CASE REPORT

A RARE CASE OF BERARDINELLI SEIP SYNDROME

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Berardinelli Seip Syndrome is a rare disorder associated with loss of adipose tissue leading to a myriad of findings owing to derangements of carbohydrate and lipid metabolism. There is no cure and the management comprising low fat diet, metformin and leptin replacement is aimed at preventing complications. We report this syndrome in a male child from Afghanistan.

Keywords: Lipodystrophy; Leptin; Hepatomegaly

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INTRODUCTION

Congenital generalized lipodystrophy is a rare disorder associated with loss of adipose tissue from various body parts with consequent derangements in carbohydrate and lipid metabolism.[1] The first case of congenital generalized lipodystrophy, BerardinelliSeip Syndrome was reported in Brazil in 1954 by Berardinelli followed by documentation of similar symptoms in three other patients by Seip in 1959.[2,3] It is an extremely rare autosomal recessive disorder with a prevalence of 0.96/million population and approximately 500 cases reported worldwide.[4]

The mutations in AGPAT 2 and BSCL2 are reported in the majority of cases with this disorder and at least three different types of the disorder have been identified based on these mutations. The cardinal feature of the disease is the lack of adipose tissue with resultant metabolic derangements of carbohydrates and lipids manifested as low leptin levels, hypertriglyceridemia, fatty liver, insulin resistance, and progression to diabetes mellitus. Subcutaneous fat is absent from the thorax and abdomen.[5] Leptin replacement therapy has been shown to halt and revert the metabolic derangements like insulin resistance and dyslipidaemia thereby preventing the development of diabetes.[6] Here we report a case of a male child from Afghanistan with this disorder.

CASE REPORT

A 3 years 9 months old male child from Afghanistan was brought for evaluation of multiple problems. He was reported to have aggressive behaviour; increased appetite, muscular built, and increased hair growth all over the body. The child was born to consanguineous parents and had no history of any significant problems in the immediate postnatal period. There was some degree of developmental delay having achieved walking at 2 years of age and could just speak 2–3 words at 3 years of age. There was a history of the death of one male sibling at the age of six months (cause unknown). On examination, the child had a muscular built and a coarse facies. His weight(20kg) and height (108cm) were at 95th centile for age with a normal upper to lower segment ratio (1.3). His blood pressure was 130/90 mm of Hg (high). There were generalized hypertrichosis and pigmentation in the axilla (acanthosis nigricans).

He had large hands and feet and prominent blood vessels. His Tanner staging was 1 with normal genitalia. He had a protuberant abdomen with multiple striae with a firm, nontender hepatomegaly (total span 12 cm). Cardiovascular system examination showed a hyperdynamic precordium. CNS and respiratory system examination were unremarkable. He was investigated for endocrine and musculoskeletal problems keeping in view the findings of hypertrichosis, acanthosis nigricans, enlarged hands and feet, and muscular built. He had a normal complete blood count, blood sugar, serum electrolytes, LFT's, and renal profile. His 17 OH progesterone and DHEA levels were normal. His serum triglycerides was high (316 mg/dl). Ultrasound abdomen revealed an enlarged fatty liver. Echocardiography and the skeletal survey was normal. His HbA1C and serum insulin levels were also normal at the time of presentation.

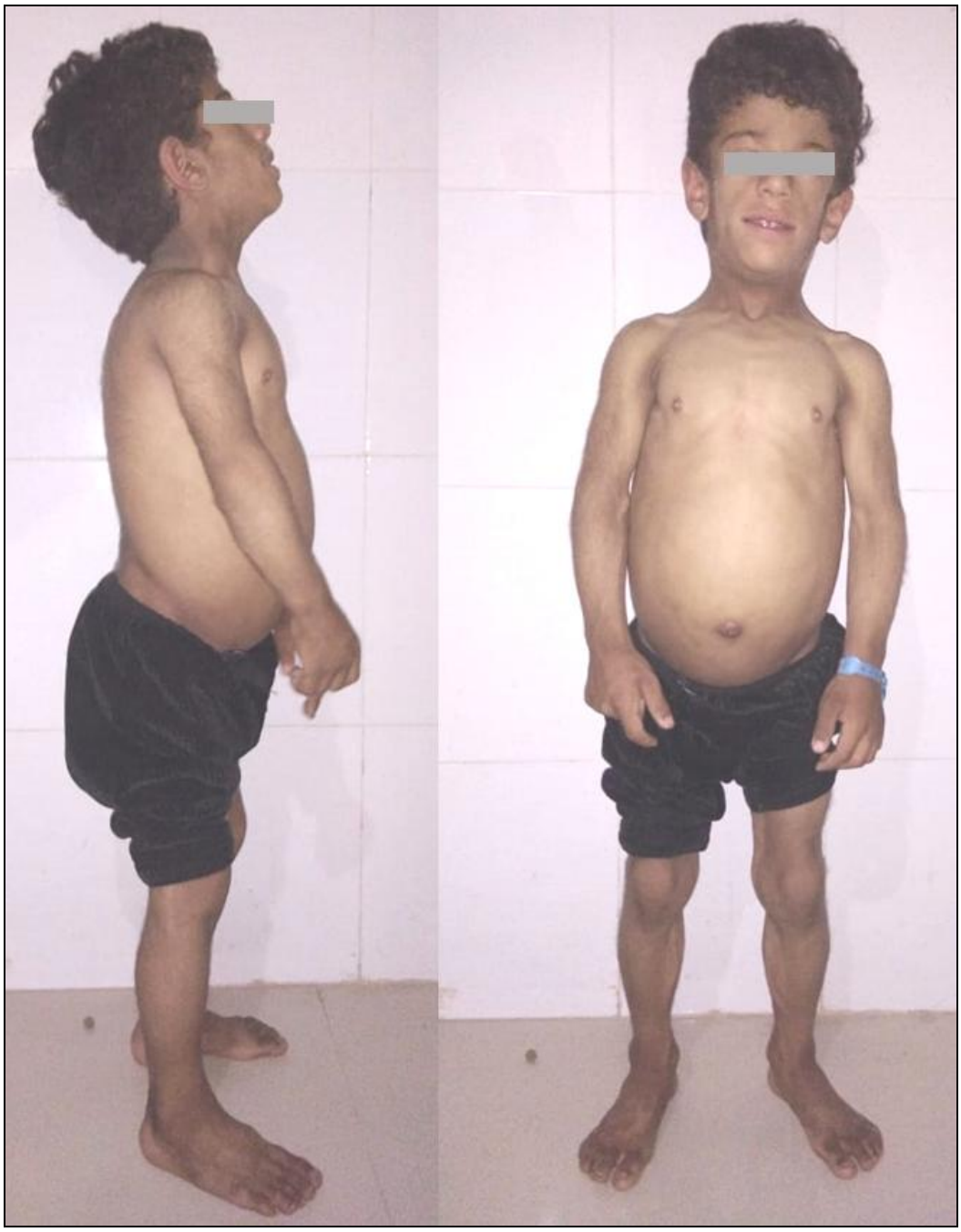

Figure-1: Large hands and feet, protuberant abdomen, hypertrichosis and muscular appearance

DISCUSSION

Our patient presented with lipoatrophy, acromegalic features, hypertriglyceridemia, hypertrichosis, hypertension, and fatty liver that fulfilled the diagnostic criteria of BSCL as reported in the literature. Similar findings in other patients diagnosed as BSCL have also been reported by Cheema HA *et al*[7] and Arif A *et al*[8]. Patients with this syndrome experience an increased appetite and have increased growth rates. The acromegalic features and hepatomegaly with fatty infiltration are attributable to increased levels of IGF-1 which is produced due to hastened anabolic rates. The fatty liver can ultimately progress to non-alcoholic steatohepatitis and cirrhosis.[9] Acromegaloid features and hepatomegaly were documented in our patients as well. The major metabolic problems are related to reduce leptin levels secondary to reduced-fat stores leading to abnormal lipid and carbohydrate metabolism manifested as

triglyceridemia and insulin resistance. Acanthosis nigricans, hirsutism, and increased external genitalia size are the manifestations due to insulin resistance. Developmental delay, cognitive impairment[5,] and Hypertension have also been reported in children[10]. Our patient also exhibited the features of hypertension and developmental delay in addition to acanthosis nigricans and hirsutism. The cornerstone of management includes dietary intervention with 50–60% carbohydrates, 20–30% fats, and 20% proteins and Metreleptin. Metreleptin lowers triglycerides and blood glucose and improves HbA1C. Other therapies include metformin and statins.[11] Metreleptin is very beneficial in children with lipodystrophy as it improves metabolic derangements and biomarkers of NAFLD. Although it improves the quality of life, further long-term studies are needed to establish its impact on life expectancy.[12]

Genetic studies could not be performed on our patients due to the non-availability of the facility. Based on the clinical features and lab reports, a management plan was formulated for our patients. The attendants were thoroughly counselled about the disease, its progression, outcomes, and available interventions. He was started on metformin for insulin resistance, a statin to lower triglycerides and a calcium channel blocker for hypertension. He was advised to strictly follow a low-fat diet. The attendants were counselled to keep a check on his blood pressure and blood glucose levels. They were advised to repeat his HbA1C, serum triglycerides, and ultrasound abdomen every three months and to return for follow-up after six months.

Until now there is no cure for patients with this syndrome. Patients with congenital generalized lipodystrophy need regular follow-up for monitoring of complications due to metabolic derangements to prevent morbidity and mortality associated with this syndrome.

Competing interests: None

Patient Attendant's consent: Obtained

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