CASE REPORT

LAURENCE MOON BARDET BIEDL SYNDROME WITH ANAEMIA

Mariam Asif, Tariq Aziz*, Samer Altaf*, Rukhsana Abdul Sattar*

Medical Student, Sind Medical College, Dow University of Health and Sciences, *Department of Medicine, Jinnah Post Graduate Medical Centre, Karachi, Pakistan

Laurence Moon Bardet Biedl Syndrome is a rare genetic disorder. Consanguineous marriage is usually the common cause. Principal features of Bardet Biedl Syndrome are red cone dystrophy, obesity, polydactyl, hypogonadism and renal anomalies. The diagnosis was overlooked in our patient until he came in our hospital. We here report an infrequent case of autosomal recessive disorder with Anaemia.

Keywords: Congenital Syndrome, Polydactyly, Bardet Biedl, Laurence Moon Syndrome

J Ayub Med Coll Abbottabad 2014;26(4):625–7

INTRODUCTION

In 1866 Laurence and Moon explained a case of 7 years old female with rod-cone dystrophy, hypogenitalism, mental retardation, obesity and polydactyly. Her three elder brothers were also suffering from the same clinical state. In 1920 Bardet described a female patient of 4 years old with the rod-cone dystrophy, fatness and polydactyly (11 toes). She also had dubious mental retardation. After two years of Bardet's report (1922), Biedl studied two cases and highlighted the complete scenario of clinical signs which could be conceivable including skull abnormalities, anal atresia and gastrointestinal conflicts.[1] Since these discoveries, presence of symptoms such as obesity, hypogonadism, retinal pigment defects, psychological hindrance and polydactylism in several conditions as combinations, frequently in children with normal parents (cousin marriages) has been labelled as Laurence-Moon - Bardet -Biedl Syndrome (LMBBS).[1]

Laurence Moon Bardet Biedl Syndrome is an exceptional autosomal recessive disorder characterized by the features of short stature, polydactyly and small penis with hypoplastic scrotum. General learning disability, retinopathia pigmentosa, speech delay and renal abnormalities are also common.[2,3] Vision loss is amongst the major symptoms of LMBBS. It occurs when retina steadily worsens.[2]

We here report a rare and interesting case of LMBBS in 15 years old boy with the additional finding of Anclystoma Duodenale in stools causing anaemia.

CASE REPORT

A 15 years old Muslim boy presented in the outpatient department of a Government hospital, Karachi, Pakistan with chief complaints of shortness of breath since 3 months, loose motions in association with blood, vomiting for 3 days and fever for two days. According to the patient's attendant he was in his usual state of health three months back when he developed shortness of breath which was gradual in onset but progressed relentlessly over months from grade-1 to grade-3. Patient felt shortness of breath even on walking few steps associated with palpitation and dizziness. It was not associated with orthopnea, paroxysmal nocturnal dyspnea, cough, chest pain, hemoptysis and wheeze.

Patient had watery loose motions for 3 days which were black in colour with foul smell, 6–7 times per day associated with abdominal pain and vomiting. Vomiting was projectile in nature and contained food particles. There was no blood in vomits. He had high grade intermittent fever (102 degree F) with the fever free interval of 2–3 hours. It was associated with rigors and chills mostly occur at the night time and relieved by taking antipyretics.

Birth history revealed that he was born out of inter-relative marriage. His mother was normal during pregnancy and had no history of taking any medication during gestation period. He was born at full term by normal vaginal delivery via wet- nurse. History of Birth asphyxia, jaundice, cyanosis and feeding difficulties was negative. The baby was immunized. According to the patient's mother, baby had delayed physical and mental growth with delayed developmental milestones. He started walking at the age of 3 years and spoke when he was 5 years old. The baby had night blindness since birth with decreased vision (both far and near) and polydactyly which was treated surgically. He gained weight promptly.

Patient was admitted multiple times in other tertiary care hospitals for the last three years due to the same complaints and had positive history of multiple transfusions. His parents and siblings are alive and healthy. Physical examination showed young boy with the weight of 60 kg, height 150 cm, BMI of 28 kg/m^2. According to the WHO criteria, he lies under the category of overweight. His pulse was 110 beats/ minute, blood pressure 90/60 mm Hg, respiratory rate 25 breaths/minute and temperature of 100° F. JVP was raised up to 8cm and patient was dehydrated. Signs of jaundice, pedal oedema, cyanosis, koilonychias and clubbing were absent. Axillary hairs were also absent.

Cardiovascular examination depicted the apex beat palpable at the 6th inter-costal space, there was no radio- femoral delay, thrill or left sternal heave. On

Auscultation, both heart sounds were of normal intensity with flow murmur. Normal findings were noted on chest examination. Inspection of pericardium indicated normal shape with no scar and visible palpations.

Genital examination revealed the overextended penile length 2 cm, testicular volume of 2 ml bilaterally, pubic hair were absent and small penis with no scar, redness or swelling. Scrotum was small in size, both testes were present within the scrotum, 2cm in size, firm in consistency, mobile and with irregular borders. There were no signs of varicocele and inguinal hernia.

On Abdominal examination, the patient was found to have a distended abdomen with the absence of shifting dullness fluid thrill. Normal shape and position of umbilicus with invisible pulsations. Stria mark was spotted on the right lower quadrant of abdomen. Spleen was palpable 2 finger breadth below the left costal margin. Digital rectum examination was unremarkable. CNS examination revealed the patient's feeble mind, low IQ level, decreased memory and fluent speech which didn't make sense. Motor and sensory system were normal. His gait was normal with no signs of tremors and nystagmus. Fundoscopy illustrated bony spicules, thin attenuated vessels and mild disc pallor. Findings were evocative of retinitis pigmentosa.

Ultrasound of Abdomen demonstrated the borderline enlargement of liver with coarse texture. Reports indicated splenomegaly (13.3 cm) and small sized kidneys with irregular margins. The results showed normal Liver functions, normal thyroid and coagulation profile and Normal Pattern Haemoglobin Electrophoresis. Serum proteins were also with in normal limits.

Figure-1: Polydactyly in feet of the patient, normal hands and abdominal obesity

Laboratory Investigations of the patient

Complete Blood Count (CBC)		
Laboratory Test	Patient's Value	Reference Range
Hemoglobin (Hb)	34 g/L	12–18 years male: mean 145 g/L
Mean Corpuscular Volume (MCV)	70.1 fL	76.5–96 fL
Platelets (PLT)	122×10^9/L	Adult: $140–400\times10^9$/L
Total Leukocyte Count (TLC)	14.08×10^9/L	4.3- 10.8×10^9 /L
Peripheral Blood Smear: Dimorphic population, Normocytic normochromic & microcytic hypochromic, Target cells, Tear drop cells		
S/U/C/E		
Blood Sugar	144 mg/dL	130–200 mg/dL
Blood Urea	46 mg/dL	20.0–40.0 mg/dL
Serum Creatinine	1.5 mg/dL	0.7–1.1 mg/dL
Sodium	140 mmol/L	136–140 mmol/L
Potassium	2.8 mmol/L	3.8–5.2 mmol/L
Chloride	114 mmol/L	98–107 mmol/L
Blood Biochemistry		
Calcium	7.11 mg%	8.6–10.2
Uric Acid	7.01 mg%	M: 3.4–7.0, F: 2.4–5.7
Stool D/R		
Color	Brown	
Mucus	Nil	
Consistency	Soft	
Reaction	Acidic	
Red Cells	Occasional/HPF	
Leukocytes	2–4/HPF	
Macrophages	Nil	
Ova of Pathogenic Protozoa	Anclystoma Duodenale Present	
Vegetative Cyst	Not seen	
Undigested Food	Not seen	
Biochemistry		
Serum FSH level	0.42	Adult male 1.4–15.4 mIU/ml
Serum LH level	0.46	Adult male 1.2–7.8
Serum Testosterone Level	1.21	1-5yr male 0.07–0.87, 6–9 yr male 0.10-1.04 Adult male 9.0–34.72
Echocardiography		
■ Normal sized LV with normal function, Normal valves, EF 79**%**		

In the past 3 years, he was admitted several times in other tertiary hospitals but was never diagnosed. After all investigations, we observed all the primary features of a very sporadic disorder and diagnosed LMBBS. On stool examination, the main cause "Anclystoma Duodenale" was found. It is a blood sucking nematode, which causes gastrointestinal septicity with severe blood loss that leads to iron deficiency anaemia and protein malnutrition.[4]

DISCUSSION

The patient described above was a typical case of LMBBS with the unassociated clinical presentation of anaemia due to the presence of parasite known as Anclystoma Duodenale. The syndrome is very rare usually characterized by retinal degeneration, obesity, extra digits on the hands and feet and intellectual impairment. It was initially explained (1920's) by Bardet and Biedl.[3]

Modern genetic techniques have enabled the scientists to explain the syndromes by specific transformations.[3] Recently at least 14 genes have been reported in associated with this disorder.

These genes often referred as BBS genes are assumed to cause alterations in the cell structures called cilia. BBS genes form proteins which are helpful in maintenance and function of cilia. Mutated genes cause the structural and functional defects in the cilia. Impaired cilia then interrupts the imperative chemical signalling pathways during development and leads to decreased sensual perception. Scientists consider malfunctioned cilia the main cause for the characteristics of LMBBS.[2] Therefore this syndrome is a rare ciliopathy caused by the mutations in different proteins.[5]

Almost 1/4th of all the cases of LMBBS are due to the mutations in the BBS1 gene and 20% cases occurs due to the mutation in BBS10 gene. Other genes are less responsible for such cases. However the cause of syndrome is unidentified in 25 % of patients with LMBBS.[2]

The incidence of renal diseases varies in several reported cases.[5] Most common factor in clinical phenotype of BBS is renal dysfunction. Before 1980's, renal abnormalities were seldom reported while many structural anomalies were observed after the post-mortem. Recent researches have specified that renal dysplasia can be present in such patients without the evidence of renal disease.[6]

Structural renal changes were identified in our patient with renal failure. Laboratory tests revealed elevated levels of Blood urea and serum creatinine.

Management of renal failure in case of LMBBS patients is the same as that for other causes i.e., usually by long- term renal replacement therapy (RRT). RRT includes haemodialysis, long-lasting peritoneal dialysis and kidney transplantation.

This case represents atypical cause of anaemia in LMBBS, which, to the best of our knowledge, has not been described before in literature.

CONCLUSION

The patient showed all the principal features of infrequent autosomal recessive disease called Laurence Moon Bardet Biedl Syndrome. Diagnosis of this syndrome is usually missed due to its scarcity. Pediatricians and other specialties should have enough information on LMBBS for accurate and spontaneous diagnosis due to its conflicting prognosis.

REFERENCES

1. 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;321:1002–9
2. Genetics Home Reference. Bardet-Biedl syndrome. http://ghr.nlm.nih.gov/condition/bardet-biedl-syndrome (accessed 18th Dec 2013).
3. Sahu JK, Jain V. Laurence-Moon-Bardet-Biedl Syndrome. JNMA J Nepal Med Assoc 2008;47(172):235–7
4. Dhawan VK. Anclystoma infection. http://emedicine.medscape.com/article/996361-overview (accessed 12th December, 2013).
5. Mihai CM, Marshall JD, Stoicescu RM, Bardet-Biedl syndrome with end-stage kidney disease in a four-year-old Romanian boy: a case report. J Med Case Rep 2011;5:378
6. Katsanis N, Lupski JR, Beales PL. Exploring the molecular basis of Bardet–Biedl syndrome. Hum Mol Genet 2001;10:2293–9

Address for Correspondence:

Mariam Asif, House No. R-4, Street No. 1, Gulshan Banglows, Gulistan-e-Johar, Block-19, Karachi, Pakistan.
Cell: +92-334-2787852
Email: dr.mariamasif@gmail.com