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Case Report

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Bardet Biedl Syndrome-Report of three Cases and Review of Recent Articles

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ABSTRACT

Purpose: To report three cases of a rare inherited familial disorder of Bardet-Biedl Syndrome (BBS).

Study Design: Observational case report.

Method: Two out of eight siblings presented in their second decade of life with dimness of vision in both eyes since birth. The third one is the only person of the family presented also in second decade of life with gradual blurring of vision in both eyes and outward deviation of left eye. Detail clinical history was taken. Physical, anthropometric, ophthalmic, psychological examination was done and appropriate clinical investigations were performed to exclude other systemic disorder. Review of recent literatures was done.

Result: First two cases were brothers, who were mentally retarded child with delayed developmental mile stone. They were short, obese and had polydactyly, gynecomastia, hypogonadism. Their vision was poor and had retinitis pigmentosa with optic atrophy. The third one was also mentally retarded and had polydactyly, trunkal obesity, atypical retinitis pigmantosa with optic atrophy. They did not had deafness or any systemic abnormalities. Depending on clinical findings they were diagnosed as a case of BBS.

Conclusion: The retinitis pigmentosa in BBS is progressive and visual loss can not be halted. So proper rehabilitation and counseling is only the way to help the BBS child and to protect them from being social burden.

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Introduction

Bardet-Biedl Syndrome (BBS) is an autosomal recessive genetic disorder characterized by structural and functional abnormalities of organ and tissue with diverse embryonic derivatives. The defective gene was mapped to four chromosames with complete penitrance and different expresibility [1]. The gene loci have been termed – BBS1, BBS2, BBS3, BBS4 mapped to chromosome 11q 13 (BBS1), 16q 21 (BBS2), 3p 13 (BBS3), 15q 22 (BBS4) [1,2].

The five cardinal features of BBS are Pigmentary retinopathy (87 to 90%), Polydactyly or Syndactyly (66 to 75%), Trunkal obesity (75 to 92%), Oligophrenia/mental retardation (73 to 87%), Hypogonadism (24 to 80%) [3]. Other associated features are short stature 35%, brachycephali 50%, congenital heart disease, renal disease, sensory deafness [1-3].

BBS is not so uncommon. The prevalence of this disorder is suggested of about 1: 16,0000 of the population [4]. Occasionally ophthalmologist encounter this problem. These patients deserve social awareness and sympathized helpful attitude, which can facilitate their life easy and effective. So the responsibility of the ophthalmologist to these babies is remind able, they must make proper diagnosis, counseling and proper referral.

Case Report

Case 1 & 2:

Yusuf and Zakir two brothers of about 17 years and 15 years old were presented in paediatric out patient department, Chittagong Eye Infirmary and Training Complex on 4th April ,2004 with the complaints of blurred vision since birth. Their attendant gave no history of consanguineous marriage of their parents & abnormal birth events. He also stated that the two boys showed poor mental performance since birth and delayed developmental mile stone. They did not have any chest pain or abdominal pain and any problem with urination.

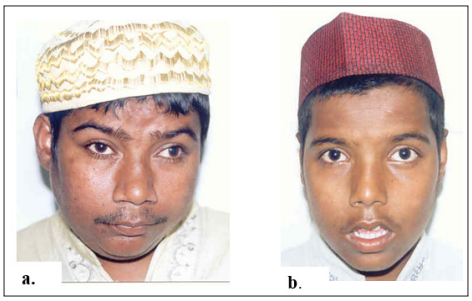

Figure I: Showing a) Yusuf with non-fixing eyes b) Zakir with apathetic look

Physical examination revealed that both the boys are dull looking, apathetic. They are obese and Yusuf is shorter than Zakir. The body weight of Yusuf was 44 kg and Zakir was 48 kg.

Figure 2: Showing Yusuf and Zakir, Yusuf was shorter than Zakir

Yusuf had polydactyly in both hands, syndactyly in right hand, polydactyly in both legs while Zakir had polydactyly in right leg.

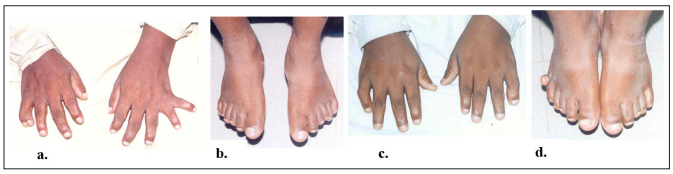

Figure 3: Showing:

a) Hands of Yusuf with polydactyly in both hands and syndactyly between little and ring finger of right hand.
b) Legs of Yusuf with polydactyly in both legs
c) Hands of Zakir showed no abnormality
d) Legs of Zakir showed polydactyly in right leg

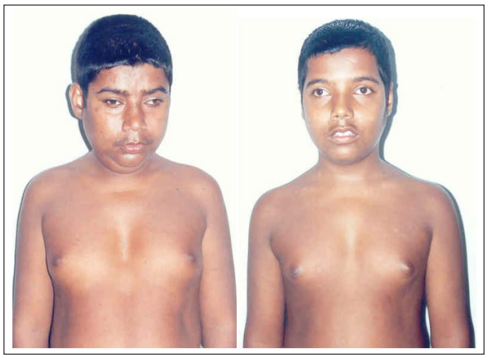

Figure 4: Showing both brother are obese with gynecomastia

Both of them had hypogonadism, gynecomastia.They do not had any deafness.

Their pluse, blood pressure was within normal limit. No abnormalities were detected in CVS and respiratory system.

Psychological assessment done by Shishu Bikash Centre, Chittagong. They use RZS scale which showed mental age of Yusuf was about four yrs whether he was seventeen yrs old, Zakir had moderate mental, intellectual functional levels.

Yusuf had no light perception in his both eyes. Left eye was exodeviated of about 450, did not take fixation on cover test. He also had mid dilated poorly reacting pupil and posterior subcapsular cataract in both eyes.

Fundus revealed (through hazy media due to cataract) similar findings in two eyes which were waxy pale optic discs, narrowing of retinal vessels, bone spicules pigments distributed at mid retinal periphery. According to fundus findings we diagnosed the case as retinitis pigmentosa with optic atrophy. We could not document the colour fundus photography due to hazy media.

Zakir had light perception in his both eyes and projection of rays were normal in all four quadrants of retina. Anterior segment examination was unremarkable except mid dilated poorly reacting pupil. Refraction showed 7DS myopia but no improvement of vision with correction. His retina also showed similar findings in both eyes, these were waxy pale optic discs, vascular narrowing, bull's eye pattern maculopathy, bone spicule pigments distributed at mid retinal periphery. So with all these he also suffered from retinitis pigmentosa with optic atrophy.

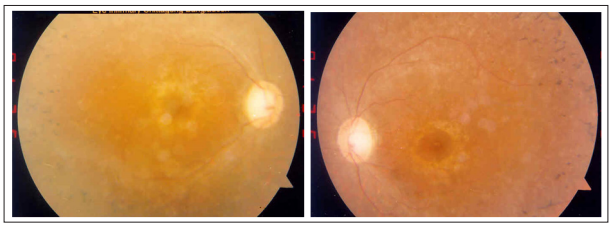

Figure 4: Colour fundus photography of both eyes of Zakir with retinitis pigmentosa with optic atrophy (waxy pale optic discs, vascular narrowing, bull's eye pattern maculopathy, bone spicule pigments distributed at mid retinal periphery).

Routine blood examination, urine examination, blood urea, serum creatinin, ECG of both brothers were normal.

Depending on all history and clinical findings they were diagnosed as cases of "Bardet-Biedl Syndrome".

For vision concern as we had nothing to do so for social rehabilitation, they were referred to Shishu Bikash Centre, Chittagong, Bangladesh.

Case 3:

Mr. Akbar Husain 14 years old came on 02-02-2005 with the complaints of gradual loss of vision both eyes, which initiated with night blindness for last one year. He also complaints of outward deviation of his left eye for last six months.

His parents did not give any history of their consanguinous marriage. They also mentioned about their child's poor mental performances.

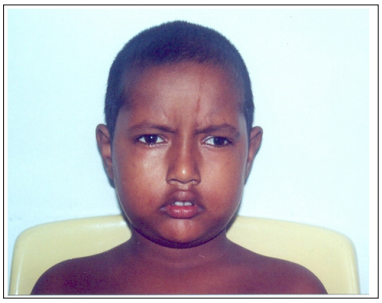

Figure 5: Ali Akbar with left extropia

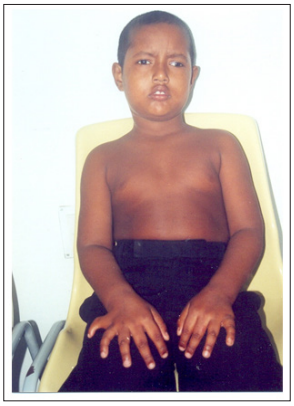

Figure 6: Ali Akbar with trunkal obesity, gynecomastia & polydactyly

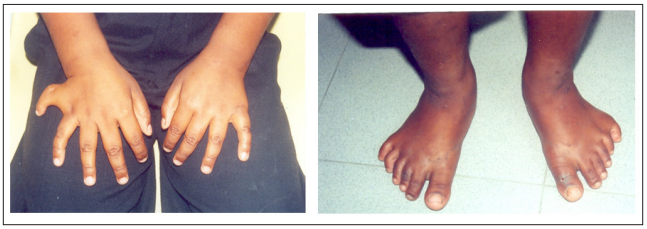

Figure 7: Hands & legs of Akbar showed polydactyly

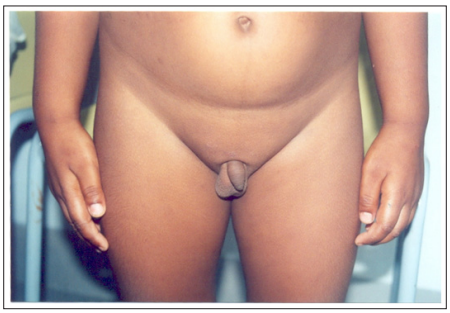

Figure 8: Akbar showed Hypogenitalism

This boy also had trunkal obesity, gynecomastia, hypogenitalism, polydactyly in right hand.

Ocular Examination revealed best corrected visual acuity in his right eye was 6/60 and left eye was 3/60, left extropia (15°), no abnormalities were detected in the anterior chamber. Fundus showed atypical retinitis pigmentosa, bull's eye pattern maculopathy, waxy pale disc in both eyes.

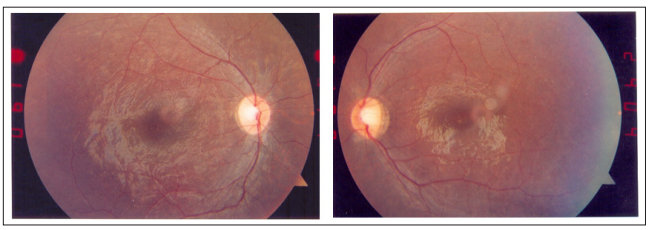

Figure 7: Fundus photograph of Akbar showed atypical retinitis pigmentosa with waxy pale disc and bull's eye pattern maculopathy both eyes

Systemic examination showed no abnormalities in the CVS and kidneys. USG of KUB region was normal. No abnormalities were found in routine blood and urine examination.

With all these findings he was diagnosed as BBS syndrome.

Discussion

BBS is a rare inherited disorder commonly approach to ophthalmologist with reduce vision. BBS is a member of atypical retinitis pigmentosa family, presented with multi system disorder.

This syndrome initially reported by John Zacheriah Laurence and Robert Moon in 1866 [5]. They reported the four cases of "retinitis pigmentosa" in a family. In that report they described four out of eight sibilings with atypical pigmentary retinopathy, mental retardation, hypogonadism, spastic paraplegia, short stature. But the three of five cardinal signs of BBS **first defined** by George Bardet in 1920. These are **pigmentary retinopathy, polydactyly and obesity**. In 1922 Artur Biedl an Austrian professor of pathology and endocrinology added mental retardation and hypogonadism with these disorder in his case report of two siblings. Finally in 1925 Solis –Cohen, Weiss rediscovered the paper of Laurence & Moon and connected it to this syndrome. Then they coined the name- "**Laurence Moon Bardet Biedl Syndrome**" [6,7]. The terminology gained universal acceptance in the world literature. But many of the authors considered the **Laurence Moon** and **Bardet Biedl Syndrome as two separate entities** with overlapping features (retinitis pigmentosa, mental retardation, hypogenitalism) [1,3]. Spastic paraplegia is the predominant features in the Laurence Moon syndrome (LMS) while polydactyly and obesity are predominant in the Bardet Biedl Syndrome (BBS).

Visual problem in BBS starts with in first ten to twenty yrs of life [1-3]. Initially poor night vision followed by loss of central vision, The macula is involved early and showed bull's eye pattern macular lesion [1,8,9]. Loss of central vision being the general rule. Nystagmus is a common feature [10]. Abnormal ERG amplitude is diagnostic tools in early stage [1-3].

BBS have fundus changes similar to retinitis pigmentosa like-constricted arteriole, bone spicule pigments at mid retinal periphery and waxy disc atrophy.

Histopathological study of retinal lesion shows diffuse retinal degeneration and loss of both rod and cone with diffuse migration of pigment. Most patient (73%) are legally blind by age 30 yrs [3].

Here we report three cases of BBS. First two siblings out of eight who were suffering form BBS. They didn't give any history of consanguinity like other reported cases [1]. They showed mental retardation and delayed developmental mile stone. The elder one of them lost his vision completely but younger one had only light perception and projection of rays in all quadrants. Younger one was myopic like reported cases by other authers [1]. The eyes of elder one was more affected with left exotropia, (could not fix on cover test) and posterior subcapsular cataract. The third case also showed mental retardation and profound visual loss with initial night blindness for last one year, like reported cases of Ruth Riise etal [1].

Fundus of all three cases showed extensive pigmentary retinopathy with optic atrophy. In addition the fundus of Zakir and Akbar showed bull's eye pattern maculopathy, similar to cases (16) reported by Jacobson SG and co-worker [8].

Like other reported cases our patients were also short stature, obese, having polydactyly of hands and legs, hypogonadism, hypogonadism and gynecomastia. There were no cardiac and renal abnormalities in our cases. As our cases had more than three cardinal signs so they were diagnosed as BBS [11].

BBS may be confused with Alstrom hallgren syndrome, having similarity in pigmentary retinopathy, obesity, perceptual deafness, diabetes mallitus but no polydactyly, mental retardation or hypogonadism[1,3]. Prader Willi Syndrome also showed mental retardation, hypogonadism, diabetes mallitus which are like BBS but have no retinitis pigmentosa, polydactyly.

Some routine investigation should done like routine urine test, serum urea, blood creatinine, ECG echocardiography, USG of KUB region to evaluate the concern systemic involvement.

There is no definite treatment, nothing can halt the progression of disease. Social rehabilitation (special schooling is needed for mental retardation), genetic counselling (is needed to reduce incidence of BBS) should be done. Management of kidney or cardiac problems if present. Death may occur at an earlier age for cardiac and renal problem.

These poor children need our sympathetic attention. We must not consider them as social handicap but as social part. So, we should properly guide the family to overcome the difficulties for reduce social burden.

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