A Rare Classical Presentation of Bardet-Biedl Syndrome in a Three-Year-Old Male from South East Nigeria: A Case Report

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Abstract

Bardet-Biedl Syndrome (BBS) is a rare autosomal recessive ciliopathy characterized by obesity, post-axial polydactyly, renal abnormalities, mental retardation, pigmentary retinopathy and hypogenitalism. Diagnosis is rare in early childhood, and only few of the features are present at that age. This is because the disease is slow evolving. However, it is possible to find majority of the component of this syndrome in very young children. A 3-year old very obese male presented with clinical features of sepsis and congestive cardiac failure. He is a product of non-consanguineous marriage with unremarkable family history. Both parents are of the Ibo tribe in Nigeria. Polydactyly was noticed at birth. There was delay in some aspects of his developmental milestone. Examination revealed mild hypertelorism and retrognathia, polydactyly of both feet with syndactyly of the big and second toes. Other findings were short broad hands, mottled pigments on the retina, moderate mental retardation, hypogenitalism, nephrotic syndrome, renal tubulopathy, hyperglycaemia and hypopigmented skin lesions. A case of BBS with all the primary features and some secondary manifestations in a very young child is hereby reported. A high index of suspicion for BBS should be shown in any young child with at least one of the features of this syndrome. This will enhance earlier diagnosis and improve disease outcome.

Keywords

Bardet-Biedl Syndrome, Early Childhood, South East Nigeria, Classical Presentation, Case Report

1. Introduction

Bardet-Biedl Syndrome (BBS) is a rare autosomal recessive ciliopathy characterized primarily by obesity, post-
axial polydactyly, renal abnormalities, mental retardation, pigmentary retinopathy and hypogenitalism [1]-[4]. It is a genetic multisystemic disorder with mutation in 16 different genes [1]. The obesity is mainly truncal, while the retinopathy includes rod-cone dystrophy with childhood onset night blindness and visual loss. Truncal obesity manifests during infancy and remains problematic throughout adulthood. Mental retardation can present with specific learning and behavioral difficulties [1].

The estimated prevalence rate is 1:140,000 - 1:160,000 worldwide [4]. However, higher incidence of 1:1700 - 1:13,500 has been reported from Kuwait and Newfoundland, because of higher consanguinity marriages in these areas [1] [5].

Diagnosis is mainly clinical, and made in late childhood or early adulthood. This is because the disease is slow evolving with gradual loss of night vision and delayed puberty [1]. Significant intrafamilial and interfamilial variations exist in the clinical expression of BBS [4]. Polydactyly may be the only feature at birth [1]-[5].

For ease of diagnosis, the clinical features of BBS are divided into primary and secondary features. The primary features are as aforementioned earlier. The secondary features include developmental delay, behavioral problems, neurological problems, dental anomalies, speech disorders, brachydactyly/syndactyly/clinodactyly, nephrogenic diabetes insipidus, hypertension, diabetes mellitus, anosmia, pigmented naevi, cardiovascular anomalies etc. [1] [3].

A clinical diagnostic criterion of BBS consists of at least four primary features, or three primary features plus two secondary features [1] [3].

I hereby present a case of Bardet-Biedl Syndrome in a 3-year-old male child.

2. Case Report

A 3-year-old male child was referred to us with history of infantile obesity, inability to walk, cough, generalized edema, frequent micturition and difficulty in breathing. There was orthopnoea and paroxysmal nocturnal dyspnoea but no wheezing.

Pregnancy history was uneventful. He was a product of non-consanguineous marriage. Both parents are of the Ibo tribe in Nigeria. He was big at birth but mother could not remember the birth weight. Polydactyly and syndactyly were noticed at birth. His developmental milestone was normal until 12 months of age when it seemed to be halted. He started walking with support at 12 months of life, but yet to walk without support at 3 years of age. His parents attributed this to the infantile obesity. He was yet to speak bi-syllable words or make sentences at 3 years. His appetite was said to be very voracious since infancy, but not to the extent of binging. There was no history of failure to thrive. Family history was not remarkable.

Examination revealed a very obese child (brought in on wheel chair because he could not walk, even with support). He had mild retrognathia and mild hypertelorism. He also had anasarca with short, broad hands (Figure 1). There were hypopigmented macular lesions over the neck, shoulders and back, with unilateral genu varus deformity of the right leg. There was also polydactyly (six toes) on both feet with bilateral syndactyly of the big and 2nd toes (Figure 2). He was severely dyspnoeic, acyanosed, anictenic, febrile (T-38.2˚C), but not pale.

Weight was 60 kg (>97th centile for age) and height was 99 cm (50th centile for age) with a body mass index of 50.5 kg/m² (>97th centile for age). Occipito-frontal circumference was 57 cm, and Mid Upper Arm Circumference was 18 cm (>97th centile for age).

Respiratory rate was 50 cycles/min with decreased air entry both lung fields. There were vesicular breath sounds with generalized coarse crepitation and few rhonchi. Blood pressure was 120/70 mm of Hg, with a heart rate of 140 beats/min. Apex beat was located at 6th LICS–MCL. Only 1st and 2nd heart sounds were heard.

His intelligence quotient, determined by “The Draw-A-Person Test” revealed moderate mental retardation. Muscle tone was normal globally. Abdomen was moderately distended with a tender hepatomegaly of 6 cm. He had micro testis and micro phallus on genital examination.

Dipstick urinalysis showed proteinuria (3+), haematuria (2+), glucosuria (1+), bilirubinuria (1+), urobilinogenuria (2+) Urine.

PH was 8.8, with spot urine protein-creatinine ratio of 2.9. Serum urea and creatinine were normal. Thyroid and liver function tests were also normal. Serum cholesterol was 450 mg/dl. All serum electrolytes were normal but for mild hyperkalaemia (K+ = 5.7 mmol/L) and acidosis (HCO3 = 18 mmol/L). Total serum protein was 30 g/l while albumin was 24 g/l. Random blood glucose was 7.5 mmol/L.
Complete blood count revealed absolute neutrophilia, while urine culture yielded heavy growth of *Escherichia coli*. Ophthalmological examination revealed mild nystagmus and retinal pigment motting on both eyes. Abdominal ultrasound was normal, but for moderate hepatomegaly. Chest X-ray showed gross cardiomegaly.

He was admitted at presentation and commenced on Nebulised Salbutamol 5 mg stat, and then Tablet Salbutamol 4 mg 8 hourly for a week, IV Sodium Bicarbonate 30 mmol slowly stat, IV Frusemide 30 mg 12 hourly for 5 days, Tablet prednisolone 30 mg 12 hourly for a month, IV Augmentin 1.2 g 12 hourly for a week, Tab Paracetamol 500 mg 3× daily for 5 days and a 3 day course of oral antimalarial was also given. He was also placed on a “weight reduction” diet by the dietician.

He did well clinically on the above regimen and was able to walk with support again after 5 days of treatment. Most biochemical derangements resolved except the urinary abnormalities (new values were protein 2+, blood 1+) and the serum cholesterol (450 mg/dl). His blood glucose also normalized on the hospital diet. He was discharged after one week of admission on oral prednisolone (60 mg every morning because of the nephrotic syndrome). Parents were also given nutritional counseling concerning his weight.

3. Discussion

BBS varies in its manifestation in different patients [1]-[10]. Apart from the primary features of obesity, post-axial polydactyly, renal abnormalities, mental retardation, pigmentary retinopathy and hypogenitalism; other secondary manifestations exist [1]-[4] [9]. These secondary characteristics include cardiac anomalies, neurological problems, nephrogenic diabetes insipidus, diabetes mellitus, dental anomalies, hypertension, speech disorders, behavioral problems, brachydactyly/syndactyly/clinodactyly, anosmia, lipid disorders, hepatic abnormalities

![Figure 1. Truncal obesity with polydactyly/syndactyly of both feet.](image-url)
and skin disorders [1]-[4] [9] [11]. Retrognathia, and hypertelorism are inconsistent features of BBS, and may not be very obvious [1].

At least three primary and two secondary features are enough to make the diagnosis of BBS in a patient [1], [9]. The index patient had all the primary features, plus cardiac pathology and skin lesions. This supports the diagnosis of BBS in our 3-year-old patient [1]-[11]. BBS is the standard term that has replaced the older Laurence-Moon-Bardet-Biedl syndrome after it was found that the phenotypes overlap and may be allelic [1] [12].

The index patient posed a diagnostic challenge initially because of his clinical overlap with syndromes like Alström syndrome and Prader Willi Syndrome (PWS). Alström syndrome shares most features with BBS, however, there is no polydactyly nor cognitive dysfunction in the former [9].

PWS also shares common features with BBS, but unlike in the former, there is no hypotonia, failure to thrive, nor sleeping disturbance in BBS [13]. The patient under discuss has normal muscle tone, and there was no history of feeding difficulties, failure to thrive, nor excessive sleeping. Although the patient’s appetite was said to be voracious, there was no history of binging.

Majority of the cases reported in children worldwide were diagnosed either in late childhood or among teenagers [2] [4] [6] [7] [10]. Diagnosis in early childhood is rare [1] [9]. However, few cases have been reported in younger children. Ahmed and Hassan once documented a case of Laurence-Moon-Biedl Syndrome in a 3-year-old Nigerian female who was screened for the disease after the diagnosis was made in her 8 years elder sister [8]. Also, Cristina et al reported a case of BBS with end-stage kidney disease in a 4-year-old Romanian male [9].

Diagnosis is usually not made early because the disease phenotypes are variable and slow evolving [1]. Initial loss of the rod photoreceptors is followed by early macular involvement, with the degeneration of the cone cells. This causes a gradual functional loss of vision [1] [10]. Visual impairment and probably, poor school performance, are the common reasons for coming to hospital in affected patients [1] [4]. The visual pathology then becomes a pointer to the diagnosis in a child with other components of the syndrome.

Our patient presented with sepsis and congestive cardiac failure (CCF). The polydactyly, obesity and mild nystagmus prompted further examination that led to the diagnosis. His parents did not complain about his vision, but were rather worried about the obesity, fever, cough and difficulty in breathing.

Polydactyly and obesity are well documented features of BBS [1]-[10]. Polydactyly when present in BBS, is seen at birth. The incidence of obesity is reported to be 72% - 86% in the BBS population [1] [11] [12] [14]. Although majority of the patients have normal weight at birth, obesity usually sets in by infancy [1] [14]. Polydactyly in a child, more especially with obesity should stimulate a high index of suspicion for syndromic disorders,
including BBS.

The unilateral genu varus deformity found in our patient is likely a complication of his severe obesity. Various types of lower limb deformities result from childhood obesity [15].

Cardiac pathology is a recognized part of BBS [1]-[3]. The CCF in our patient could not be totally explained by the sepsis he had. His cardiac symptoms started 6 months before the onset of cough, fever and frequent micturition. The later symptoms started a week before presentation. Cardiac anomalies, including congenital heart defects and dilated cardiomyopathy, are reported in up to 50% of patients with BBS [1] [2]. Echocardiography was not done for our patient due to financial constraints. Elbedour et al. suggested that echocardiographic evaluation be done for all cases of BBS [2].

Liver pathology is found in BBS, though it is considered a secondary feature of the disorder [1] [4] [9] [11] [14] [16]. However, the hepatomegaly in the index patient may be due to the CCF, rather than the BBS. This is because of the normal liver function test, and nil significant hepatic pathology on abdominal ultrasound.

Renal involvement was recently included as a primary feature of BBS [1] [4] [9] [11] [14]. Various kinds of renal pathologies (structural and functional) including nephrotic syndrome and renal tubular acidosis can be found in patients with BBS [1] [4] [8] [10] [11] [17]. End stage renal failure is a major cause of death in these patients [16]. Our patient had both nephropathy and a renal tubulopathy. While Singh et al. documented steroid sensitive nephrotic syndrome in a 10-year-old Indian male, Lin & Lin found bilateral dilatation of the renal minor calyces in an 8-year-old female [4] [10].

Skin disorders varying from hyper to hypopigmented lesions and recently multiple pigmented nevi have been reported in patients with BBS [1] [11]. The patches of hypopigmented skin lesions on the index patient may be part of the syndrome. Karaman documented multiple pigmented nevi in a Turkish female with BBS [11].

Early retinal dystrophy, which is slowly progressive in these patients, is the most common component of the syndrome [1] [9] [11]. Mild retinal anomaly is usually the finding in younger patients, while severe retinopathy (retinitis pigmentosa and macular degeneration) is found in older patients. The retinal mottling in our patient depicts early sign of retinitis pigmentosa. Iwuala et al reported nystagmus and retinal mottling in another Nigerian male child with BBS [6].

Although developmental delay and cognitive deficit are common in BBS, mental retardation tends to be variable in these patients [1] [11]. It has been reported that decrease in IQ level correlates with the presence of visual handicap [11] [17].

The hypercholesterolemia in the index patient either reflects the presence of nephrotic syndrome alone, or the deranged hyperlipidaemia that can also occur in patients with BBS [1]. The BBS 5 - 9 and BBS 11 genes are expressed in adipose tissues [11] [18]. Hypercholesterolemia is seen as a secondary feature of BBS.

Both diabetes insipidus and diabetes mellitus are inconsistent findings in some patients with BBS [1] [8] [11]. The index patient had glucosuria and hyperglycaemia.

Hypogenitalism, which is one of the primary features of BBS, is more obvious as the child gets older. Tanner staging in pubertal patients reveals delayed sexual maturation [1] [6]-[11]. In affected children, primary gonadal failure may occur later in life [8]. The index patient, though still very young, has external genitalia that is grossly small for age.

Our patient had financial constraints and this was a major limitation because some important investigations could not be done. Again, his parents were defaulting to the follow-ups. However, the detailed documentations at his initial presentation and the available investigation results made this case report possible.

4. Conclusion

A classical presentation of BBS in very young children is rare. The presence of all the primary features of BBS, along with some of its secondary manifestation in a 3-year-old male, makes this case report very unique. Therefore, the finding of any of the primary features of this syndrome in a younger child should prompt the search for other manifestations of this disorder. This may improve earlier diagnosis of BBS, and possible improvement in disease outcome.

Consent

Written informed consent was obtained from the patient’s legal guardian for publication of this case report and
any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Competing Interest**
There is no competing interest.

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