

## Bardet-Biedl Syndrome – A Rare Cause of Cardiomyopathy

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Bardet-Biedl syndrome (BBS) is a rare autosomal recessive condition characterized by retinitis pigmentosa, polydactyly, obesity, learning disabilities, hypogonadism and renal anomalies. Cardiomyopathy in association with BBS has previously being reported only twice in literature. We report a case of a patient presenting with features of cardiomyopathy, who was subsequently diagnosed to have BBS.

**Key words:** Bardet-Biedl syndrome, Cardiomyopathy.

**B**ardet-Biedl syndrome (BBS) is an autosomal recessive condition with a wide spectrum of clinical features. The principal manifestations are rod-cone dystrophy (sometimes called atypical retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. 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 [1,2]. Significant cardiac abnormalities in isolated BBS were first reported by Elbedour, *et al.* [3] in 1994, which included 2 cases of IVS hypertrophy and 1 case of DCM with no identifiable cause. Cardiomyopathy in association with BBS has previously been reported only twice in literature.

### CASE REPORT

A 13-year male child was admitted to the intensive care unit with complaints of progressive breathlessness and cough for three months and recent swelling of his entire body. There was no history of a preceding viral illness, weight loss, haemoptysis, joint swelling, palpitations and decreased urine output. There was no past or family history of tuberculosis or cardiovascular disease. He was tachypneic and tachycardic with a low volume pulse, low BP and pitting edema. On systemic examination, heart sounds were muffled with B/L rhonchi, crepitations and hepatomegaly. Chest X-ray showed cardiomegaly with basal pulmonary infiltrates and ECG was normal. Echocardiography revealed dilated left atrium and ventricle with mild mitral and tricuspid regurgitation with normal sized coronary arteries and no pericardial effusion. Fractional shortening and ejection fraction were 18.5% and 0.38 respectively with no evidence of diastolic dysfunction. A provisional diagnosis of a recent

myocarditis or dilated cardiomyopathy was made. Known risk factors for cardiomyopathy *i.e.* recent viral infections, rheumatic fever, congenital heart diseases, hyper-tension, connective tissue disorders, inborn errors of metabolism, muscular dystrophies, Kawasaki disease etc were ruled out and thus a possible familial/genetic cause was sought. The patient was stabilized and transferred to pediatric cardiology.

Patient had delayed motor and mental development milestones and was the second offspring of non-consanguineous marriage. There was facial dysmorphism, hypertelorism, downward slanting palpebral fissures, flat nasal bridge, long philtrum, and thick upper lip. Postaxial polydactyly and syndactyly was present in the right foot with brachydactyly in all the limbs. He had micropenis, absent axillary and pubic hair, although both testes were palpable in the scrotal sac. His height was 135.5cm, falling between 3-10 centile. On neurological examination: hypotonia, broad based gait, poor coordination, balance, dysdiadochokinesia and past pointing were present without sensory disturbance. Speech was hypernasal and slow. Fundus examination showed retinopathy, bilateral optic atrophy and ERG showed grossly abnormal retinal function in both the eyes, suggestive of atypical retinitis pigmentosa. The IQ was 56. Hearing assessment was normal. Investigations revealed a low hemoglobin (Hb-8 g/dL) and low calcium-(7.9 mg/dL) with raised phosphorus (5.9 mg/dL) and abnormal KFT (BU-117 mg/dL, creatinine-6.4 mg/dL, GFR-9 mL/min/m<sup>2</sup>BSA, serum sodium-115 mmol/L and potassium-4.6 mmol/L) implying chronic kidney disease. Urine examination, GTT, LFT, ABG, C3/C4 levels, ASO and ANA were within normal limits however TSH levels were raised. Ultrasonography revealed bilateral shrunken kidneys with loss of corticomedullary distinction. CECT head was normal. Clinical and echocardiographic screening of other family members was normal.

The constellation of polydactyly, hypogonadism, retinitis pigmentosa, mental retardation and CKD suggested a possibility of Bardet Biedl syndrome. Other supporting features were overcrowding of teeth, gall bladder stones, and primary hypothyroidism.

## DISCUSSION

Till 1970, Laurence Moon Bardet Biedl syndrome (LMBBS) was considered a single entity. However, due to the presence of two distinct phenotypic patterns, it was split into Laurence- Moon and Bardet-Biedel syndromes, with the former characterized by paraparesis and the latter by polydactyly [1]. The characteristic combination of findings in Bardet Biedl syndrome are rod cone dystrophy (93-100%), polydactyly (58-69%), obesity (72-88%), learning disabilities (41-62%), hypogonadism in males (85-90%) and renal anomalies (25-100%) [2,4]. Bardet-Biedl syndrome (BBS) is a rare, genetic multisystem disorder; a ciliopathy secondary to the basal body dysfunction [4,5]. It is associated with mutations in 14 genes [6,7].

Our patient presented with CHF and had 5 primary and six secondary features in accordance with Beales, *et al.* [4] classification. The patient had significantly low ejection fraction with dilatation of the left ventricle suggestive of underlying cardiomyopathy. All other predisposing causes of cardiomyopathy were absent. The alliance of cardiomyopathy with this syndrome has been rarely documented.

McLoughlin, *et al.* [5] surveyed 330 published cases of LMBBS and documented 9 congenital heart diseases which included ASD, VSD, PDA, pulmonary stenosis, hypoplasia of aorta, dextrocardia, and L-TGA. Of these, 6 patients had polydactyly and may be considered as BBS patients although the presence/absence of paraparesis is not mentioned. Seven patients had acquired heart disease most commonly left ventricle hypertrophy, biventricular hypertrophy and rheumatic heart disease. All patients with acquired heart disease also had some form of renal involvement but only 3 were hypertensive [5].

Significant cardiac abnormalities in isolated BBS were first reported by Elbedour, *et al.* [2] in 1994, which included 2 cases of IVS hypertrophy and 1 case of DCM with no identifiable cause. Most of the patients studied were young, thus limiting the discovery of acquired heart disease but authenticating the reported lesions to the basic syndrome. There was no association of cardiac abnormalities with presence of renal involvement, hypertension or high creatinine levels. In these studies, male predominance was apparent and patients were asymptomatic in contrast to our patient who had

symptomatic cardiac disease. In a survey of 109 BBS patients, two were found to have cardiomyopathy [4].

Dilated cardiomyopathy in our patient without an antecedent apparent viral infection might still be late sequelae of a subclinical viral infection of the myocardium. However, with no evidence of metabolic, hereditary, systemic and toxic exposure our case possibly belongs to that of "idiopathic cardiomyopathy" group. BBS thus may be a genetic/familial cause of the same. We thus report the 3rd association of BBS and cardiomyopathy. However, unlike most other documentations, CHF with cardiomyopathy was the presenting complaint leading to the first time diagnosis of this syndrome in our patient. Periodic follow up by echocardiography is required in order to monitor possible progression of heart disease [3].

Alström syndrome is a rare autosomal recessive ciliopathy, which clinically closely resembles BBS and is characterized by childhood obesity, progressive cone-rod dystrophy, sensorineural deafness, dilated cardiomyopathy, hepatic dysfunction, renal insufficiency and endocrinological features. It shares many of the complex spectrums of phenotypic features with BBS. Cognitive function is preserved in Alström syndrome and polydactyly is not a feature, thus distinguishing it from Bardet-Biedl syndrome.

BBS must be considered as a rare cause of cardiomyopathy. The association has been sparsely documented. The absence of predisposing factors and rarity of both conditions makes coincidence less likely.

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## REFERENCES

1. Amman F. Investigations cliniques et génetiques sur le syndrome de Bardet-Biedl en Suisse. *J Genet Hum.* 1970;18:1-310. [Article in French].
2. Green J, Parfrey PS, Harnett JD, Farid NR, Cramer BC, Johnson G, *et al.* The cardinal manifestations of Bardet Biedl syndrome, a form of Laurence-Moon-Biedl syndrome. *New Engl J Med.* 1989;321:1002-9.
3. Elbedour K, Zucker N, Zalstein E, Barki Y, Carmi R. Cardiac abnormalities in the Bardet-Biedl syndrome: echocardiographic studies of 22 patients. *Am J Med Genet.* 1994;52:16
4. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA.

- New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *J Med Genet.* 1999;36: 437-46.
5. McLoughlin TG, Krovetz LJ, Schiebeler GL. Heart disease in the Laurence-Moon- Biedl-Bardet syndrome: A review and a report of three brothers. *J Pediatr.* 1964;65:388-99.
  6. Ross AJ, Beales PL. Bardet-Biedl syndrome [internet] Gene Reviews. Available from <http://www.geneclinics.org/profiles/all.html>. [cited 2008 December]. Accessed on 1 January, 2013.
  7. Yang Z, Yang Y, Zhao P, Chen K, Chen B, Lin Y, *et al.* A novel mutation in BBS7 gene causes Bardet-Biedl syndrome in a Chinese family. *Mol Vis.* 2008;14:2304-8.

## Meningitis due to *Neisseria meningitidis* Serogroup B in India

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Invasive meningococcal disease has a fulminant course and high mortality. *Neisseria meningitidis* serogroup A is predominantly responsible for meningococcal disease in India and the developing countries. Group B meningococcus, which is prevalent in the developing world is uncommon in India. We herein report the second case of group B meningococcal infection from the country, two decades after the reporting of the first case. Ineffective vaccines against serogroup B warrant the need for close surveillance of this disease.

**Key words:** Child, India, *N. meningitidis* serogroup, Surveillance.

Invasive meningococcal disease commonly follows a fulminant course and has high mortality [1]. Thirteen serogroups of *Neisseria meningitidis* have been identified, but six of these serogroups (A, B, C, W135, X and Y) are responsible for majority of the infections worldwide [1]. Serogroup A strains are predominantly responsible for meningococcal disease in developing countries, including India [2]. Serogroup B strains are responsible for outbreaks of meningitis in the developed world where vaccines against serotypes A,C,Y and W135 are extensively used [3]. Group B meningococcus is not prevalent in India, with only one previous report [4]. We herein report the second case of group B *N. meningitidis* infection from the country.

### CASE REPORT

The patient was a one-year-old, boy weighing 7kg who presented to the pediatric emergency with seizures, history of high-grade fever, vomiting, lethargy and decreased oral acceptance since three days. He had multiple episodes of generalized tonic clonic seizures in last 24 hours. He was delivered at full term through an uneventful vaginal delivery. Immunization history was appropriate for age. No history of similar illness was present in the family and immediate contacts. On examination, child was conscious, had no cyanosis and

had bilaterally constricted pupils with sluggish reaction to light. He was febrile (101<sup>0</sup>F) with heart rate of 172 beats per minute and respiratory rate 42 per min. Capillary filling time was less than 3 sec. Anterior fontanelle was full and pulsatile. Neck rigidity was present. There was increased tone in all four limbs, deep tendon reflexes were brisk with bilateral extensor plantars. He had no skin rash. Initial clinical diagnosis of meningitis was made and therapy with intravenous ceftriaxone and anticonvulsants was started, in addition to supportive management.

Laboratory reports revealed that the child had hemoglobin of 8.1 g/dL with total white blood cell count of 10,610/mm<sup>3</sup> (56% neutrophils, 38% lymphocytes, 3.9% monocytes and 1.2 % eosinophils), and platelet count of 5.9 lakh/mm<sup>3</sup>; C-reactive proteins was raised (178.97 mg/L). The blood pro-calcitonin levels were 118.23 ng/mL (≥10 ng/mL and plasma lactate levels were also raised (30.5 mg/dL). Renal function tests and serum electrolytes were within the normal range. The cerebrospinal fluid showed raised protein levels (113 mg/dL), and low levels of glucose (26 mg/dL). CSF cytology could not be reported because of hemorrhagic nature of tap. CSF lactate levels were increased at 83.93mg/dL and CSF chloride levels were 123 nmol/L. Latex agglutination was performed on the CSF sample and was