Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 02/02/2024
Approved on: 19/03/2024

CASE REPORT

Berardinelli syndrome: clinical criteria and the importance of early management

Sara Silveira Brandão[1], João Paulo Farias da Silveira[1], Maria Clara Duarte de Figueirêdo[1], Wallace William da Silva Meireles[2], Erlane Marques Ribeiro[1]

Keywords:
Genetic counseling, Lipodystrophy, Congenital generalized, Rare diseases.

Abstract

Berardinelli lipodystrophy is a rare disease of autosomal recessive inheritance characterized by important changes in the metabolism of carbohydrates and lipids. FDSS, a 5-year-old Brazilian boy, son of consanguineous parents, is admitted to the Medical Genetics clinic due to growth deficiency, acromegaloid aspect, protrusion of the umbilical scar, hypertrophy of skeletal muscle and hypertriglyceridemia. Diagnosis of Berardinelli lipodystrophy was made by the presence of 3 major criteria and instituted therapy with a multidisciplinary team. Confirmed genetic mutation from the gene panel for hypertriglyceridemia. The case described corroborates the fact that knowledge about the disease is relevant, because the realization of clinical diagnosis from the specific criteria in order to establish early management of these cases can direct more correct conducts that may reduce the morbidity and mortality of the disease.

[1] Centro Universitário Christus (Unichristus) - Fortaleza - CE - Brazil.
[2] Hospital Infantil Albert Sabin (HIAS), Serviço de Genética Médica - Fortaleza - CE - Brazil.

Correspondence to:
Erlane Marques Ribeiro.
Centro Universitário Christus (Unichristus). Av. Dom Luís, 911, Meireles, Fortaleza, CE, Brazil. CEP: 60160-230. E-mail: erlaneribeiro@yahoo.com.br

Resid Pediatr. 2025;15(2). DOI: 10.25060/residpediatr-2025.v15n2-1230

Este trabalho está licenciado sob uma Creative Commons Attribution 4.0 International License.

INTRODUCTION

Berardinelli-Seip congenital lipodystrophy (BSCL) is a rare condition characterized by reduced or absent adipose tissue and skeletal muscle hypertrophy[1]. BSCL is typically identified by striking physical characteristics such as acromegalic features, a triangular face with prominent cheeks due to the loss of the buccal fat pad, hypertrophied muscles, hepatomegaly, protrusion of the umbilical scar, and phlebomegaly[2]. This condition was first described by Brazilian physician Berardinelli in 1954. It is a rare genetic disorder belonging to the category of lipodystrophies, characterized by the absence or abnormal reduction of adipose tissue in the body[3]. The objectives of this report are: (1) to alert physicians about this condition and its consequences in the patient's daily life; (2) to emphasize the importance of early diagnosis, even in the absence of molecular tests, and its effect on reducing comorbidities related to BSCL.

CASE PRESENTATION

A 5-year-old boy with dysmorphic features was brought to the genetics outpatient clinic of a public referral hospital for rare diseases in Ceará. His parents were consanguineous relatives; the mother was 21, and the father was 42. They stated that their family had no other cases of the disease. The boy was born via vaginal delivery, sat up at six months, walked at one year, spoke at two years, and gained sphincter control at one year and three months. He had no issues at school. His parents reported a history of agitation and hyperphagia. During physical examination, he weighed 14.4 kg (Z score = -3 and -2) and was 100 cm tall (Z score = -2). His head circumference measured 51 cm (Z score = -2 and 0), and he exhibited facial lipoatrophy, limbs with hypertrophied muscles, lipodystrophy, an anal plicoma, and flat feet (Figures 1 and 2). Computed tomography images of the head, abdominal ultrasound, and total skeletal radiography revealed no significant findings. Triglyceride levels were noted at 218 mg/dL (RV <75 mg/dL between 0 and 9 years). The patient met three primary diagnostic criteria for BSCL: lipodystrophy affecting the trunk, limbs, and face; acromegalic features; and elevated serum triglyceride levels (>80 g/L). Clinical diagnosis was followed by a gene panel for hypertriglyceridemia, which identified a mutation in the AGPAT2 gene (1-acylglycerol-3-phosphate O-acyltransferase 2). A geneticist, an endocrinologist, and a dietitian are monitoring the patient, and genetic counseling was provided.

DISCUSSION

BSCL is a rare disease with incidence rates varying among populations, 1 in 1,000,000 in the USA and 1 in 500,000 in Portugal[4]. Although we lack epidemiological data for Brazil, it is reasonable to assume that the incidence is similar to that



Figure 1. A 5-year-old boy with BSCL (full body, front view).



Figure 2. A 5-year-old boy with BSCL (full body, back view).

of Portugal due to the Portuguese ethnic ancestry of most Brazilians. Furthermore, there are reports of a potential cluster in Rio Grande do Norte, a state neighboring Ceará, where the patient resides. The case we present involves a patient with a clinical suspicion of BSCL, which was confirmed by laboratory tests. We believe that recognizing the clinical diagnosis of this disease is crucial so that management measures can be implemented early.

The diagnosis can be established based on the identification of

- three primary criteria or
- two primary criteria and two or more minor criteria or
- identification of biallelic pathogenic variants in the AGPAT2 gene[5].

The primary criteria include the following: (1) lipodystrophy affecting the trunk, limbs, and face; (2) acromegalic features; (3) hepatomegaly; (4) elevated serum triglyceride level (>80 g/L); and (5) insulin resistance[5]. For the minor criteria, (1) hypertrophic cardiomyopathy; (2) mild to moderate neurological or intellectual developmental delay; (3) hirsutism/hypertrichosis; (4) precocious puberty in girls; (5) bone cysts; and (6) phlebomegaly[5]. Our patient satisfied three primary diagnostic criteria for BSCL (1, 2, 4). Accurate diagnosis is crucial to prevent complications and to initiate appropriate treatment, thereby mitigating dyslipidemia, the effects of insulin resistance, and heart disease.

The accumulation of visceral fat around the internal organs, particularly the liver, leading to hepatomegaly, can contribute to insulin resistance and the development of type 2 diabetes mellitus, which should be avoided as much as possible. This highlights the importance of having an endocrinologist and a dietitian in the multidisciplinary care team[6].

BSCL is caused by mutations in specific genes that develop and regulate adipose tissue. The AGPAT2 gene is primarily involved in lipid synthesis, playing a crucial role in the formation of adipose tissue. Mutations result in abnormalities in the body's production and distribution of fat, leading to the characteristic lack of subcutaneous adipose tissue[7]. In typical cases, the diagnosis can be made using the abovementioned criteria; however, molecular testing is essential for defining the etiology of cases with incomplete phenotypes and determining the prenatal diagnosis of other family members. It can also aid in genetic counseling. However, waiting for the results to begin therapeutic interventions is not advisable, as they can be costly and may be challenging for patients in the public health system to access.

Parental consanguinity increases the occurrence of autosomal recessive diseases, such as BSCL; however, not every consanguineous couple will have children with these genetic diseases[8]. The family of the patient described in this report was informed about the disease and given a 25% chance of recurrence. The identified mutation can be used to diagnose other cases if necessary. The clinical management of BSCL involves strategies to address its metabolic complications, with dietary management being the most crucial aspect in controlling biological effects by limiting total energy, saturated

fat, and simple carbohydrate intake while prioritizing complex carbohydrates, soluble fibers, medium-chain triglycerides, and unsaturated fatty acids, alongside encouraging exercise[9]. Implementing a diet can be challenging, particularly for patients with hyperphagia. Many caregivers struggle to understand why their children might need treatment since they appear athletic. If the disease is poorly understood, families often interrupt treatment when faced with challenges such as traveling long distances to a care facility and the quality and availability of public transport. Engaging families in playful activities to raise awareness of the medical facts about the disease helps them comprehend and adapt to living with it while following medical recommendations. Pediatricians play a key role in coordinating the multidisciplinary team, which may include professionals from education and law.

CONCLUSION

The patient was diagnosed with BSCL for meeting three primary criteria: lipodystrophy affecting the trunk, limbs, and face; acromegalic features; and elevated serum triglyceride levels. A molecular test provided confirmatory evidence. Treatment must be initiated early to avoid complications. There is no need to wait for molecular test results to manage the patient, as diagnosis based on clinical criteria is sufficient. Genetic counseling and therapeutic actions by a multidisciplinary team, including health, education, and legal professionals, are essential. They should be coordinated by a pediatrician, the healthcare professional who maintains close contact with the family.

RFERENCES

1. Loureiro JC, Araújo BC, Duarte RH, Brito AM de, Santos MCO, Pena VL da S, et al. Síndrome de Berardinelli-Seip com acometimento familiar em Patos de Minas - MG: um relato de caso. Brazilian J of Tech. 2022 Sep 10;5(3):181–92.
2. Lima JG de, Campos JTA de M, organizadores. Síndrome de Berardinelli-Seip Aspectos genéticos e morfofisiológicos. 1. ed. Natal: EDUFRN; 2020. p. 51-64.
3. Damasceno E de B, Figueiredo JG de, França JMB, Veras JCD, Borges REA, Melo LP de. Experiência de pessoas que vivem com a Síndrome de Berardinelli-Seip no Nordeste brasileiro. Sci Saúde Coletiva. 2018 Feb;23(2):389–98.
4. Centre de Référence des Pathologies Rares de l'InsulinoSécrétion et de l'Insulino-Sensibilité (PRISIS). Lipodystrophies généralisées congénitales. Paris: Haute Autorité de Santé; 2022 Nov 15.
5. Giori SF, Palhares LGA, Castro IAF, Salgado P de O. Lipodistrofia Generalizada Congênita: Relato de caso. Braz Journal of Surg Clin Research BJSCR. 2019;29(3):29-32.
6. Czepielewski MA, Tavarone V, Riera N, Boschi A, Paula LPD. Síndrome de Berardinelli-Seip: Menino com Baixo Peso e Tecido Subcutâneo Ausente. Clin Biomed Rese. 2010 Nov 19;30(3).
7. Barra C, Savoldelli RD, Manna TD, Kim CA, Magré J, Porta G, et al. Síndrome de Berardinelli-Seip: descrição genética e metabólica de cinco pacientes. Arq Bras Endocrinol Metab. 2011 Feb 1;55(1):54–9.
8. Santos SC dos, Melo US, Lopes SS dos S, Weller M, Kok F. A endogamia explicaria a elevada prevalência de deficiências em populações do Nordeste brasileiro? Sci Saúde Coletiva. 2013 Apr;18(4):1141–50.
9. Bispo MB, Freitas ACC de. Lipodistrofia generalizada congênita: uma revisão bibliográfica. Rese Soc and Develop. 2023 Feb 7;12(2):e21812240288.