A Rare Case of Berardinelli-Seip Syndrome in a Four Month Old Child

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Introduction

Berardinelli-seip syndrome is a rare genetic autosomal recessive disorder1, first described in 1954 by Berardinelli and Seip2, affecting approximately 1 in 10 millions births worldwide. The earliest genetically confirmed case of Pakistani origin is reported in 2013 in a consanguineous family.

On the basis of alterations, 4 types of BSCL have been recognized as BSCL 1-4, with their etiology linked to mutations in four distinct genes: AGPAT2, BSCL2, CAV1 and CAVIN1, respectively3. The common feature in all of these is loss of adipose mass, accompanied by metabolic abnormalities, muscular hypertrophy and distinct physical features. This syndrome is associated with severe insulin resistance, dyslipidemia, and high risk of developing type 2 diabetes mellitus, cardiovascular disease, and other comorbidities. The diagnostic criteria has been described in literature, which include major and minor criteria. The major criteria include lipoatrophy, acromegaloid features, hepatomegaly, hypertriglyceridemia, bone cysts and cardiomyopathy. Diabetes mellitus, hypertriglyceridemia, and hepatic steatosis ordinarily develop in these patients, and most girls suffer from menstrual abnormalities. We report a case of an 8-year-old female child presented multiple times in the hospital with complaints of failure to thrive and a marasmic look. She has lipoatrophy affecting the face, limbs and trunk, acromegaloid features, hepatomegaly, hypertriglyceridemia, phlebomegaly and hirsutism. Such patients need to be identified and monitored for complications like diabetes mellitus and cardiomyopathies.

Case Report Presentation

A 4-month-old female child presented at the pediatric department of POF hospital, Wah Cantt, in September 2016, with complaints of failure to thrive, a marasmic look and abdominal
distention for 1 month. Her parents are first cousins, residents of Busti, Wah Cantt. Birth history was unremarkable. She has 2 siblings with normal development. On examination, her OFC was 39 cm [below 3rd centile], and her weight was 5.2 kg [below 5th centile], and length was 63 cm.

[above 25th centile] with a BMI of 13.11 kg/m². She had a muscular build with generalized loss of fat, mainly from buttock, face, legs and arms; thick hands and feet; hirsutism; and prognathism. She also had distended abdomen, firm hepatomegaly without any signs of cirrhosis or portal hypertension (Figure 1).

Figure 1: Loss of subcutaneous fat, protuberant abdomen, phlebomegaly and acanthosis nigricans [pictures taken after consent from family].

It was rare for patients with Berardinelli-seip syndrome to develop diabetes during the first decade of life as our patient affected by this complex syndrome. Because of the absence of functional adipocytes, lipids, are stored in other tissues, including muscle and liver. It is a rare disease, with a prevalence of approximately 0.96 cases/million and 500 cases described in literature with fewer than 10 cases in Pakistan to date, with greater frequency reported in some ethnic groups, mainly in Latin Americans and Arabians [individuals of Portuguese and Norwegian ancestry]. It was first described in 1954 by Berardinelli in a 2-year-old boy and later by Seip in three patients. BSCL etiology involves genetic variations in four different genes: AGPAT2, BSCL2, CAV1 and CAV1N1. The four different biochemical subtypes of the disease are distinguished depending on which gene is mutated. The defect in BSCL is in the 1-acylglycerol-3-phosphate-O-acyltransferase-2 [AGPAT2] gene on chromosome 9q34 in the type 1 variant and in the BSCL2 gene on chromosome 11q13 in the type 2 variant.

Affected individuals develop insulin resistance [T2DM] and approximately 25-35% develop diabetes between the ages of 15 and 20 years. Hepatomegaly secondary to hepatic steatosis and skeletal muscle hypertrophy occur in all affected individuals. Hypertrophic cardiomyopathy is reported in 20%-25% of affected individuals and is a significant cause of morbidity from cardiac failure and early mortality. Our patient developed firm hepatomegaly, generalized lipodystrophy and hypertriglyceridemia. Clinically 4 major and 2 minor criteria for diagnosis were met by our patient. Our patient developed diabetes in the first decade which is rare and usually developed in the second decade of life.

Diagnosis of the disease is a challenging task. For a definite diagnosis, genetic studies must be carried out. To date, no definitive treatment has been approved for BSCL. The management plan of these patients revolves around the clinical manifestations and basic pathophysiology i.e. loss of metabolically active adipose tissue and leptin deficiency which were the primary causes of metabolic complications. A leptin analogue called Metreleptin has been approved by United States Food and Drug Authority (FDA) for use in BSCL patients. Management in our patient included restriction of total fat intake to 20-30% of dietary calorie intake, enhanced physical activity and oral Antidiabetic i.e Metformin.

Conclusion

This case report highlights the clinical presentation, diagnostic journey, and management challenges associated with this rare syndrome. There is a need for increasing awareness about this condition among physicians so that early diagnosis and management with a multidisciplinary approach can be carried out to prevent metabolic and systemic complications. Genetic counseling plays an integral role in the management of this disease. Continued research and patient follow-up are essential to improve therapeutic strategies and outcomes for individuals affected by this complex syndrome.

Patient consent

Written consent was obtained from the patient’s father to publish this case.

References


