A RARE CASE REPORT ON BARDET BIEDL SYNDROME ASSOCIATED WITH SITUS INVERSUS

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ABSTRACT
Bardet Beidl Syndrome is a rare, autosomal recessive inherited disorder. A few cardinal features of Bardet Beidl Syndrome include central obesity, hypogonadism, retinitis pigmentosa, mental retardation, delay of speech, syndactyly and polydactyly. Other manifestations like Diabetes mellitus, heart disease and neurological manifestations are common. Situs describes the anatomic position of cardiac atria and viscera. Situs inversus is a genetic condition that causes the organs in the chest and abdomen to be positioned in a mirror image from their normal position. We report a case of Bardet Beidl Syndrome with Situs inversus and secondary feature of Type I Diabetes mellitus.

KEYWORDS: Bardet Beidl Syndrome, Situs Inversus, Type I Diabetes mellitus.

INTRODUCTION
Bardet Biedl Syndrome (BBS) is a rare ciliopathic human genetic disorder with involvement of multisystem and wide spectrum of clinical features.1,2 It is characterized by cardinal symptoms of marked central obesity, rod-cone dystrophy (sometimes called atypical retinitis pigmentosa), postaxial polydactyly, mental retardation, renal dysfunction, hypogonadism in males and menstrual irregularities in females, as well as other minor frequent features such as anosmia, ataxia or Hirschspring disease.2,3,4 Bardet Biedl Syndrome occurs throughout the world with prevalence rate of 1:14,000 to 1:16,000 in North America and Europe respectively. Population with a high rate of consanguinity or from isolated regions have been characterized with a higher frequency of Bardet Beidl Syndrome such as Kuwait (1:17,000) and Newfound land (1:18,000).5 In India the actual prevalence rates are unknown and a few cases have been reported. Bardet Beidl Syndrome is distinguished from much rarer Laurence-Moon Syndrome, in which retinal pigmented degeneration, mental retardation and hypogonadism occurs in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly.5 We report here a rare case of Bardet Beidl Syndrome in 32year male with additional findings of Situs Inversus, Dextrocardia, Congenital Heart Disease and Type-I diabetes mellitus which is rarely seen in clinical practice.

CASE REPORT
A 32year male patient presented to emergency medical department of SVRRGG Hospital, Tirupati with complaints of sudden loss of consciousness followed by altered sensorium. On careful history, he had frequent loss of consciousness for 10-15minutes followed by regain of consciousness. No history of fever, chest pain, vomiting, loose stools, seizures, weakness of limbs. He was a known case of Congenital Heart Disease, Situs Inversus by birth; at the age of 5years he attained complete blindness (Fig-1). He was a known case of Type-I diabetes mellitus for past 4years and was on therapy with Injection Insulin Mixtard 20units at morning and 15units at night with good drug compliance.

On examination he was unconscious. His pulse rate was 78beats/min with normal volume; blood pressure was 150/90 mm of Hg. He had no signs of pallor, pedal edema, raised JVP, cyanosis, clubbing, jaundice. There was polydactyly in all four limbs (Fig-2), syndactyly in three limbs, central obesity and ataxia was present. His height was 140cm, weight was 55kg and BMI was 28.1kg/m². The fundus examination had suggestive features of retinitis pigmentosa. On cardiovascular system examination the apex beat was present on right side in 5th intercostal space, mid clavicular line with normal first and second heart sounds and no murmur were heard. On other system examinations no abnormalities were detected.
Lab investigation showed Hb-14.7g/dl, WBC-7,700cell/cc mm, platelets-1.57lakh cells/cc mm, FBS-274mg/dl, RBS-384mg/dl, blood urea nitrogen-50mg/dl, serum creatinine-2.2mg/dl, serum Na⁺-131mmol/lit, serum K⁺-3.4mmol/lit, serum Cl⁻-92mmol/lit and testosterone- 172.52ng/dl (Normal range-241-827ng/dl) which indicates presence of hypogonadism. Urine analysis showed presence of albumin with no sugar and deposits in urine. US abdomen was normal i.e., no obvious sonological abnormalities detected. ECG findings showed positive P waves in lead 2, 3, avf and negative P waves in lead 1, avl; in lead 1 all waves P, QRS, and T are negative; in lead avr all waves are positive (Fig-3). Chest X-ray showed dextrocardia (Fig-4).
Fig 4: XSitus Inversus.
DISCUSSION

Bardet Beidl Syndrome is named after Georges Louis Bardet, a French physician and Arthur Beidl, a Hungarian pathologist and endocrinologist (3). It is a genetically heterogenous recessive disorder and about 18 genes (BBS1 – BBS18) and 7 BBS proteins (BBS1, 2,4,5,7,8 and 9) have been identified, which are located in the basal body and cilia of the cell (6). The most common defective gene associated with Bardet Beidl Syndrome is BBS1 gene located in the long arm (q) of chromosome 11(11q13). Researchers have determined that approximately 20-30% of individuals with Barder Beidl Syndrome do not have a mutation in one of the 18 identified genes indicating that more genes yet to be identified which causes Bardet-Beidl Syndrome. The most plausible hypothesis regarding a shared function for BBS protein is that they assist microtubule-related transport and cellular organization processes, in particular relating to ciliary flagellar and centrosomal activities (2,7). Recently a study by using round worm C.elegans as a model system, biologist found that BBS proteins are involved in a process called Intraflagellar Transport (IFT), a bidirectional transportation activity within the cilia along the long axis of the ciliary shaft that is essential for cilogenesis and maintenance of cilia. A theory that photoreceptor cells are nourished by the Intraflagellar transport (IFT) of retinal cilia now offers a potential explanation for the retinal dystrophy common in Bardet-Beidl Syndrome patients after their early years of life (8).

Diagnosis is usually done at childhood by detection of characteristic findings (e.g. visual problems due to retinal dystrophy, obesity, polydactyly). In 1999, modified diagnostic criteria were defined after a study conducted in England in 109 Bardet-Beidl Syndrome patients. Patients who had four primary characteristics/ three primary and two secondary characteristic criteria were identified as BBS (1). Genetic testing may assist in diagnosing the disorder, as it is not available at all places especially in developing countries like India.

Our patient has polydactyly, syndactyly, retinitis pigmentosa, mental retardation, obesity, hypogonadism, ataxia, congenital heart disease, Type-I Diabetes mellitus i.e. 4 primary and 4 secondary clinical features along with situs inversus. Type-I diabetes mellitus was the presenting complains which made this case rare.

A multidisciplinary approach is needed for managing this syndrome based on the clinical manifestations. Treatment may require the coordinated efforts of a team of pediatricians, orthopedic, surgeon, cardiologist, dental specialist, speech pathologist, audiologist, ophthalmologist, neurologist and other healthcare professionals. Surgery may be performed to correct certain genitourinary abnormalities, abnormalities of the fingers or congenital heart defects. Regular monitoring of renal, liver, glucose, lipid and endocrine profile and ECG is necessary. Attention should be paid to high blood pressure, weight management with regular ophthalmological examination. Early intervention is important in ensuring that children with BBS reach their highest potential. Genetic counseling may be of benefit for affected individuals and their families (7).

CONCLUSION

BBS is a genetic disorder with variable expressivity and a wide range of clinical variability. The diagnosis was made on the clinical features. So far there are limited cases reported on Bardet Beidl Syndrome in association with situs inversus and secondary feature of Type I Diabetes mellitus.

REFERENCES