INTRODUCTION

Laurence-Moon-Bardet-Biedl Syndrome (LMBBS) is characterized by obesity, mental retardation, retinitis pigmentosa, polydactyly and hypogonadism. LMBBS is genetically transmitted by the autosomal recessive pattern of inheritance. For diagnosis, four primary features are required to be present or three primary plus two secondary features. Primary features are rod-cone dystrophy, polydactyly, obesity, learning disabilities, hypogonadism in males and renal anomalies. Secondary features are speech disorder, brachydactyly, developmental delay, polyuria/polydipsia, ataxia, poor coordination/clumsiness, diabetes mellitus, left ventricular hypertrophy, hepatic fibrosis, spasticity and hearing loss.

In addition to these features, short stature, crowding of teeth, hypermobile or lax joints and early osteoarthritis are also reported. The following case reports present two additional symptomatology in patients with LMBBS, which, to the best of our knowledge, have not previously been reported in literature.

CASE REPORT

Case 1: A 16-year-old boy presented to the accident and Emergency Department of Jinnah Postgraduate Medical Centre (JPMC), Karachi, in December, 2007 and was admitted in Medical Ward 7 with diarrhea, vomiting since one month and weakness of all limbs for 2 days. Clinical diagnosis of hypokalemic periodic paralysis was made. Detailed clinical examination revealed a blind Pathan boy of average height and built, pale, lethargic, lying on bed, not moving his limbs, having polydactyly (Figure 1), high arched palate, crowding of teeth and hypermobile joints. The boy’s height and weight was 152 cm and 44 kg respectively. The testis was small, 3 cm (measured by orchidometer) in size, with buried penis. His voice was breathy and with high pitched nasal quality. The ophthalmological examination revealed optic atrophy, bony spicules, and attenuated blood vessels (Figure 2). He was mentally retarded with minimental score of 15/30. These features were consistent with LMBBS. The mother and father had consanguineous marriage. Patient had 7 brothers and 3 sisters. His one elder brother and sister also had similar features, which were consistent with LMBBS. His sister was also obese and died 2 months back following a similar episode of illness.

Complete blood count revealed WBC count 14.0 x 10^3/L with hemoglobin at 9.2 g/dl, MCV of 100 fl, MCH of 32.2 pg/cell and platelet count of 212 x10^3/L, morphology was normochromic, anisocytosis and macrocytosis. Blood glucose was 117 mg/dl, serum urea was 29 mg/dl, and serum creatinine was 1.04 mg/dl. Serum electrolytes measured sodium at 148 mEq/l, potassium at 1.9 mEq/l, chloride at 114 mEq/l, bicarbonate at 18 mEq/l and calcium at 8.8 mg/dl. Urinalysis showed an acidic pH with specific gravity of 1.025 and one + proteinuria, while sugar and acetone were absent. Urinary potassium was 18 mEq/l; 24-hour urinary potassium was 25 mEq/l and urine volume was 1380 ml. ECG showed inverted T-waves. Patient's potassium was replaced intra-venously for the first 24 hours followed by oral potassium supplementation. After the
replacement of potassium, symptoms were improved gradually. Despite treatment, serum potassium remained on the lower side, measuring 2 mEq/l. The patient was discharged on 7th day and advised of oral intake of potassium supplement and acetazolamide 1000 mg/d in divided doses for prophylaxis of hypokalemic paralysis.

Case 2: A 30-year-old male (brother of case 1) presented to outpatient department of JPMC with history of yellow discoloration of skin and sclera, breathlessness, weakness and right hypochondrial pain for 3 months. He was also blind and mentally slow since 3 years of age. Initially, the patient had night blindness. He also had polydipsia, polyuria, increase frequency and urgency since 6 months. Clinical examination revealed a young male of short stature, average built, pale as well as jaundiced, lethargic, having polydactyly, high arched palate, crowding of teeth and hypermobile joints. His height and weight was 152 cm and 53 kg respectively. The right testicle was small (4 cm in size- measured by orchidometer) and left testicle was undescended with buried penis. His voice was also breathy with high pitched nasal quality. Ophthalmological examination revealed optic atrophy, bony spicules and attenuated blood vessels (Figure 3). Mini- mental score was 17/30. His blood pressure was 110/60 mmHg in lying position. ECG and echocardiography were normal. Ultrasound abdomen showed mild splenomegaly and cholelithiasis. Complete blood count showed WBC at 4.8 x 10³/L, hemoglobin at 2.4 g/dl, MCV of 114.3 fl, MCH of 37.5 pg/cell and platelet count of 22 x10³/L. Red cell morphology was normochromic with anisocytosis and macrocytosis. Fasting blood glucose was 160 mg/dl; random blood glucose was 110 mg/dl; serum urea was 29 mg/dl, and serum creatinine was 1.04 mg/dl. Serum electrolytes measured sodium at 155 mEq/l, potassium at 2.90 mEq/l and chloride at 112 mEq/l. Urinalysis revealed pH of 5, specific gravity of 1.025 and one + proteinuria with 20-25 pus cells. Sugar and acetone were absent. Liver function tests showed total bilirubin of 1.6 mg/dl, direct bilirubin of 0.6 mg/dl, indirect bilirubin of 1.0 mg/dl, alanine aminotransferase level of 97 U/l, aspartate aminotransferase level of 22U/l, alkaline phosphatase at 211 U/l and gamma-GT level of 27 U/l. Serum lactate dehydrogenase was 582 U/l. Bone marrow examination revealed megaloblastic changes. Four units of packed cell volume were transfused and potassium and vitamin B₁₂ replaced. Potassium was replaced orally 40 mEq/day in the form of syrup. Intramuscular injection of 100 mcg of vitamin B₁₂ was initially given daily for one week, weekly for first month, and then advised monthly for one year. He continued to do well on long-term follow-up.

DISCUSSION

Laurence-Moon-Bardet-Biedl Syndrome is an uncommon disorder. It is an autosomal recessive disorder. Both parents must be carriers of the defective gene and both must pass on the defect to the child in order for the child to be affected. If both parents carry the defective gene, responsible for causing LMBBS, there is 1 in 4 chance of having a child with the syndrome. Prevalence rates in North America and Europe range from 1:140,000 to 1:160,000 live births. However, in Kuwait and Newfoundland, the rate is much higher, with an estimated incidence of 1:13,500 and 1:17,500, respectively. In our country, there is high frequency of consanguineous marriages, especially in Pathans and other ethnic groups. The exact prevalence of this syndrome in our population is not known. LMBBS are no longer considered as valid terms; recently, the syndrome split into Laurence-Moon Syndrome (LMS) and Bardet-Biedl Syndrome (BBS). Where LMS is characterized as the cases involving mental retardation and spastic paresis and BBS involves obesity, polydactyly, and learning disabilities. The significant point about these cases was that obesity was not a common feature. Only one affected sibling was obese. One possible reason for the overestimates may lie in the definition of obesity. Retinal dystrophy is the first major
feature of the disorder. It is occasionally found in the first
decade but present in almost all patients by the second
decade. Limb-abnormalities are the second major
feature of BBS. Limb deformities have been reported at
varying frequency. Of these, post-axial polydactyly,
and brachydactyly of hands and feet are the most
common. The decrease in IQ level correlates with the
presence of visual handicap. Hypogenitalism is
reportedly more frequent in BBS-affected males than
females. The cause of megaloblastic anemia in these
cases may be due to gastrointestinal fibrosis which
leads to malabsorption. Renal malformations in BBS
had been reported infrequently, although a high
frequency of structural abnormalities were observed
postmortem. Polyuria and hypokalemia, as seen in
these cases, may be explained by renal abnormalities
common in this condition.

REFERENCES
1. Flier JS, Maratos-Flier E. Obesity. In: Karper DL, Fuci AS,
Harrison's principles of internal medicine: 16th ed. New York:
2. Bonita F, Craig I, Sheila K. Renal histopathological changes in a
30:1077-81.
2008 May 10]. Available from: http://www.blindness.org/
visiondisorders/causes.asp.
4. Laurence-Moon-Bardet-Biedl syndrome - more than meets the
eyes. Laurence-Moon-Bardet-Biedl Society. [Updated 14 Nov
2004; cited]. [Cited 2008 May 10]. Available from:
www.lmbbs.org.uk/-9k.
5. Special child: disorder zone archives - Laurence-Moon-Bardet-
Biedl syndrome. [Cited 2008 May 10]. Available from:
http://www.specialchild.com/archives/dz-035.html
6. Katsanis N, Lupski JR, Beales PL. Exploring the molecular basis
7. Bardet-Biedl syndrome – Wikipedia, the free encyclopedia
[Internet]. San Francisco (CA): Wikipedia Foundation Inc
Bardet-Biedl syndrome
8. Fulton AB, Hansen RM, Glynn RJ. Natural course of visual
111:1500-06.
Smith's recognizable patterns of human malformation. 3rd ed.
criteria for improved diagnosis of Bardet-Biedl syndrome: results