International Journal of Research in Medical Sciences
Panuganti SK et al. Int J Res Med Sci. 2024 Oct;12(10):3948-3951
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242970

Case Report

A case report on unusual cause of childhood obesity and visual disturbances-Bardet-Biedl syndrome

Suresh Kumar Panuganti*, Sujeeth Kumar Modi, Pooja Nilesh Patel, Sudha Boda, Radha Reddy Syamala

Department of Paediatrics, Yashoda Hospitals, Somajiguda, Hyderabad, Telangana, India

Received: 06 August 2024
Accepted: 19 September 2024

***Correspondence:**
Dr. Suresh Kumar Panuganti,
E-mail: drskpanuganti@gmail.com

ABSTRACT

Bardet-Biedl syndrome (BBS) represents a rare genetic condition distinguished by a multifaceted set of clinical features, including obesity, retinal dystrophy, polydactyly, renal dysfunctions, and cognitive dysfunction. BBS mostly affects children of consanguineous marriages. It is frequently overlooked during initial pediatric examinations. The lack of syndromic diagnostic strategy for identifying genetic disorders by healthcare professionals is being acknowledged as a significant concern. Here, we reported a patient (9 year 4 months old male) born to second degree consanguineous parents, who presented with major features of Bardet-Biedl Syndrome (BBS). The patient came to us with the symptoms including increasing weight gain and visual disturbances. In our case, the diagnosis was made after a comprehensive clinical assessment and genetic testing. Genetic testing showed that the patient had a heterozygous missense variant of the BBS10 gene (chr12: g.76347012 C>A; Depth: 117x). This result confirmed the diagnosis of Bardet-Biedl-Syndrome. This case report highlights a patient diagnosed with BBS, focusing on the clinical manifestations, genetic characteristics and potential avenues for future research.

Keywords: Obesity, BBS10 gene, Bardet-Biedl-syndrome, Retinal dysfunction

INTRODUCTION

Bardet Biedl Syndrome is a ciliopathy that affects various organ systems. It is autosomal recessive disorder originates from the mutations in genes involved in the development and function of cilia, which play a essential role in cellular signaling and development. The incidence of BBS is approximately 1 in 160,000 individuals, but it might be higher in some specific populations. To date, only 15 cases have been reported in India.[1,2] Despite the growing understanding of the genetic basis of Bardet Biedl Syndrome (BBS), it remains a clinical diagnosis. The diagnosis can be established if the patient exhibits four out of six primary features: rod cone dystrophy, obesity, genital anomalies, renal anomalies, postaxial polydactyly, and cognitive impairment.[3] Genetic testing is recommended to verify the diagnosis, and it is estimated that 80% of patients will possess a recognized genetic etiology for BBS.[4] Here we present a 9-year-old male patient who was diagnosed with Bardet Biedl Syndrome (BBS) based on his clinical presentation and genetic analysis. After carefully reviewing the literature, this case will be the 16th case of this syndrome to be published from India. By making this case study publicly available, our objective is to enhance understanding and expertise in this uncommon disorder among healthcare professionals and researchers, as well as to underscore the challenges and potential approaches for improving the well-being and treatment outcomes for patients with BBS.

CASE REPORT

A 9 years 4 months old male patient, born to second degree consanguineous parents, presented in the

pediatrics department with progressively increasing weight, visual disturbances suggestive of tubular vision and easy fatiguability. There were no similar complaints reported within the family. On clinical examination, the child has BMI above the 95th percentile for age and sex (weight of 60.5 kg, height of 137.5 cm and BMI 32 kg/square meter) that indicated obesity (Figure 1 A). Additionally, child had velvety, brown to black hyperpigmented plaques seen in the body's intertriginous sites, such as the neck, axillae and groin indicating significant acanthosis nigricans. The child had post-axial polydactyly (hexadactyly) on both hands and feet (Figure 1B, 1C). Ultrasound examination showed renal agenesis on the left side, but the renal functions were normal. Mild developmental delay was noted, with cognitive testing revealing a score below the average range.

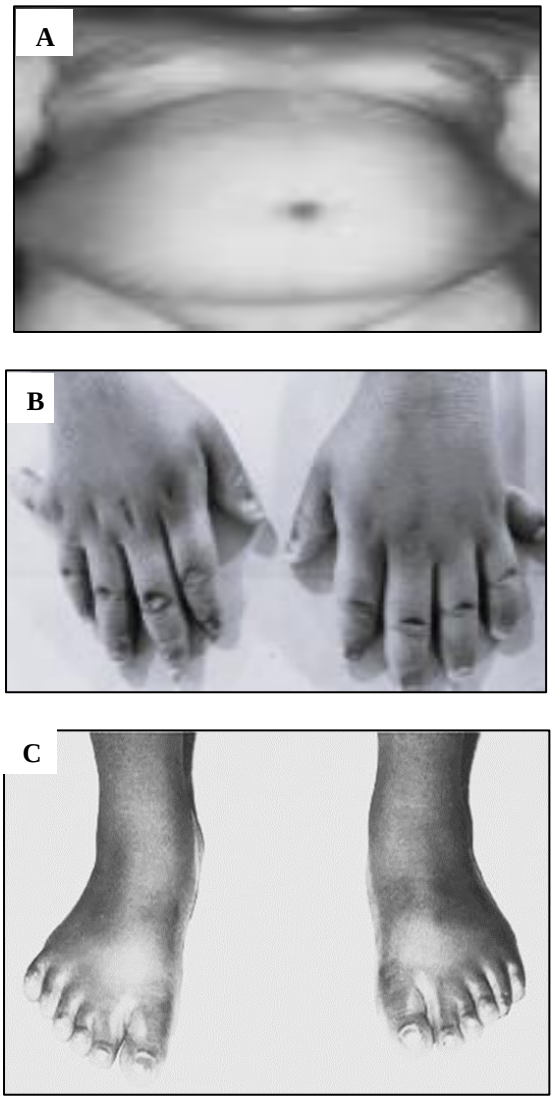

Figure 1: A) Central obesity. B) and C) post-axial polydactyly (hexadactyly) on both hands and feet.

On ophthalmological examination, electroretinography (ERG) showed diffuse retinal dysfunction with extinguished peaks on pattern ERG, scotopic ERG, maximal combined and oscillatory potential in both the eyes. Laboratory findings show an elevated triglycerides (170 mg/dl) and low HDL cholesterol (36 mg/dl). To confirm the diagnosis and to identify the potential underlying genetic mutations associated with BBS in this case, which is one of the few cases of the syndrome in India, targeted gene sequencing was performed. The analysis revealed a heterozygous missense variant in exon 2 of the BBS10 gene (chr12: g.76347012C>A, Depth:117x) that results in the amino acid substitution of Leucine for Valine at codon 325 (Val325 Leu; ENST00000650064.2) was detected. This finding confirmed the diagnosis of Bardet-Biedl Syndrome.

DISCUSSION

Bardet-Biedl Syndrome (BBS) exhibits a variable phenotype, leading to potential challenges in its diagnosis. The proteins associated with BBS are elements of the centrosome that are crucial for the function of ciliary transport; thus, the condition has been categorized as a "ciliopathy".[5] This case underscores the importance of recognizing the hallmark features of BBS, particularly in pediatric population with obesity and retinal issues. Early intervention, including nutritional counseling and regular ophthalmologic evaluations is crucial to manage the symptoms and prevent the complications.

The genetic basis of BBS is characterized by alterations in a minimum of 21 recognized genes implicated in causing BBS. This group contains the BBS1-BBS20 gene family and the NPHP1 gene, which produces the nephrocystin-1 protein. Each of these genes plays a crucial role in ensuring the proper functioning of primary cilia. The two main genes associated with BBS are BBS1 and BBS10, each gene having been identified in over 20% of diagnosed cases.[6]

One of the clinical characteristic features of this uncommon genetic disorder is the impairment of vision, particularly in the form of Retinitis dysfunction. Retinal dysfunction in BBS is primarily characterized by retinal dystrophy along with optic atrophy deteriorating vision.[7] The electroretinography (ERG) findings in our case was in alignment with the established fact that 93% of BBS patients exhibit retinal dysfunction. Based on prior research, no approved therapies exist to alleviate vision deterioration and prevent blindness; nevertheless, frequent ophthalmological follow-up is utmost essential for visual prognosis. The utilization of low-vision aids can improve visual acuity by preserving the residual vision, thereby fostering increased independence in daily life activities.

Consequently, obesity has established the second most crucial feature among the BBS characteristics. Obesity has been observed in these individuals throughout the childhood. The prevalence of increased body mass index (BMI) is noted with the progression of age. It is typically identified by their parents within the initial decade of life,

in contrast to their siblings and peers of a similar age.[3] Our patient was with progressively increasing weight, and there was also noticeable acanthosis nigricans. He had increased levels of triglycerides and low HDL along with increased body mass index (BMI). Therefore, it is imperative that healthcare professionals engage in counseling sessions with parents concerning lifestyle modifications at an early stage. Implementing a low-calorie, low-protein diet can help in managing obesity and may also slow down the progression of renal failure in individuals with BBS.[8]

Postaxial polydactyly is another characteristic of Bardet-Biedl syndrome (BBS) manifests at the time of birth, while other traits continue to develop and evolve throughout the individual's lifetime. The incidence of simultaneous involvement of both the upper and lower extremities is observed in approximately 21% of patients. It is noteworthy that lower limb involvement is present in 21% of these cases, whereas upper limb involvement is documented in 9% of the cases9. In our patient, we observed post-axial polydactyly (hexadactyly) on both hands and feet.

A comprehensive review of the literature reveals a variety of renal abnormalities associated with Bardet-Biedl Syndrome (BBS). These include unilateral agenesis, chronic kidney disease (CKD), parenchymal cysts, dysplastic kidneys, renal scarring, calyceal clubbing, fetal lobulation, renal calculi, and vesicoureteral reflux.[10] In our case, ultrasound examination showed renal agenesis on the left side and renal functions were normal.

The majority of children diagnosed with BBS are noted to exhibit cognitive impairments and developmental delays. Genetic testing is now recommended for all children with global developmental delay.[11] The cognitive dysfunction linked to BBS is typically classified as mild to moderate severity.[12] In our case, mild developmental delay was observed, accompanied by cognitive testing results that indicated a score below the average range.

In this case report, a heterozygous BBS (Val325Leu; ENST00000650064.2) was identified using targeted gene sequencing, that results in the amino acid substitution of leucine for valine at codon 325.[10] This mutation has been classified as having a high likelihood of being pathogenic, in accordance with the guidelines and criteria established by the American college of medical genetics and genomics (ACMG).[13] BBS10 is located on chromosome 12q21 and consists of a total of two exons, collectively spanning a length of 23.97 kb. This sequence is responsible for encoding a protein with 723 amino acids, which is part of a Chaperonin-like complex.[14] The human gene mutation database (HGMD) contains information on 115 variants, that are spread throughout the entire BBS10 gene.[15]

The diagnostic criteria for BBS are primarily based on clinical criteria, so patients may remain in a quiescent state for several years before the disease has progressed significantly. In some cases, diagnostic dilemmas have been encountered. Challenges in diagnostics emerge when children, born without any congenital abnormalities, yet face issues related to learning disabilities and excessive weight gain. Visual impairment leads to the initial recognition of its associated abnormalities by parents upon seeking assistance from healthcare professionals. For the confirmation of this diagnosis, genetic testing could potentially play a crucial role. Emerging research suggests that gene therapy and other targeted treatments may offer hope for affected individuals in the future. Additionally, awareness and education regarding BBS are essential for healthcare providers to ensure timely diagnosis and management.

CONCLUSION

This case exemplifies the multifaceted nature of Bardet-Biedl Syndrome and the necessity of a multidisciplinary approach to care the patients. Persistent investigation into the genetic basis and therapeutic alternatives for BBS will augment our comprehension of this intricate condition.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Klein D, Ammann F. The syndrome of Laurence-Moon-Bardet-Biedl and allied diseases in Switzerland. Clinical, genetic and epidemiological studies. J Neurol Sci. 1969;9(3):479-513.
2. Hooda AK, Karan SC, Bishnoi JS, Nandwani A, Sinha T. Renal transplant in a child with Bardet-Biedl syndrome: A rare cause of end-stage renal disease. Indian J Nephrol. 2009;19(3):112-4.
3. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. J Med Genet. 1999;36(6):437-46.
4. Niederlova V, Modrak M, Tsyklauri O, Huranova M, Stepanek O. Meta-analysis of genotype-phenotype associations in Bardet-Biedl syndrome uncovers differences among causative genes. Hum Mutat. 2019;40(11):2068-87.
5. Nachury MV, Loktev AV, Zhang Q, Westlake CJ, Peränen J, Merdes A, et al. A core complex of BBS proteins cooperates with the GTPase Rab8 to promote ciliary membrane biogenesis. Cell. 2007;129(6):1201-13.
6. Mandal RK, Pande R, Kc RS, Acharya B. Bardet-Biedl syndrome: a case report from Nepal. Asian J Med Sci. 2021;12(8):158–63.
7. Andrade LJ, Andrade R, França CS, Bittencourt AV. Pigmentary retinopathy due to Bardet-Biedl

syndrome: case report and literature review. Arq Bras Oftalmol. 2009;72(5):694-6.
8. Dervisoglu E, Isgoren S, Kasgari D, Demir H, Yilmaz A. Obesity control and low protein diet preserve or even improve renal functions in Bardet-Biedl syndrome: a report of two cases. Med Sci Monit. 2011;17(1): 12-4.
9. Li H, He J, Leong I, Huang R, Shi X. Central precocious puberty occurring in Bardet-Biedl syndrome-10 as a method for self-protection of human reproductive function: A case report. Exp Ther Med. 2022;24(3):574.
10. Elawad OAMA, Dafallah MA, Ahmed MMM, Albashir AAD, Abdalla SMA, Yousif HHM, et al. Bardet-Biedl syndrome: a case series. J Med Case Rep. 2022;16(1):169.
11. Savatt JM, Myers SM. Genetic testing in neurodevelopmental disorders. Front Pediatr. 2021;9:526779.
12. Koscinski I, Mark M, Messaddeq N, Braun JJ, Celebi C, Muller J, et al. Reproduction function in male patients with Bardet Biedl Syndrome. J Clin Endocrinol Metab. 2020;105(12):4417–29.
13. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. ACMG laboratory quality assurance committee (2015) standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-24.
14. Álvarez-Satta M, Castro-Sánchez S, Valverde D. Bardet-Biedl syndrome as a chaperonopathy: dissecting the major role of chaperonin-like BBS Proteins (BBS6-BBS10-BBS12). Front Mol Biosci. 2017;4:55.
15. Dong X, Li Z, Wang D, Xiong Y, Li H, Yang P, et al. Prenatal diagnosis of Bardet-Biedl syndrome due to novel variants in the BBS10 gene in a fetus with multiple anomalies: A case report. Exp Ther Med. 2022;24(6):721.

Cite this article as: Panuganti SK, Modi SK, Patel PN, Boda S, Syamala RR. A case report on unusual cause of childhood obesity and visual disturbances-Bardet-Biedl syndrome. Int J Res Med Sci 2024;12:3948-51.