Case Report

Bardet-Biedl Syndrome Associated with Dextrocardia and Situs inversus

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Abstract
Bardet-Biedl syndrome is a rare, autosomal recessive inherited disorder. A few cardinal features of Bardet-Biedl syndrome include central obesity, hypogonadism, retinitis pigmentosa, mental retardation, delay of the speech and polydactyly. We report a case of Bardet-Biedl syndrome with typical phenotype in conjunction with dextrocardia and Situs inversus with review of literature.

Key words: Bardet-Biedl syndrome, Hypogonadism, Obesity, Polydactyly, Retinitis pigmentosa.

Introduction
Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder.1 BBS is named after Georges Louis Bardet, a French physician (born 1885) and after Artur Biedl, a Hungarian pathologist and endocrinologist (born 1869) who described this syndrome in 1920.2 It was later erroneously coupled with another disorder described by Laurence and Moon, and was consequently referred to as Laurence- Moon-Biedl syndrome. BBS is distinguished from the much rarer Laurence- Moon syndrome, in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly.3 The principal manifestations are rod-cone dystrophy (Retinitis pigmentosa), post-axial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction.1 We report here a typical case of Bardet-Biedl syndrome in a seven year old boy with additional finding of dextrocardia and situs inversus which is rarely seen in clinical practice.

Case Report
A seven year old male child resident of Kohinoor Mill, Rawalpindi, presented with complaints of poor vision especially at night, learning difficulties, and rapid weight gain. He was born from consanguineous marriage, through normal vaginal delivery at full term with no antenatal, natal or postnatal complication. However his developmental milestones were delayed. He started walking at 1 year and 10 months. He learned to speak at 3 years of age. His vision gradually decreased especially in dim light while hearing and social milestones were normal. Currently he is studying in main stream school but his performance is not optimum. His writing and reading abilities are more affected than his memory. He is the eldest among the three siblings. His parents and 2 year old sister are healthy, while one sister who is 5 year old is also having similar features.

On examination his weight was 29.5 kg at 95th centile, height was 113cm at 5th centile, BMI 23.10 kg/m², head circumference 51.5cm at 50th centile and blood pressure was 130/90 mmHg (both systolic and diastolic blood pressure above 95th centile). Other findings were short, stubby hands and feet, polydactyly of all 4 limbs, (Figure 1 and 2) low IQ, micro penis with normal testes, Talipes equinovarus at birth which has now been treated successfully with serial casting. Visual acuity without glasses was 6/60 in right eye and 6/36 in left eye and with glasses 6/12 in both eyes. Fundoscopy showed retinitis pigmentosa as shown in Figure 3. On Cardiovascular system examination, apex beat was on right side in 5th intercostal space, midclavicular line with normal first and second heart sounds and no murmur.

Laboratory investigations showed raised fasting blood sugar, fasting serum cholesterol and triglycerides. Blood complete

Figure 1: Post axial polydactyly of hands.
picture, renal function tests, liver function tests and thyroid function tests were within normal limits.

Figure 2: Post axial polydactyly of feet.

Figure 3: Retinitis Pigmentosa

Figure 4. Chest x-ray showing dextrocardia and situs inversus.

Radiological investigations showed dextrocardia on chest x-ray as shown in Figure 4. Echocardiography showed no abnormality other than dextrocardia. Ultrasound abdomen revealed situs inversus with cholelithiasis and no urinary tract anomalies.

He has been receiving multidisciplinary management. In infancy, orthopedic surgeon treated Talipes equinovarus successfully with serial casting. Due to short stubby feet and polydactyly he cannot wear normal shoes. So he uses special shoes manufactured by limb centre of Fauji Foundation Hospital, Rawalpindi. His vision is much improved with the help of glasses prescribed by ophthalmologist and he regularly receives antioxidant therapy in form of high dose of vitamin A drops at 6 month interval to slow the progression of retinitis pigmentosa. As echocardiography showed dextrocardia with situs inversus and functionally normal heart so no treatment is needed. His speech is much improved through speech therapy and he is advised to join special education school to improve his skills for independent living. Low fat and carbohydrate diet and regular exercise is advised and he is advised for follow-up after 3 months. He will specifically need to be followed up for pubertal development for the next few years as hypogonadism is a likely problem.

Discussion

The prevalence of BBS is 1:160000 in Europe and North America although higher incidence has been reported in the isolated populations of Newfoundland [1:13000] and Kuwait [1:17000].4,5 Incidence in Pakistan is not known. So far there is no reported case of Bardet-Biedl Syndrome with Dextrocardia and Situs inversus in world literature although other congenital heart disease like aortic stenosis, patent ductus arteriosis, unspecified cardiomyopathy, valvular stenosis and atrial/ventricular septal defects are the commonly reported lesions.1 Retinal dystrophy (100%) is the first major feature of the disorder. It is found occasionally in the first decade but is present in almost all patients by the second decade.6 Obesity is the second major feature of BBS, with a frequency of 72-96% depending on measurement criteria. Obesity usually begins in childhood and the severity increases with age. The mean body mass index (BMI) in females is estimated to be 31.5 mg/m² while in males it is 36.6 mg/m².6,7

Limb-abnormalities are the third major feature of BBS. Limb deformities have been reported at varying frequencies. Of these, post-axial polydactyly, (ulnar side of the hand and on the fibular side of the foot) and brachydactyly of both hands and feet are the most common. Partial syndactyly, fifth finger clinodactyly, and a prominent gap between the first and second toes are sometimes associated.1,6 Mental retardation is a more disputed feature of BBS. Recently, objective IQ tests determined that only a minority of patients are mentally retarded. The decrease in IQ level correlates with the presence of visual handicap.1,7 Acquisition of intelligible speech and proper sentence formation is commonly delayed until age of four years, but children tend to respond to early therapy.1,7 Hypogonitalism is reported more frequently in BBS males than females.8 In BBS females, genital abnormalities encompass a wide range, including hypoplastic fallopian tubes, uterus, and ovaries, partial and complete vaginal atresia, absent vaginal orifice, and absent urethral orifice.9 Bardet-Biedl syndrome males have small penis and testes (88%).9 Renal failure is the major cause of morbidity and early mortality in BBS. A wide range of renal abnormalities have been described. These include chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral
Bardet-Biedl syndrome is recessively inherited with both parents being phenotypically normal. The risk of subsequent offspring being affected is 25%. There is a 50% chance that unaffected siblings will be carriers. When a new case is seen, a careful family history should be taken and other relatives examined. Management consists of multidisciplinary approach. The paediatrician should be involved in the overall care of the patient. The child may need referral to ophthalmologist, orthopaedic surgeon, cardiologist, nephrologist, endocrinologist, nutritionist, speech therapist and occupational therapist.

BBS has an adverse prognosis, with early onset of blindness, obesity, hypertension, and diabetes mellitus. Renal impairment is frequent and often goes undetected leading to early death in these patients. 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. Surveillance includes regular ophthalmologic evaluation, annual blood pressure measurement, monitoring of renal function, and regular testing for blood sugar levels 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. Paediatricians, ophthalmologists, endocrinologists and nephrologists should be aware of BBS because of its adverse prognosis.

References