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Bardet-Biedl Syndrome: A Rare Case Report

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Abstract: The Bardet-Biedl syndrome (BBS) is a rare genetically heterogeneous, autosomal recessive inherited disorder with wide variability in expression. It presents with varied clinical manifestations like retinitis pigmentosa, post-axial polydactyly, central obesity, mental retardation and renal dysfunction. Other rare manifestations include diabetes mellitus, heart disease, hepatic fibrosis and neurological manifestations. Its presentation with type 1 diabetes mellitus is a rare manifestation. We report a case of Bardet-Biedl syndrome presenting with type1 diabetes mellitus.
Keywords: inherited disorder, diabetes mellitus, Bardet-Biedl syndrom

INTRODUCTION

The Bardet-Biedl syndrome (BBS) is a rare cilio-pathicautosomal-recessive disorder, characterized by cardinal symptoms of marked central obesity, rod-cone dystrophy (retinitis pigmentosa), post-axial polydactyly, mental retardation, hypogonadism and renal dysfunction [1]. BBS occurs throughout the world, with prevalence rates of 1:140000 to 1:1,60,000 in North America and Europe respectively [2]. The incidence is much higher in some populations with a high level of consanguinity or those that are geographically isolated, with disease incidence of 1 in 13,000 in the isolated populations of Newfoundland and1 in 17,000 live births in Kuwait. Male to female ratio is approximately 1.3:1. [1, 3]In India, the actual prevalence rates are unknown and a few cases have been reported.

CASE REPORT

A 27-year-old male patient presented to our emergency medical services, with history of polyuria and polydipsia of one-month duration. He also had a history of significant weight loss in the past one month. There was no history of anorexia, nausea, vomiting, dysuria, hematuria, recurrent urinary tract infection, or nocturnal enuresis. His past history included poor school performance and diminished distant vision since eight years of age. He was born out of a non-consanguineous marriage and birth history was not significant except for the anomaly of polydactyly in three of his four limbs. There was no history of any illness in the neonatal period. He had delayed developmental milestones.

Examination at presentation showed, height of 150 cms, weight 43 kgs, BMI of 19.1kg/m^2, pulse 80/bpm, and BP 130/90 mmHg. There was crowding of teeth. He had polydactyly in three of his four limbs (Fig. 1). He had no signs of pallor, pedal edema, cyanosis, clubbing or jaundice. The fundus examination of both the eyes revealed features suggestive of retinitis pigmentosa (Fig. 2). Borderline mental retardation with an IQ of 71–75 was found. Systemic examination was unremarkable.

Laboratory examination including complete blood count, urine analysis, fasting lipid profile, liver function tests and renal function tests were normal. His random blood sugar was 484 mg/dl at presentation. The glycated haemoglobin (HbA1c) was 11 and fasting C – peptide levels were 0.03ng/ml(Ref. Range 1.1- 4.4 ng/mL).

Ultrasonography of abdomen revealed bilateral multiple small renal cysts and no evidence of pancreatic calcification or cysts. The electrocardiogram and chest X-ray were normal. The echocardiography of heart showed mild mitral regurgitation with normal pulmonary artery pressure. The Auditory Steady-State Responses (ASSR) test revealed mild conductive hearing lossin both the ears.

He was managed initially in emergency ICU, as his blood sugars were high (484 mg/dl), with continuous intravenous infusion of short acting insulin. His blood sugars came to control after 8 hours of insulin infusion. After control of diabetic state with insulin he

was discharged from the hospital on day seven. The patient is in regular follow up.

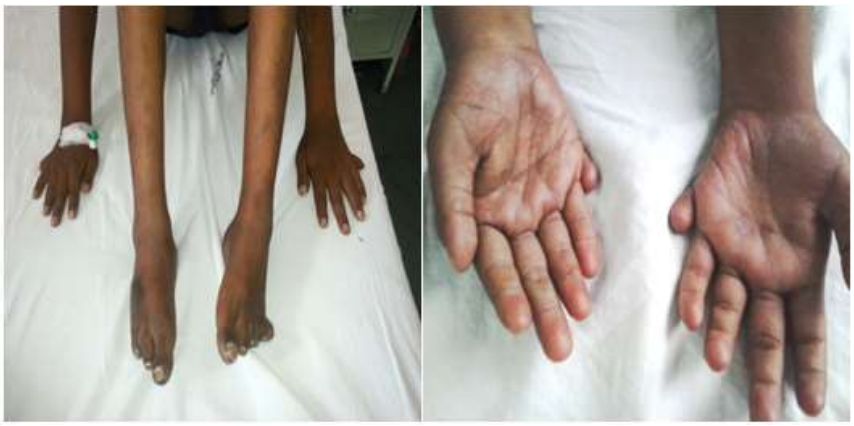

Fig. 1: postaxial polydactyly with hexadactyly of hands and feet

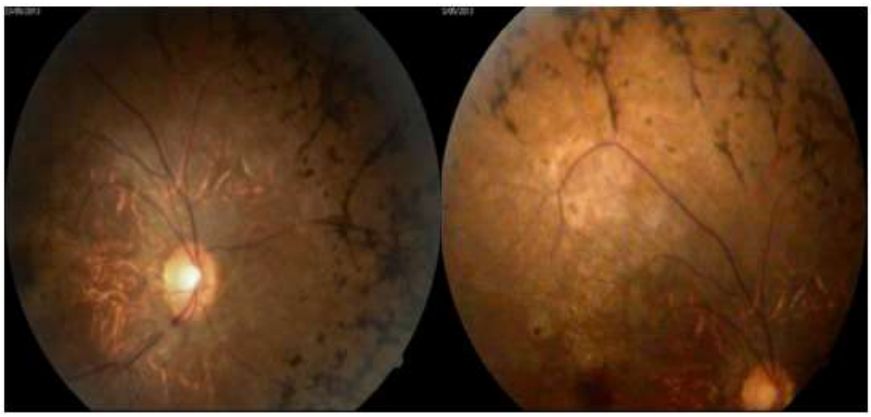

Fig. 2: Optic fundi photography reveals atypical retinitis pigmentosa in both eye

DISCUSSION

Bardet-Biedl Syndrome is named after Georges Louis Bardet, a French physician and Artur Biedl, a Hungarian Pathologist and endocrinologist. It is a genetically heterogeneous autosomal recessive condition and about 16 genes have been identified till date [4]. The first known case was reported by Laurence and Moon in 1886 and there was a controversy in medical literature with the condition described by Laurence and Moon, referred as Laurence-Moon syndrome (LMS). After 22yearsof prospective cohort study of Newfoundland families with BBS, Moore et al concluded that BBS and LMS are different spectrum of same entity [5].

The detailed biochemical mechanism that leads to BBS is still unclear. BBS is caused due to defects in the cellular ciliary structure and hence it is a ciliopathy [6].

The primary and secondary features of BBS are given in table 1.

The diagnosis of BBS can be made if four primary, or three primary and two secondary following features are observed. [1]

Rod-cone dystrophy (atypical retinitis pigmentosa) is one of the hallmarks of this disorder and found occasionally in the first decade but present in almost all patients by second decade. Obesity usually begins in the childhood and the severity increases with age and majority of cases exhibit symptoms within the first year of life [1].

Limb abnormalities include post-axial polydactylyin majority and others in varying frequencies are brachydactyly, syndactyly and clinodactyly. And also hypogonadism in males and menstrual irregularities in females are common. Renal failure can occur when there is involvement of renal tubular cilia [7, 8].

Diabetes mellitus is diagnosed in 32-45% of cases with BBS [10 ,11]. It is usually Non-insulin dependent diabetes but occasionally insulin-dependent [9, 11]. Renal disease is the major cause of morbidity

and mortality and 25% die by the age of 44 years [11]. A wide range of renal abnormalities has been described (chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi and vesico-ureterix reflux).

Table 1: The primary and secondary features of BBS

Primary features	Secondary features
• Rod-cone dystrophy • Polydactyly • Obesity • Learning disabilities • Hypogonadism in males • Renal anomalies	• Speech disorder/delay • Strabismus/cataracts/astigmatism • Brachydactyly/syndactyly • Developmental delay • Polyuria/polydipsia (nephrogenic diabetes insipidus) • Ataxia/poor coordination/imbalance • Mild spasticity (especially lower limbs) • Diabetes mellitus • Dental crowding/ hypodontia/small roots/high arched palate • Left ventricular hypertrophy/congenital heart disease • Hepatic fibrosis

Table 2: Differential diagnosis of BBS

Differential diagnosis of BBS
• Laurence Moon syndrome • Cohen's syndrome • Ahlstrom's syndrome • McKusick Kaufmann syndrome

Diagnosis of BBS is mainly based on characteristic clinical features. The other investigations are performed to assess for the secondary features that may help in the diagnosis. Genotyping may not always be required to make the diagnosis as it is not available at all places specially developing countries like India. But Genetic testing of family members facilitates carrier detection, genetic counselling and the early diagnosis of affected family members.

Our patient had polydactyly, retinitis pigmentosa, mental retardation, renal abnormalities, type1 Diabetes mellitus, conductive hearing loss, congenital heart disease, dental anomalies i,e four primary and four secondary clinical features. Type 1 diabetes mellitus was the presenting complaint, which made this case very rare. The differential diagnosis of BBS is shown in table 2.

A multidisciplinary approach is needed for managing thissyndrome based on clinical manifestations. Regular monitoringof renal, liver, glucose, lipid and endocrine profile is necessary. Attention should be paid to blood pressure and weight management along with regular ophthalmological examination. Visual aids, special schools, educational programmes to over come learning disabilities are important. Speech therapy, behavioral therapy and hormone replacement therapy are required in many cases. Surgical removal of accessory digits may be necessary for cosmetic purpose.

CONCLUSION

The diagnosis of BBS in this case was made on the basis of clinical features and the case is reported for its rare presentation with type 1 DM.

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