

Case Report

A rare case of polydactyly with multiple defects

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ABSTRACT

Bardet-Biedl Syndrome (BBS) is a very rare genetically heterogenous disorder. Here is a case of 27 yr. old obese male presented with acute gastroenteritis with shock in our department. He had polydactyly in both upper limb and left lower limb, blindness since childhood, with difficult in learning and delayed onset of milestones. Patient's sibling (younger brother 20-year-old) also had same problems since childhood and one female baby died within few days of birth. He was having single testis. Patient was managed conservatively. The available literature on this syndrome was reviewed.

Keywords: Bardet-Biedl Syndrome, Blindness, Heterogenous disorder, Milestone, Obese, Polydactyly

INTRODUCTION

Bardet-Biedl Syndrome (BBS) is a very rare inherited disorder as autosomal recessive. BBS characterized by polydactyly, hypogonadism, obesity, in eye retinitis pigmentosa and also involve other system also. The sign and symptoms vary among affected individuals, even among members of the same family. Bardet-Biedl syndrome affects males and females equally. The disorder was first described by doctors Bardet and Biedl in the 1920s. Associated features can be helpful in making a diagnosis and are important in the clinical management of BBS.

The diagnosis is based on clinical findings and can be confirmed by genetic study in 80% of patients. BBS genes encode proteins that localise to the cilia and basal body and are involved in cilia biogenesis and function.¹ A multidisciplinary approach is required to effectively manage this pleiotropic condition. Although research is in progress, but no targeted treatment for BBS. Prognosis is poor if renal failure occurs.

CASE REPORT

A 27-year-old male was admitted with chief complaints of fever, diarrhea, vomiting and pain abdomen since 3 days. Diarrhea was watery type not associated with blood and mucus and vomiting non-projectile type. There was no history of taking food outside and travelling.

Physical examination

Fever was not recorded during hospital stay. On head to toe examination in eye icterus present and fundus suggestive of retinitis pigmentosa, in oral cavity missing of teeth in lower jaw bilaterally and high arched palate, post axial polydactyly in bilateral upper extremity and left lower extremity (Figure 1).

Preliminary workup showed deranged urea 58.42 and creatinine 3.98, in LFTs SGOT/PT was 130/75, PT/INR 19.8/1.72, total bilirubin 7.9 (direct 4.4 and indirect 3.5), urine routine and microscopy findings were normal. In CBC Hb was 13.1, total counts 31.74×10^3 /cu mm (N 94%, L 3%) and platelet counts 1.28 lakhs/ml. PBF was

normal. Dengue (NS1 and Ig M), widal and malaria parasite was negative. Blood and urine culture sensitivity were sterile. Viral markers (Anti Hcv, HbsAg, Anti H A V Ig M, Anti H E V Ig M and HIV) were negative. In thyroid profile T4, T3 and TSH were 0.57 ng/ml, 1.19 pg/ml and 9.61 mIU/ml respectively and anti-TPO was negative. Serum cortisol, insulin, FSH, LH and testosterone level were within normal limits. Chest x ray and ECG were normal. X-ray of jaw suggestive of missing teeth in lower jaw bilaterally (Figure 2).



Figure 1: Polydactyly in bilateral hand and left feet.



Figure 2: X ray of jaw s/o missing teeth in lower jaw bilaterally.

USG shows splenomegaly and 2D ECHO suggestive of global hypokinesia of left ventricle. CT urography s/o a heterogenous density lesion with multiple foci of fat and soft tissue in left adrenal? myelolipoma? adenoma (Figure 3). Both kidneys are normal in position and structure. BERA s/o B/L moderate to moderate severe hearing loss.

Patient was treated symptomatically with supportive treatment IV fluids, antibiotics, initially with inotrop support, probiotics and ORS solution. Patient was recovered from gastroenteritis and multiple organ dysfunction syndrome in a week. There was no specific treatment for this syndrome. At the time of discharge patient was stable and all parameters (Complete blood counts, Renal function test and Liver function tests) were within normal limits.



Figure 3: CT urography s/o a heterogenous density lesion with multiple foci of fat and soft tissue in left adrenal? myelolipoma? adenoma.

DISCUSSION

Bardet-Biedl syndrome is an autosomal recessive. It is genetically heterogeneous ciliopathy characterized by retinitis pigmentosa, obesity, kidney BBSome, a stable complex involved in signalling receptor trafficking to and from cilia summary by Scheidecker et al.²

Its frequency in Europe and North America falls below 1:100,000 Forsythe and Beales. Some isolated human communities are characterized by unusually high occurrence of this disease Sheffield, BBS prevalence in Newfoundland was reported to approach 1:18,000 Moore et al. BBS is relatively common in the Middle East, with a frequency of 1:13,500 in some Bedouin communities. Ashkenazi Jews, being apparently the most genetically studied founder community, have not yet been subjected to an exhaustive BBS epidemiologic research Fedick et al.³

BBS is a genetically heterozygous disorder. Till now 19 genes described so far (BBS1 to 19). All BBS genes are related to cilium biogenesis and/or function.⁴ Studies have reported a more severe phenotype in those carrying the third mutation suggesting the possible effect of modifier allele. This has been called 'tri-allelic inheritance', or 'recessive inheritance with a modifier of penetrance'.⁵ Nineteen forms have been identified with differing phenotypes.⁶ There is no clear correlation between the genotype and clinical expression of BBS. Few BBS gene mutations (e.g., BBS1) have been found to be associated with a milder phenotype.⁷

Based on a review of 109 BBS patients, Beales et al, proposed modified diagnostic criteria that requiring the presence of either 4 primary features, including rod-cone dystrophy, polydactyly, obesity, learning disabilities, hypogonadism (in males), and/or renal anomalies; or 3 primary plus 2 secondary features, including speech

disorder or delay; strabismus, cataracts, or astigmatism; brachydactyly/syndactyly; developmental delay; polyuria/polydipsia (nephrogenic diabetes insipidus); ataxia, poor coordination, or imbalance; mild spasticity, especially of lower limbs; diabetes mellitus; dental crowding, hypodontia, small dental roots, or high-arched palate; left ventricular hypertrophy or congenital heart disease; and/or hepatic fibrosis.⁸

Bardet-Biedl syndrome treatment is directed toward the specific symptoms that are apparent in each individual. There are currently no proven therapies available for retinal dystrophy associated with Bardet-Biedl syndrome. Standard care from an ophthalmologist is required for management of refractive errors (e.g., myopia) and assistance with low vision aids as vision decrease.

Measures to manage obesity may include age-appropriate diets, exercise programs, and behavioural modifications. In addition, affected individuals should be evaluated by kidney specialists to determine appropriate intervention for kidney disease. Hormone replacement therapy may be necessary for males with hypogonadism. Bardet-Biedl syndrome individuals should undergo regular ophthalmologic examinations as well as periodic assessments to determine the presence of complications.⁹

CONCLUSION

Bardet-Biedl syndrome is a disorder that affects different parts of the body. The signs and symptoms of this condition vary among affected individuals, even among members of the same family. In the coming years, it is likely that other disease-causing genes will be identified so there will be further improvement of the clinical diagnostic services allowing for faster diagnosis and prenatal testing.

The ability to more accurately predict the level of disability an affected individual is likely to experience may be improved by furthering our understanding of the molecular processes leading to phenotypic variation. Understanding the epigenetic factors that may account for intrafamilial variation and other modifiers of the condition will be imperative in this process.

At present no cure for BBS, but that does not mean that there is nothing that can be done to help people with BBS. Research is ongoing to understand the basic mechanisms at the cellular level that ultimately cause BBS. This research will provide clues to develop future treatments.

Elucidation of the molecular pathogenesis of the clinical features of BBS and research into therapeutics may yield

novel treatment options that target organ-specific aspects of the condition, such as renal cysts or rod-cone degeneration, or have a more general modulating effect on several aspects of the condition.

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