A Case Of Bardet Biedl Syndrome

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Citation

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Abstract

Bardet Biedl syndrome is a rare autosomal recessive condition with a wide spectrum of clinical features. The accepted major criteria for diagnosis include retinal dystrophy, obesity, polydactyly male hypogonadism, mental retardation and renal dysfunction. We report on an 11 year old boy patient exhibiting characteristic features of this syndrome. In the light of this case, the literature regarding Bardet Biedl syndrome has been reviewed.

INTRODUCTION

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive disorder (MIM 209900). BBS was first described by Bardet and Biedl in the 1920[1]. The principal manifestations are rod-cone dystrophy (Retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. Other features, not always present, include hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dental anomalies and developmental delay [2,3]. We presented here a case of BBS which is rarely seen.

CASE REPORT

An 11 year old boy was admitted to our hospital complaining of loss of vision, speech deficit, learning difficulty, poor balance, and ataxic gait. He was the seventh child of healthy consanguineous parents (first- degree relatives). His oldest two brothers had died (one at the age of 1 and, the other at 3 months old) and the etiologies of their deaths are unknown.

On physical examination he had facial dysmorphism, he weighed 46 kg,his height was 134 cm and body mass index (BMI) was 25.6. Exotropia (Figure 1), horizontal nystagmus, rod-cone dystrophy (atypical retinitis pigmentosa) in his left eye was noticed on ophthalmologic examination. Neurological examination showed sings of ataxia, poor coordination, dysmetri, dysdiadochokinesia and intentional tremor. Maldescended testes were detected on genital examination and his penis was small and buried in adipose tissue (Figure 2). He had a postaxial polydactyly (extra digit was on the left foot; Figure 3). He had mild mental retardation.

Figure 1

Figure 1: Exotropia, horizontal nystagmus, rod-cone dystrophy (atypical retinitis pigmentosa) in left eye of the patient

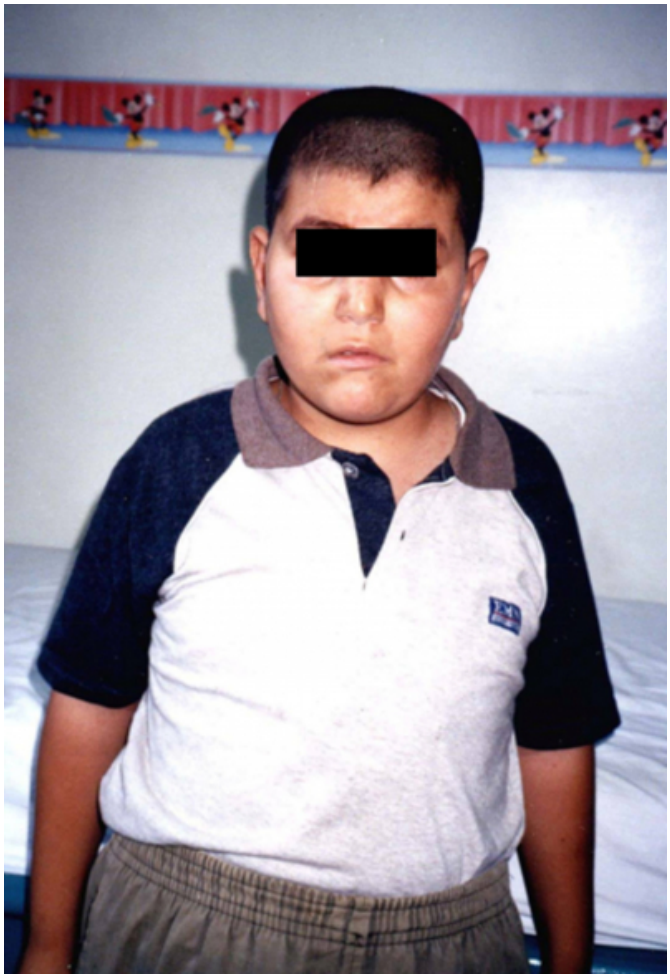


Figure 2

Figure 2: Maldescended testes and small penis buried in adipose tissue

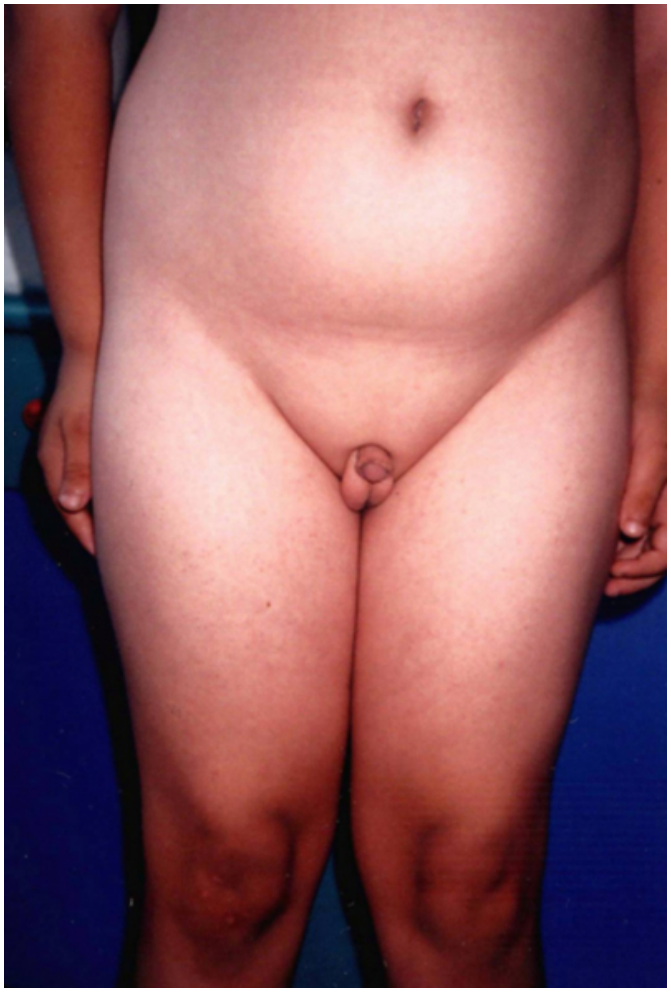
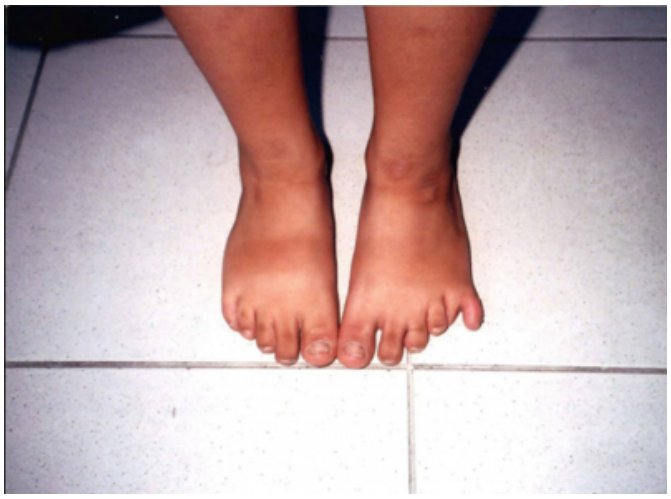


Figure 3

Figure 3: Extra digit on the patients left foot.



Laboratory analyses including complete blood count, urinalysis, biochemical and thyroid hormone parameters, transthoracic echocardiography as well as magnetic resonance imaging (MRI) scans of brain and hypophysis were normal. Renal ultrasonography revealed few renal parenchymal cysts of 7-12mm diameter bilaterally.

DISCUSSION

The syndrome was described by Bardet Biedl in the 1920s. It was later erroneously coupled with another disorder described by Laurence and Moon, and was consequently referred to as Laurence- Moon-Biedl syndrome. BBS is distinguished from the much rarer Laurence- Moon syndrome in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly [4,5].

The prevalence of BBS generally considered a rare disorder is 1:160000 in Europe and North America[6], although higher incidence has been reported in the isolated populations of Newfoundland [1:13000[2]] and Kuwait [1:17000[7]].

Obesity, mainly of the trunk is one of the most common features in BBS. It develops in early childhood and is aggravated with age. Ocular manifestations are also common and become apparent between the ages of 4 and 10 years. Hypogonadism in affected males is common. Most affected men have small external genitalia with primary testicular failure. Postaxial polydactyly is one of the earliest and most common manifestations of BBS. Renal failure is the major cause of morbidity and early mortality in BBS. A wide range of renal abnormalities has been described (Chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, vesicoureterix reflux). Despite the presence of underlying renal malformations, only a small number of BBS patients were symptomatic at the time of the survey. Mild to moderate mental retardation and learning difficulties are additional features of the syndrome[2,3]. In 1999, modified diagnostic criteria were defined following a study conducted in the UK in 109 BBS patients[3]. Patients who had 4 primary characteristics or 3 primary and 2 secondary criteria were identified as BBS (Table 1). Our case had all of the primary and 3 of the secondary diagnostic criteria.

Figure 4

Table 1: Modifield diagnostik criteria

Primary Features
Rod-cone Dystrophy
Polydactyly
Obesity
Learning Disabilities
Hypogonadism in males
Renal Anomalies
Secondary Features
Speech disorder/Delay
Strabismus/cataracts/astigmatism
Brachydactyly/syndactyly
Developmental delay
Nephrogenic diabetes insipidus
Ataxia/poor coordination/inbalance
Mild spasticity
Diabetes mellitus
Dental crowding/hypodontia/small roots
Left ventricular hypertrophy/congenital heart disease
Hepatic fibrosis

BBS is an autosomal recessive disorder characterized by non-allelic heterogeneity. Genetic analysis has mapped the disease to several independent loci, all of which produce similar phenotypes. Linkage analysis studies have so far identified eight distinct loci responsible for the syndrome [BBS1:11q13$_{8}$, BBS2:16q21$_{9}$, BBS3:3p13-p12$_{10}$, BBS4:15q22-3q23$_{11}$, BBS5:2q31$_{12}$, BBS6: 20p12$_{13}$, BBS7: 4q27$_{14}$, BBS8: 14q32.11$_{15}$]. Six genes associated with BBS have been identified, but their sequences have not illuminated the molecular and cellular etiology of the disease. The most plausible hypothesis regarding a shared function for BBS proteins is that they assist microtubule-related transport and cellular organization processes, in particular relating to ciliary/flagellar and centrosomal activities. This hypothesis is supported by several studies using different model organisms15-18. Some of the phenotypes exhibited by BBS proteins, including retinal degeneration, skeletal anomalies and renal cysts/malformations bear resemblance to human diseases associated with abnormal cilia function15, 19.

Further larger scale studies should be conducted in order to understand the exact pathogenesis of this syndrome.

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