Case Report

BARDET BIEDL SYNDROME WITH MEGALOBLASTIC ANEMIA

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ABSTRACT
Bardet Biedl Syndrome (BBS) is a multisystem autosomal recessive rare disorder having variable symptoms ranging from peripheral obesity, retinal degeneration, polydactyly, hypogonadism, and renal impairment among many other features. We present a case of 16 years old female exhibiting characteristic features of Bardet Biedl Syndrome.

Key Words: Bardet Biedl syndrome, Obesity, Polydactyly, Hypogonadism

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INTRODUCTION

Bardet Biedl Syndrome is a ciliopathic autosomal recessive rare disorder with variable expressivity and a wide range of clinical variability within families. It was 1st reported by Bardet and Biedl in 1920.[1] It was once thought that the syndrome, described by Lawrence and Moon in 1866, was the same as described by Georges Bardet and Artur Biedl in the early 1920s, but these syndromes are now recognized as two separate entities.[2,3] The main features are Rod-Cone dystrophy with childhood-onset of visual loss preceded by night blindness, postaxial polydactyly, truncal obesity, specific learning difficulties, male hypogonadism, and complex female genitourinary malformations along with renal dysfunction.[4,5]

In this report, a case of Bardet Biedl Syndrome is being presented that is not very common in clinical practice. It exemplifies the need for multidisciplinary management in such cases.

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CASE DESCRIPTION

Clinical situation and course of events

A 20yrs old girl presented to the emergency department of mayo hospital with a complaint of dyspnea for three months for which she had repeated blood transfusions at some local care. The last transfusion resulted in the development of some rash along with worsening dyspnea. Later she presented to Mayo hospital with the same complaint. For the past 2 weeks, she also developed jaundice along with exertional dyspnea of grade III, relieved with rest, not associated with orthopnea, paroxysmal nocturnal dyspnea, cough, hemoptysis, wheeze, and chest pain. She developed a fever after the last blood transfusion, low grade in intensity, not recorded properly, intermittent, not associated with rigors & chills or vomiting.

No history of cough, sputum, palpitations, sweating, sore throat, diarrhea, dysuria, burning micturition, and night sweats. No history of itching, clay-colored stools abdominal pain, hematemesis, or Malena was there with jaundice. A major source of history was her mother. According to her, the patient is also gaining weight for the last 2 years with normal hair patterns & growth along with hyperpigmentation on fingers, toes, and nape of the neck. She also developed polyuria for the last 2 years with

no polydipsia or polyphagia. No history of heat or cold intolerance was there.

Born out of consanguineous marriage, she was delivered through normal vaginal delivery at full term at a local setup and was given immunization. No history of jaundice, birth asphyxia, difficulty in feeding, and cyanosis. She had delayed mental and physical growth with delayed developmental milestones as told by her mother. She started sitting at the age of 1yr, walking at the age of 4 years and started talking at the age of 6 years. She has had polydactyly and night blindness since birth along with decreased vision (both far and near). In the past 2 years, she developed some problems with daylight vision as well. She is more agitated and rational towards fellows while playing, having abnormal eating habits as well. Menarche was achieved at the age of 14 with normal menstrual history from then onwards. She has 4 siblings; all of them are normal and healthy.

The young girl weighed 88 kg, height 170 cm, BMI of 30.4 kg/m2 with stable vitals. Pallor, jaundice along with hyperpigmented fingers, toes and nape of the neck were present. Buffalo hump, central obesity, depressed nasal bridge, high arched palate and short stubby hands and feet & postaxial polydactyly were present in left hand &foot.

CNS examination revealed the patient's poor memory, low IQ and scanning speech which didn't make sense. The sensory and motor systems were normal. She had gait ataxia with no signs of nystagmus, tremors and positive glabellar tap. Cranial nerve examination revealed visual acuity reduced to the perception of light in both eyes. Fundoscopy illustrated features of retinitis pigmentosa. She had a Mini-mental state examination score of 9 showing severe cognitive impairment. Cardiovascular, respiratory, GIT and genitourinary examination remained unremarkable.

Her Labs revealed a Hb level of 5.7g/dl with an MCV of 103.1fl. Peripheral blood film revealed macrocytosis, poikilocytosis and anisocytosis. Serum Vitamin B12 levels were markedly reduced with normal folate levels. Serum cortisol n ACTH was normal. Her HbA1C turned out to be 6.8%. LFTs revealed raised bilirubin level of 5.8mg/dl with predominant indirect bilirubin and raised alkaline phosphatase and LDH showing ineffective erythropoiesis because of Vitamin B12 deficiency. Serum calcium was normal with raised PTH. Urine examination revealed protein in traces. Echocardiography, USG abdomen and thyroid profile were also normal. X-ray of hands n feet didn't show any bony abnormality.

Clinical resolution

She was given blood transfusion along with Vit B12 replacement and oral hypoglycemics and further symptomatic management & was asked to follow regularly in OPD consultation with pediatrician and endocrinologist was also made.

DISCUSSION

The prevalence of Bardet-Biedl syndrome is 1 out of 160000 persons in North America and Europe. A higher incidence rate has been seen in Newfoundland (one out of 13000).[6] The Incidence of BBS in Pakistan is not known.

Bardet-Biedl syndrome can be due to the mutations in at least 14 different genes termed as the BBS genes. BBS genes mutations result in problems with the structure as well as the function of cilia.[7,8] Mutations in the BBS1 gene cause about one-fourth of all cases of Bardet-Biedl syndrome. Another major contributor to these stats is the BBS10 gene which results in 20 percent of cases.[8] In25% of the patients, the cause of the syndrome is still unknown.

The most prominent and major feature of BBS is complete Retinal dystrophy. The second main feature of BBS is obesity whose frequency ranges from 72-to 96% according to measurement criteria.[4]

The 3rd prominent finding in BBS is abnormalities of Limbs. The Post-axial polydactyly (ulnar side of the hand and on the fibular side of the foot) along with brachydactyly of both feet and hands are the most frequent deformities. Mental idiocy is a

complex and debatable finding of BBS. Results of recent object IQ tests showed that only a minority of patients are mentally retarded.[9]

Hypogenitalism is also reported in BBS. In females, genital abnormalities include hypoplastic fallopian tubes, ovaries, and uterus, absent vaginal and/or urethral orifices, partial and complete vaginal atresia[3] while in males the BBS small penis and testes are found in 88% of the patients.[10]

According to the criteria developed by Dr. Philip Beales, a patient who had four primary features or three primaries along with two secondary features are considered as BBS patients. Primary features include rod-cone dystrophy, polydactyly, obesity, hypogonadism in males, learning disabilities, and renal anomalies. The Secondary features include speech disorder or delay, brachydactyly/syndactyly, strabismus/cataracts/astigmatism, polyuria/polydipsia (nephrogenic diabetes insipidus), developmental delay, mild spasticity (especially lower limbs), diabetes mellitus, ataxia/poor coordination/imbalance, hypertrophy of left ventricle, other congenital heart diseases, dental crowding/high arched palate, and hepatic fibrosis.[4,5]

Our patient had four major criteria along with minor criteria that fulfill the diagnostic criteria of Bardet-Biedl syndrome.

Management consists of a multidisciplinary approach. The prognosis of BBS is adverse, with early onset of blindness, hypertension, diabetes mellitus, and obesity. Renal impairment is common and often remains undetected. Surveillance includes annual blood pressure measurement, regular ophthalmologic evaluation, monitoring of renal function, regular testing for blood sugar levels and lipid profile. Failure to diagnose partial or incomplete cases may be the reason the disease is considered rare. Pediatricians, ophthalmologists, endocrinologists, and nephrologists should be aware of BBS because of its adverse prognosis.

CONCLUSION/LESSONS TO BE LEARNT

It isn't confirmed if the presence of megaloblastic anemia is an association with BBS or only a mere coincidence, but such hematological manifestation may be of real clinical importance. As the disease is often missed in childhood and a diagnosis could be delayed later in life. Management of it consists of a multidisciplinary approach.

AUTHOR'S CONTRIBUTION

HL: Drafted manuscript
NF: Literature search & data collection
RR: Critical review
AI: Conception of idea

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