally we concluded this was a case of Laurence-Moon-Bardet-Biedl syndrome. Now he is receiving symptomatic treatment with metformin & Inj. testosterone with instruct for periodic follow up.

Discussion:

The Laurence-Moon-Bardet-Biedl syndrome was independently described by Bardet and Biedl in the 1920s. There was controversy in medical literature with the condition described in 1865 by Laurence and Moon, referred as Laurence and Moon syndrome (LMS). After a 22-year prospective cohort study of 46 patients from 26 Newfoundland families with BBS, Moore et al concluded that BBS and LMS are different spectrum of same entity[3]. The variable manifestations of this syndrome can be explained at molecular basis by ciliopathy. The condition was thought to be rare, but this may have been due to the failure to diagnose incomplete or partial cases. The prevalence of LMBBS is 1: 160 000 in Europe. However, its prevalence is markedly increased in highly consanguineous Arab-Bedouin communities in the Arab population of Kuwait (1: 13 500) [4]. Recent advances in genetics have enabled investigators to define syndromes by specific mutations. Eleven genes are known to be associated with this syndrome: BBS1, BBS2, ARL6/BBS3, BBS4, BBS5, MKKS/BBS6, BBS7, TTC8/BBS8, B1/BBS9, BBS10 and TRIM32/ BBS11[4]. The syndrome is transmitted as an autosomal recessive trait. There is considerable heterogeneity and intra familial variation in the extent and severity of clinical manifestations of LMBBS. The diagnosis of LMBBS is established by clinical criteria suggested by Beales et al that the presence of four primary features or three primary features plus two secondary features is diagnostic[5]. Primary features include rod-cone dystrophy, polydactyly, obesity, learning disabilities, hypogonadism in males and renal anomalies. Secondary features include speech disorder, brachydactyly, developmental delay, polyuria / polydipsia, ataxia, poor coordination/clumsiness, left ventricular hypertrophy, diabetes mellitus, hepatic fibrosis and spasticity. Central obesity is the commonest feature of LMBBS. It develops in early childhood and is aggravated with age. Ocular manifestations are also common and become apparent between the ages of 4 and 10 years. They include retinal dystrophic changes which progresses relentlessly leading to decreased night vision, reduced visual acuity and blindness at a young age. Mild to moderate mental retardation is an additional feature of the syndrome. Hypogonadism in affected male is common. Dysmorphism of extremities, including postaxial polydactyly, syndactyly or brachydactyly, is one of the earliest and most common manifestations of LMBBS. Renal involvement is observed in most affected individuals. It consists of structural and functional abnormalities such as calyceal or pelvic dilatation, fetal lobulation, and focal and diffuse cortical loss, as well as tubular dysfunction, hypertension and progressive renal failure[6]. Many children with LMBBS are delayed in reaching major developmental milestones and speech disorder has been reported infrequently in this syndrome.

LMBBS has an adverse prognosis, with early onset of blindness, obesity, hypertension, and diabetes mellitus. Renal impairment is frequent often goes undetected. This is significant in that early death often occurs in this condition because of the renal disease. Their survival and quality of life depend on the severity of clinical features, as well as on the quality of the medical care they receive. LMBBS with visual impairment need visual aids and educational programs. For management of obesity, diet, exercise and behavioral

therapies are advocated. Accessory digits may be removed surgically to prevent functional interference and poor fitting of footwear. Early intervention and special education is needed to address cognitive disability. Speech delay/ impairment needs early diagnosis and speech therapy. Hormone replacement therapy is advocated to correct hypogonadism. Renal anomalies and hypertension are treated as in the other affected children. Surveillance includes regular ophthalmologic evaluation, annual blood pressure measurement, monitoring of renal function, and regular testing for diabetes mellitus and lipid profile. These concerns are best addressed in the setting of a dedicated team made up of the appropriate specialties allowing proper planning and cooperation so that the patient may receive the best possible care. The main purpose of this case report, besides reporting a very rare entity was to make the reader aware of management strategies and adverse prognosis. The condition is supposed to be rare, but this may have been due to the failure to diagnose incomplete or partial cases [5-6].

Conclusion:

This is a rare disease and often diagnosis is missed. This case illustrates several common features of LMBBS. In addition he also had Diabetes Mellitus . Early recognition and effective measures might help the patient to lead a reasonably good life.

Conflict of Interest: None

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