| Case | Report |

Bardet–Biedl syndrome

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Abstract

The Bardet-Biedl syndrome is a rare genetically heterogeneous, autosomal recessive inherited disorder with wide variability in expression. It presents with varied clinical manifestations like retinitis pigmentosa, polydactyly, central obesity, mental retardation and renal dysfunction. Other rare manifestations include diabetes mellitus, heart disease, hepatic fibrosis and neurological manifestations. Mutations in 16 genes have been identified as causative factors. We, here, have presented a 12 year old male patient exhibiting characteristic features of Bardet Biedl syndrome.

Introduction

Genetic disorders are common causes of morbidity and mortality in infants and children. Among these genetic disorders, Bardet-Biedl syndrome is a rare disorder. The prevalence rates of 1:140000 to 1:1,60,000 are in North America and Europe respectively.[1] 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 and 1 in 17,000 live births in Kuwait. Male to female ratio is approximately 1.3:1.[2,3] In Bangladesh, the actual prevalence rate is unknown and so far eight cases have been reported.[4-11]

Case Report

A 12 year old boy, 3rd issue of non-consanguinous parents, admitted on July 2015 in the Pediatric ward of Bangabandhu Sheikh Mujib Medical University with the complaints of obesity, poor genital development in relation to other peers, poor vision. On query, mother also gave history of poor interest to surroundings and difficulty with learning.

There was no history of urinary problem, palpitations, hearing impairment, breathing difficulty, dental problem, and limb weakness. He was delivered at home by normal vaginal delivery at term. Birth history was not significant except for the anomaly of polydactyly in his four limbs. He had delayed developmental milestones along with speech delay.

On examination, he had moon face, alopecia and dull looking appearance (Figure 1). His weight was 54 kg (on 95th centile). Height was 142 cm (in between 10-25th centile). Body mass index was 26.8 kg/m^2 (on 97th centile). Bed side urine for albumin and sugar was negative. Musculoskeletal system examination revealed polydactyly in all limbs, short, broad, stubby fingers and toes (Figure 2). He had high arch palate with abdominal distension and hepatomegaly. His stretched penile length was 2 cm. Testicular volume was 2 mL. SMR was Tanner stage 1. On eye examination, visual acuity was 6/36 in both eye. Anterior segment was normal. There was retinitis pigmentosa on both eye. Color fundus photography showed generalized pigmented fundus, maculopathy, arterial attenuation. There were some bony spicule in the periphery (Figure 3). Psychiatric evaluation revealed moderate mental retardation, IQ was 50. CVS examination showed no abnormality.

Routine examinations including CBC, urine analysis, X-ray chest, ECG and echocardiography were normal. Bone age was approximately 8-9 years which was lower than his chronological age (Figure 4). Ultrasonography of whole abdomen revealed hepatomegaly with fatty change and both kidneys were normal. Hearing screening was normal. Biochemistry revealed normal creatinine, raised TG (1299 mg/dL) and ALT (151 U/L). Fasting blood sugar was 24.8 mmol/L. After 2 hours of glucose intake, it was 34 mmol/L. Thyroid stimulating hormone was within normal limit.

We diagnosed the case as Bardet Biedl syndrome as our patient had 4 primary and 5 secondary features.

As there is no specific curative therapy available for this syndrome. The boy was managed symptomatically. Genetic counseling was done. The patient was discharged with diabetic diet,

Table I

Features of Bardet-Biedl syndrome

Primary feature	Our case	Secondary feature	Our case
Rod-cone dystrophy	+	Speech disorder/delay	+
Polydactyly	+	Strabismus/cataracts/astigmatism	-
Obesity	+	Brachydactyly/syndactyly	+
Learning disabilities	+	Developmental delay	+
Hypogonadism in males	-	Polyuria/polydipsia (nephrogenic diabetes insipidus)	-
Renal anomalies	-	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	-

Figure 1: Shows central obesity and polydactyly upper limb

atorvastatin and oral antidiabetic drug. Regular CBG monitoring was advised.

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 determined heterogeneous autosomal recessive condition. About 16 genes have been identified till date which account for approximately 80% of clinically diagnosed cases of Bardet-Biedl syndrome.[12] Among them, BBS1 and BBS10 are the two main genes involved in BBS and each of this gene mutation is present in more than 20% of the cases.[12] The detailed biochemical mechanism that leads to Bardet-Biedl syndrome is still unclear. It is caused by defects in the cellular ciliary structure and hence it is a ciliopathy.[13] 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. After 22 years of prospective cohort study of Newfoundland families with Bardet-Biedl syndrome, Moore et al concluded that Bardet-Biedl syndrome and LMS are different spectrum of same entity.[14] Bardet-Biedl syndrome 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.[15,16]

The primary and secondary features of Bardet-Biedl syndrome are given in Table I. The diagnosis of Bardet-Biedl syndrome can be made if four primary, or three primary and two secondary following features are observed.[2]

Our patient had retinitis pigmentosa and decreased visual acuity. Retinitis pigmentosa is one of the hallmarks of this disorder and found occasionally in the first decade but usually present in almost all patients by second decade. Decreased visual acuity can result from macular involvement of the disease. The patient was obese with hepatomegaly which was may be due to fatty change of liver. He had dyslipidemia associated with obesity. Obesity present in 75% of patients usually begins in the childhood and the severity increases with age.[2] Cause of obesity is unknown but appears to be the effect of a combination of hyperphagia and altered disposal of calories.[2]

Learning disability is a primary feature of BBS, our patient had learning disability probably due to moderate mental retardation and decreased visual acuity. Limb deformities have been reported at varying frequencies. Of these, polydactyly, and brachydactyly of both hands and feet are most common.[2] Our patient had moderate mental retardation, IQ is 50 which is a more disputed feature of BBS. An IQ of 79 or below is found in 44% of BBS patients. The decrease in IQ level correlates with the presence of visual handicap.[2,17] Hypo-genitalism is reportedly more frequently present in Bardet-Biedl syndrome males than females.[2] Bardet-Biedl syndrome males have small penis and testes (88%).[17] Our patient was prepubertal with stretched penile length was 2 cm, testicular volume was 2ml and SMR was Tanner stage 1.

A wide range of renal abnormalities such as chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, vesico-ureterix reflux has been described but our patient had no

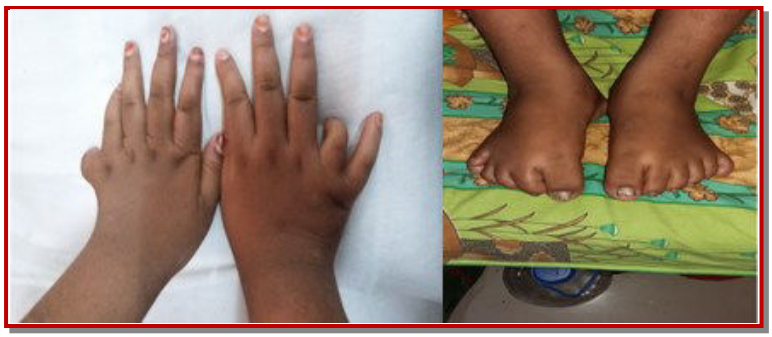

Figure 2: Shows polydactyly of both upper limb and lower limb

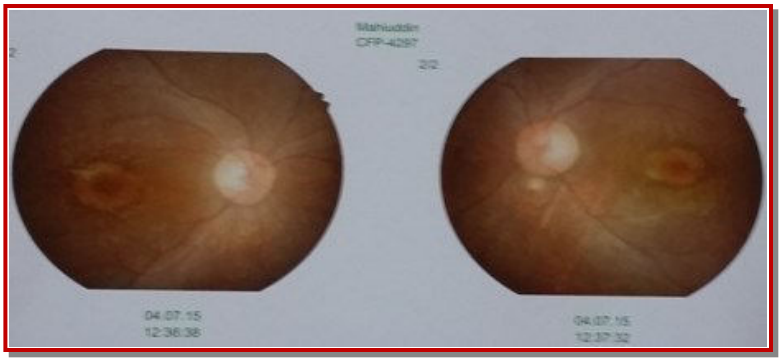

Figure 3: Color photography of fundus showing generalized pigmented fundus, maculopathy, arterial attenuation, some bony spicule in the periphery

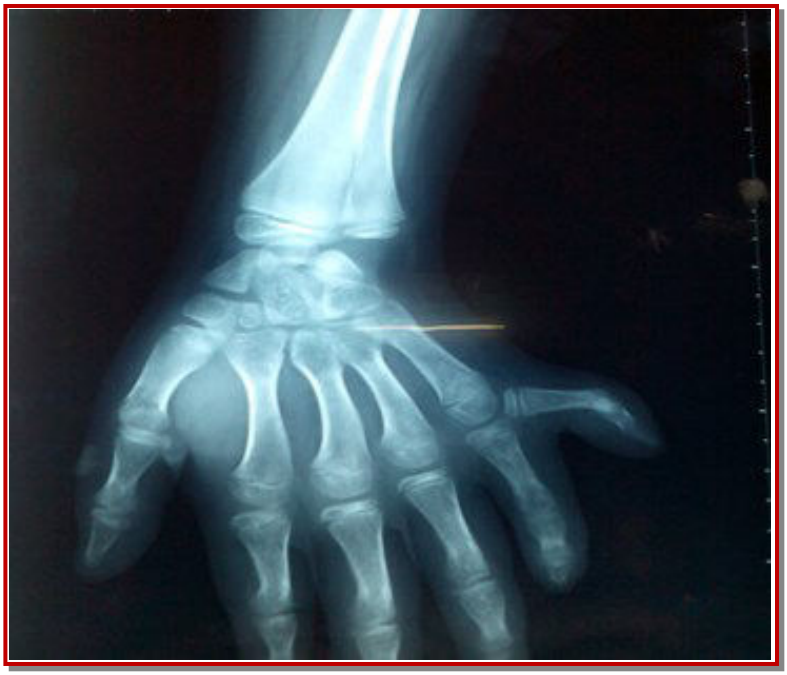

Figure 4: X-ray left hand including wrist joint including hand showing delayed bone age

renal abnormalities. Renal failure is the major cause of morbidity and early mortality in Bardet-Biedl syndrome and 25% die by the age of 44 years.[18] Renal function was found to be normal in our patient.

Diabetes mellitus is diagnosed in 32-45% of cases with Bardet-Biedl syndrome.[18,19] It is usually non-insulin dependent diabetes but occasionally insulin -dependent.[18,20] Our patient had diabetes mellitus and was controlled by oral hypoglycemic drugs. Hussain et al. (2000)[4] reported a case of Bardet-Biedl syndrome in our country in a twelve year old boy having all the cardinal features such as obesity, mental deficiency, polydactyly, syndactyly, retinopathy, genital hypoplasia and renal anomalies.[4] Our patient had 4 primary features such as polydactyly, retinitis pigmentosa, obesity, learning disabilities and 5 secondary features such as diabetes mellitus, speech & developmental delay, brachydactyly, high arch palate but no renal anomalies.

Diagnosis of Bardet-Biedl syndrome is mainly based on characteristic clinical features. Investigations are done to assess the features that may help in the diagnosis. Genotyping of Bardet-Biedl syndrome may not always be required to make the diagnosis as it is not available at all places specially developing countries like Bangladesh.

For management of Bardet-Biedl syndrome a multidisciplinary approach is needed. Regular monitoring of renal, liver, glucose, lipid and endocrine profile is necessary. Attention should be given to blood pressure and weight management along with regular ophthalmological examination. Visual aids, special schools and educational programs to overcome 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

Many progresses have been made about this disease. Further studies are needed to understand the pathophysiology and genetic complexity of the disease. Though the disease is incurable, careful evaluation and symptomatic management may provide good prognosis.

Ethical Issue

Written and signed informed consent from the guardian was taken for publishing this case report.

References

1. Klein D, Ammann F. The syndrome of Laurence-Moon-Bardet-Biedl and allied diseases in Switzerland: Clinical, genetic and epidemiological studies. J Neurol Sci. 1969; 9: 479-513.

2. 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.

3. Beales PL, Warner AM, Hitman GA, Thakker R, Flinter FA. Bardet-Biedl syndrome: A molecular and phenotypic study of 18 families. J Med Genet. 1997; 34: 92-98.
4. Hussain N, Rahman SA, Islam S, Mannan MA, Kawser CA. Bardet-Biedl syndrome: A case report. Bangladesh J Child Health. 2000; 24: 71-73.
5. Haque M, Sharmin L, Islam Q, Ekram A. Bardet Biedl syndrome- A case report. TAJ. 2009; 20: 56-59.
6. Habibullah M, Mohiuddin AA. Bardet-Biedl syndrome. Mymensingh Med J. 2009; 18: 80-83.
7. Nahar K, Chowdhury P, Mahmud N, Chowdhury M. Bardet Biedl syndrome: A case report. J Chittagong Med College Teachers' Assoc. 2011; 21: 44-46.
8. Safder AMB. Quiz: Images in clinical practice. Birdem Med J. 2012; 2: 66-69.
9. Hossain K, Badruddoza M. Bardet-Bidel syndrome: A case report. Chattagram Maa-O-Shishu Hospital Med College J. 2013; 12: 67-69.
10. Rahman M, Islam N, Biswas S, Zaved H, Dewan G. Laurence-Moon-Bardet-Biedl syndrome: A 19 years girl with total blindness and end stage renal disease. J Med. 2014; 15: 94-97.
11. Ahmed S, Shahin M, Chowdhury R, Ahammad A, Shazzad M, Alam M, Chowdhury M. A 13-year-old female with Bardet-Biedl syndrome: A case report. Bangladesh J Med. 2015; *26*: 31-34.
12. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet. 2013; 21: 8-13.
13. Kumar S, Mahajan BB, Mittal J. Bardet-Biedl syndrome: A rare case report from North India. Indian J Dermatol Venereol Leprol. 2012; 78: 288.
14. Moore SJ, Green JS, Fan Y, Bhogal AK, Dicks E, Fernandez BA, et al. Clinical and genetic epidemiology of Bardet-Biedl syndrome in Newfoundland: A 22-year prospective, population based, cohort study. Am J Med Genet. 2005; 132: 352-60.
15. Laurence JZ, Moon RC. Four cases of retinintis pigmentosa occurring in the same family, and accompanied by general imperfections of development. Obes Res. 1995; 3: 32-41.
16. Schathat AP, Maumenee IH. Bardet-Biedl syndrome and related disorders. Arch Ophthalmol. 1982; 100: 285-88.
17. Jones KL. Bardet-Biedl syndrome: Smith's recognizable patterns of human malformation. 5th edi. Saunders Company, 1997, pp 590-91.
18. O'Dea D, Parfrey PS, Harnett JD, Hefferton D, Cramer BC, Green J. The importance of renal impairment in the natural history of Bardet-Biedl syndrome. Am J Kidney Dis. 1996; 27: 776–83.
19. Green JS, 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. N Engl J Med. 1989; 321: 1002–09.
20. Ross AJ, Beales PL. Bardet-Biedl syndrome. Gene Reviews. Available from http://www.geneclinics.org/profiles/all.html.