LAURENCE-MOON-BARDET-BIEDL SYNDROME - PRESENTING WITH ACUTE ONSET OF DIABETES MELLITUS

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Introduction

Laurence-Moon-Biedl (LMB) syndrome is a rare familial disorder, inherited by autosomal recessive characteristic with variable penetrance and expressivity [1]. This syndrome is characterized by 5 cardinal features - obesity (95%), mental retardation (90%), retinal degeneration (90%), hypogonadism (75%), and polydactyly (75%) [2]. The pentad of symptoms is present in less than half of the cases. However some workers differentiate between Laurence-Moon and Bardet-Biedl syndrome by the presence or absence of polydactyly and spastic paraparesis [3-4]. Several cases have been reported with variable features [2,5]. Glucose intolerance is reported in 14-45 per cent of cases [2,4,6] but diabetes mellitus requiring drug treatment is rare. Here we report a case of LMB syndrome who has presented with acute onset of diabetes mellitus requiring insulin treatment.

Case Report

A 22-year-old male (Fig 1 - IV.2) was admitted with acute onset of polyuria, polydipsia and loss of weight for 3 weeks. He was born of a full term normal delivery at home. He had no genital ambiguity at birth and early developmental milestones were normal. However, his scholastic performance was poor and puberty was delayed. He had several episodes of generalised tonic-clonic convulsion since 3 years of age. He was treated with some tablets, nature of which parents were not aware of. The last seizure was at the age of 10 years. His parents (III.3 and III.8) were first cousins (Fig 1). There was no history of diabetes, obesity, infertility or polydactyly in the family.

Physical examination revealed height 160 cm, span 170 cm, upper segment 75 cms and body mass index 21.48 kg/m². He had gynecomastia stage 3 (Tanner and Marshall 1970). There was no polydactyly, syndactyly or brachydactyly of hands or feet. There was no facial hair. Pubic hair was stage 2 (Tanner and Marshall 1970). Stretched penile length was 4.5 cm. Right testis measured 1 cm x 1 cm and left was 1.5 cm x 1.0 cm. Visual acuity was 6/9 for right eye and 6/12 for left eye. Fundus examination revealed evidence of retinitis pigmentosa. Electroretinogram measured 15 uv

and 21 uv in right and left eye respectively. Intelligence quotient was 86. Pure tone audiometry was normal in both ears.

Investigation showed hemoglobin 14.1 gm per cent, blood glucose fasting 405 mg/dL and post-prandial 523 mg/dL (60-100), glycosylated hemoglobin 16.5 per cent, blood urea 19 mg/dL (14-38), serum creatinine 0.8 mg/dL (0.5-1.8), serum sodium 139 meq/L (130-149), serum potassium 3.7 meq/L (3.5-5.0), serum bilirubin 0.9 mg/dL (0.1-1.0), serum calcium 9.3 mg/dL (9.0-11.0), serum phosphate 3.7 mg/dL (2.5-4.5), serum alkaline phosphatase 180 IU/L (90-180), serum total protein 7.1 gm/dL (6.0-7.8) and serum cholesterol 155 mg/dL (150-250). Electrocardiogram was within normal limits. Urine revealed glycosuria without ketonuria. Radiograph hand and feet were normal. Karyotype was 46 XY. Basal leutinising hormone (LH) was 14.5 mIU/mL (5.0-20.0), follicular stimulating hormone (FSH) 40mIU/mL (5.0-20) and testosterone 0.5 ng/mL (2.9-10.9). Serum insulin level was 7.5 microU/mL (5-35). Ultrasonographic examination of abdomen did not reveal any renal or hepatic abnormality. CT scan head was normal. He was treated with insulin therapy (mixed split regimen) because he did not respond to oral hypoglycemic therapy.

Discussion

Children with LMB usually present with mental retardation, night blindness or renal disease [7]. Retinal pigmentary changes are present in 80-100 per cent of cases [3,4]. Retinal degeneration with or without the classical appearance of retinitis pigmentosa may not be evident early, though it causes blindness in many affected patients by the age of 30 years. Decreased

Fig. 1 : Pedigree chart

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visual acuity becoming apparent at the school age is often the first sign [5]. Nystagmus, optic atrophy, bilateral keratoconus, internal and external ophthalmoplegia, telecanthus, epicanthal fold and bilateral ptosis [5] have also been reported in some of these patients.

Mental retardation has been reported in 41-90 per cent [3,4]. Green et al reported relation between IQ and visual deficit. Six of 7 patients with IQ < 70 had visual acuity inadequate for counting fingers. Only minority of patients (41%) were mentally retarded if IQ is adjusted for visual impairment.

Obesity is a characteristic feature of Bardet-Biedl syndrome, with trunk and proximal part of limbs being the predominant site of involvement [4]. However, weight below 5th percentile for age has been reported in a case belonging to poor socioeconomic background [8]. Various skeletal deformities described are polydactyly, syndactyly, brachydactyly, skull defects, genu vulgum and thickening of skull vault. Polydactyly is not a universal feature of Bardet-Biedl syndrome [3].

Hypogenitalism is reported in 50-88 per cent of cases [4,9]. Common features reported are cryptorchidism, hypogenitalism and gynecomastia. Diabetes mellitus and glucose intolerance in association with LMB syndrome has been described in 14-45 per cent cases in different studies [2,5,6]. These patients rarely required treatment [5]. Furthermore, studies have reported occurrence of diabetes mellitus in blood relatives of LMB patients from various countries [10] including India [7]. The cause of diabetes mellitus in some patients of LMB and their relatives is unclear.

Our patient presented with acute onset of polyuria, polydipsia and weight loss due to diabetes mellitus and needed insulin for control of hyperglycemia. This is not a very common presentation. Inappropriately low but detectable insulin level had probably prevented ketosis in this case. Insulin mediated glucose disposal measured by hyperinsulinemic euglycemic clamp, was normal in 2 cases of LMB syndrome (Unpublished observation). It indicated absence of insulin resistant state in this syndrome. Other features of the syndrome like retinitis pigmentosa, mental retardation

and skeletal involvement though present were mild. In absence of digital anomalies our case represents incomplete form of LMB syndrome [2]. At the age of 22 years his visual acuity was still good (6/9 and 6/12 in right and left eye respectively). His IQ was > 80 and had studied till class eleven. He had gynecomastia, hypogenitalia and raised FSH consistent with hypergonadotropic hypogonadism, however normal LH in presence of low testosterone remained unexplained. He had thickening of skull vault, no other skeletal abnormality was detected.

The present case report highlights the need to screen all patients with LMB for the presence of diabetes mellitus and glucose intolerance.

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