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Case Report

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

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A B S T R A C T

Berardinelli-seip congenital lipodystrophy [BSCL] or congenital generalized lipodystrophy [CGL] is an extremely rare autosomal recessive disorder. It is one of the four subgroups of lipodystrophy syndrome characterized by varying degrees of loss of adipose mass in the body. The reported clinical presentation of this syndrome include muscular hypertrophy, gigantism, hepatomegaly, impaired glucose tolerance,acanthosis Nigricans, intellectual impairment, phlebomegaly, 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.

Keywords: Berardinelli-seip congenital lipodystrophy; Hypertriglyceridemia; Phlebomegaly; Hepatomegaly

Introduction

Berardinelli-seip syndrome is a rare genetic autosomal recessive disorder[1], 1first described in 1954 by Berardinelli and Seip[2], 2affecting approximately 1 in 10 millions births worldwide. The earliest genetically confirmed case of Pakistani origin is reported in 2013 in a consanguineous family.

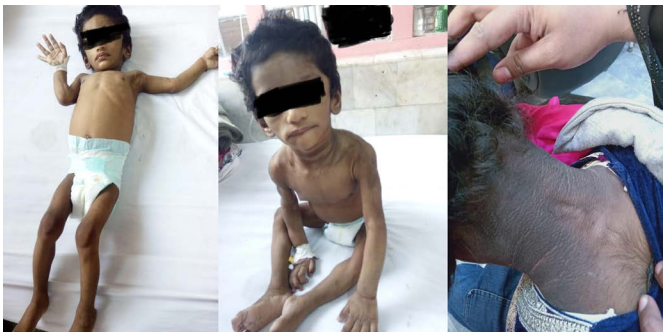
On the basis of alterations, 4 types of BSCL have been recognized as BSCL 1-4, with their etiology linked to mutations in four distinct genes: AGPAT2, BSCL2, CAV1 and CAVIN1, respectively4. The common feature in all of these is loss of adipose mass, accompanied by metabolic abnormalities, muscular hypertrophy 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 and insulin resistance. Minor criteria include hypertrophic cardiomyopathy, psychomotor retardation, hirsutism, bone cysts, precocious puberty especially in females, and splenomegaly. The diagnosis of BSCL is suggested if three major or two major plus two minor criteria is fulfilled or a specific gene mutation is identified. We report a case of an 8-year- old female child, product of consanguineous marriage that fulfilled the clinical criteria of BSCL.

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 63cm.

[above 25 th centile] with a BMI of 13.11kg/m^2. 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)**.



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

Figure 1: Loss of subcutaneous fat, protuberant abdomen, phlebomegaly and acanthosis nigricans.

Chest examination was normal. There was hypertriglyceridemia [655 mg/dl], raised ALT [122 IU/L] and ALP [322 IU/L]. CBC, Thyroid function test, ferritin, vitamin D, renal function tests, and serum electrolytes were normal. Echocardiography was done which was also normal.

Ultrasound abdomen showed hepatomegaly. Initially, fasting and random sugar was in the normal range but increased later on. Since the clinical criteria was met, the patient was diagnosed and treated as a case of BSCL, however it was not confirmed due to unavailability of genetic testing. The patient was managed conservatively with a low fat diet and increased physical activity along with close monitoring of hypertriglyceridemia and blood sugar levels.

During her course of illness, she developed acanthosis nigricans and her fasting blood sugar level rose above 200 mg/dl. Her HBA1C was 9.3% for which she was started on oral antidiabetics i.e metformin. Leptin was not offered due to non-availability.

It was rare for patients with Berardinelli-seip syndrome to develop diabetes during the first decade of life as our patient developed. Currently, the patient is on followup in our department and her blood sugars are well controlled on Metformin and she did not develop any complications. [Parental consent was obtained for publishing the data with photographs].

Discussion

BSCL is usually diagnosed at birth or soon after birth. 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 CAVIN1. 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[3] 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[5]. Management in our patient included restriction of total fat intake to 20-30% of dietary caloric intake, enhanced physical activity and oral Antidiabetic i.e Metformin[6-9].

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

1. Handelsman Y, Oral EA, Bloomgarden ZT, et al. The clinical approach to the detection of lipodystrophy-An AACE consensus statement. Endocr Pract 2013;19:107-116.
2. Lima JG, Nobrega LH, Lima NN, et al. Causes of death in patients with Berardinelli-Seip congenital generalized lipodystrophy. Plos One 2018.13(6).
3. Akinci B, Onay H, Demir T, et al. Natural history of congenital generalized lipodystrophy: A nationwide study from turkey. J Clin Endocrinol Metab 2016;101(7):2759-2767.
4. Craveiro Sarmento AS, Ferreira LC, Lima JG, et al. The worldwide mutational landscape of Berardinelli-Seip congenital lipodystrophy. Mutat Res Rev Mutat Res 2019;781:30-52.

5. Van Maldergem L. Berardinelli-Seip Congenital Lipodystrophy. Gene Reviews 1993.

6. Cheema HA, Malik HS, Waheed N, Mushtaq I, Fayyaz Z, Anjum MN. Berardinelli-Seip Congenital Generalised Lipodystrophy. J Coll Physicians Surg Pak 2018;28(5):406-408.

7. Gomes KB, Pardini VC, Fernandes AP. Clinical and molecular aspects of Berardinelli-Seip Congenital Lipodystrophy (BSCL). Clin Chim Acta 2009;402:1-6.

8. Mork NJ. Rajka G, Halse J. Treatment of acanthosis nigricans with etretinate (Tigason) in a patient with Lawrence-Seip syndrome (generalized lipodystrophy). Acta Derm Venereol 1986;66(2):173-174.

9. Ashraf S, Masood S, Naz F, Rashid J. Berardinelli Seip Syndrome: A rare case report. J Pak Med Assoc 2022;72(5):969-971.