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Case Report

Berardinelli-Seip Congenital Lipodystrophy: A Case Report and Literature Review

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ABSTRACT

Congenital generalized lipodystrophy (CGL) or Berardinelli-Seip congenital lipodystrophy is a very rare genetic disorder, characterised by severe reduction to absence of adipose tissue. They presented with very typical characteristic features but diagnosis is often difficult and if undiagnosed, it can lead to several complications. We present a case of 5-year old Bangladeshi boy who presented to us due to abnormal facies and was diagnosed as congenital generalized lipodystrophy (CGL).

Keywords: *Congenital generalized lipodystrophy (CGL), Berardinelli-Seip congenital lipodystrophy, Bangladeshi.*

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INTRODUCTION

Congenital generalized lipodystrophy (CGL) also known as Berardinelli-Seip congenital lipodystrophy (BSCL), is a rare autosomal recessive condition, characterised by the absence or severe reduction of adipose tissue, leading to a lack of fat storage and associated with insulin resistance, hypertriglyceridemia and hepatic steatosis[1]. It has 4 types and is associated with mutations of the following genes, respectively: AGPAT2, BSCL2, CAV1 and CAVIN1 (PTRF) genes[2,3]. It has an incidence of 1-10 per million populations[4]. It was first described by Waldemar Berardinelli in 1954 and later on further outlined by Martin Seip[5]. In Bangladesh, only one case report has been done by Benzamin et al. till date[6].

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CASE REPORT

A 5-year-old male baby, born to non-consanguineous parents, was admitted to the paediatric inpatient department of Sylhet M A G Osmani Medical College Hospital with complaints of abnormal facial features since 5 months of his age. He had an uneventful antenatal period. The baby was delivered by vaginal delivery with a normal birth weight. The postnatal period was uneventful. Until 5 months, he was relatively well. Then, the mother noticed her baby was getting wasted with abnormal facies and abdominal distension, which was progressively increasing day by day. The mother informed that all his developmental milestones were delayed, such as his sitting got delayed till 1 year; he started walking at 2 years. On examination, the baby had dysmorphic facies with empty

cheeks and prognathism (figure-1), decreased subcutaneous fat in all body parts, apparent muscular hypertrophy of the arm (figure-2), excessive body hair (excluding the face and axilla), an elongated penis, (figure-3) enlarged hands and feet, darkening of the skin (acanthosis nigricans) on the neck and axilla (figure-4). He had hepatomegaly without features of cirrhosis or portal hypertension such as ascites or splenomegaly. Anthropometrically, his weight was 17.8 kg (weight-for-age Z score, -0.26) and length was 120 cm (length-for-age Z score, 2.26). Laboratory investigations- haemogram, serum electrolytes, urea, and serum creatinine- revealed normal results. Liver enzymes were elevated; serum glutamic oxaloacetic transaminase was 75 IU/L and serum triglycerides were 220 mg/dL, both of which were elevated, and serum total cholesterol was normal. Blood sugar was normal (fasting blood sugar, 5.7 mmol/L). An ultrasound of the abdomen revealed an

Figure-1: *Dysmorphic facies with empty cheek, prognathism and hirsutism.*

Figure-2: *Muscular hypertrophy of arm.*

Figure-3: *Elongated penis with pubic hair.*

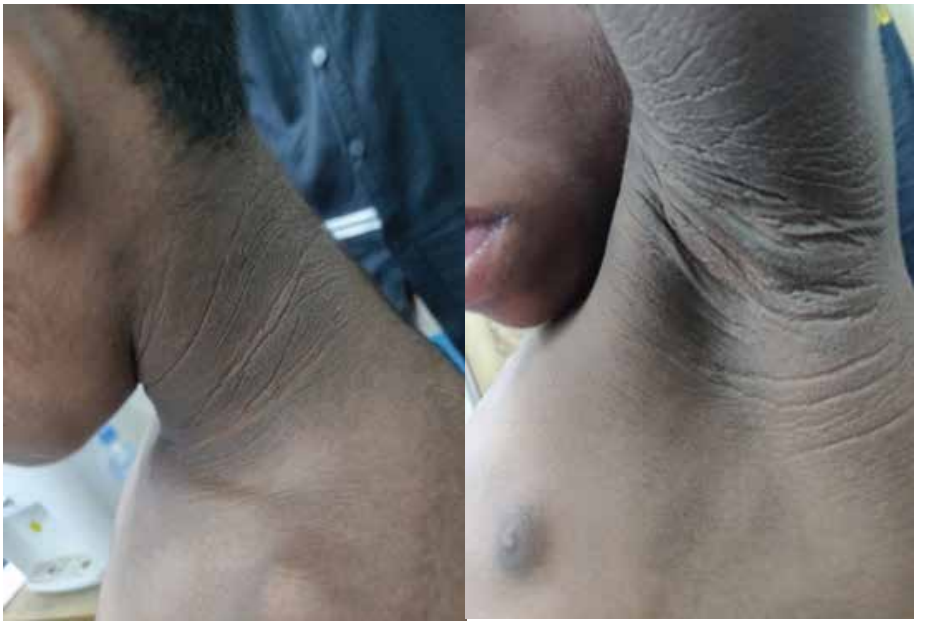

Figure-4: *Acanthosis nigricans.*

enlarged liver with increased echogenicity (suggestive of fatty liver). The possibility of tuberculosis was excluded by a normal chest X-ray and a negative Mantoux tuberculin skin test. HIV was also excluded (anti-HIV I and II were negative) and thyroid functions were normal. His intelligence quotient was 40, which indicated moderate intellectual disability. Genetic studies were not carried out because it is expensive. The presence of typical morphology and biochemical findings leads us to the clinical diagnosis of BSCL2. During the management, we counselled parents about the condition and suggested limiting fat intake and gave the patient omega fatty acid supplements.

DISCUSSION

Diagnosis of congenital generalized lipodystrophy (CGL) is frequently challenging, and partial forms may easily be confused with metabolic syndrome. Usually, the diagnosis occurs either at birth or shortly thereafter. BSCL1 is the milder variant presenting mostly in the 2nd or 3rd decade of life, BSCL2 is more common and severe form than BSCL1, with onset in the neonatal period or in early infancy[7]. Our case presented at 5 years, but his symptoms started from 5 months of age. Diagnosis of lipodystrophy syndromes is based on clinical phenotype and is confirmed by genetic testing. The diagnosis of BSCL is established in a proband with three major criteria or two major criteria plus two or more minor criteria and/or by the identification of biallelic pathogenic variants in one of the genes. Major criteria include: 1. Lipoatrophy affecting the face and both trunk and limbs; gives an athletic appearance, 2. Acromegaloid features (gigantism, muscular hypertrophy, advanced bone age, prognathism, prominent orbital ridges, enlarged hands and feet, clitoromegaly, and enlarged external genitalia in males), 3. Hepatomegaly (earlier due to fatty liver, later due to cirrhosis), 4. Elevated serum triglycerides (serum concentration of triglycerides can be elevated up to 80 g/L), 5. Insulin resistance (in the early stage, acanthosis nigricans and elevated serum concentrations of insulin; the latter overt diabetes mellitus developed). Minor criteria include a) Hypertrophic cardiomyopathy, b) Psychomotor or mental retardation, which affects a majority of BSCL2 patients. c) Hirsutism d) Precocious puberty in the female e) Bone cysts[8]. Our case has 5 major criteria, like lipoatrophy, acromegaloid features (including gigantism and muscular hypertrophy), hepatomegaly, insulin resistance (acanthosis nigricans), elevated serum triglycerides, and 2 minor criteria like mental retardation and hirsutism. In type 1 patients, they still have mechanical adipose tissue, like over the palms and soles, under the scalp, and in the retro-orbital and periarticular regions, but type 2 patients do not have any adipose tissue, including mechanical[9]. In type 2 patients, there is greater likelihood of psychomotor retardation and intellectual impairment[8]. In our patient, there are generalised absence of adipose tissue and intellectual impairment. In congenital generalized lipodystrophy 3 (CGL3), individuals have hypotonia and in congenital generalized lipodystrophy 4 (CGL4), additionally have myopathy but normal intelligence[8]. On our case, muscle tone was normal. For BSCL patients there is no cure. For the metabolic disturbances, lifestyle modification (diet and exercise as needed), metformin, fibrates (and/or statins) and omega-3 fatty acids are generally required. Insulin or other antidiabetics (e.g., metformin, thiazolidinediones) can also be used if needed. Metreleptin, a leptin analogue, is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with generalized lipodystrophy[7]. Our patient, we treated with dietary modification (low-fat diet, comprising less than 20-30% of total dietary energy) and omega-3 fatty acids.

CONCLUSION

Berardinelli-Seip congenital lipodystrophy is a rare disease with a very typical presentation. It is a complex genetic disorder that requires multidisciplinary care to address its metabolic complications effectively. Given diagnostic criteria, it can be easily diagnosed even in the countries with limited resources.

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