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Bardet-Biedl Syndrome

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A twenty-nine year old lady presented to the ophthalmology clinic with night blindness and was found to have retinitis pigmentosa in association with mental retardation, obesity, polydactyly and history of renal calculi. She is diagnosed with Bardet-Biedl syndrome which is a rare autosomal recessive ciliopathic multisystemic disorder.

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Bardet-Biedl syndrome (BBS) is a rare genetically heterogenous autosomal-recessive disorder. It is a disease of immotile cilia characterized by obesity, polydactyly, rod-cone dystrophy, mental retardation, renal dysfunction and hypogonadism[1]. Two cases, from the same family, had been reported from Bahrain in 1991[2].

The aim of this report is to present the third case of Bardet-Biedl syndrome from Bahrain.

THE CASE

A twenty-nine year old Bahraini female complained with diminished vision in both eyes, especially at night. She is mentally retarded, obese, has an extra finger in her left hand, has short stature and has hirsutism, see figure 1.

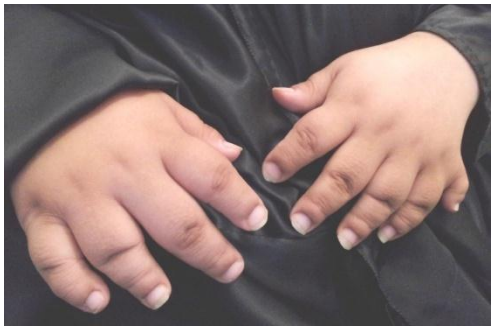

Figure 1: Extra Digit in the Left Upper Limb

Visual acuity was difficult to assess due to mental retardation. Anterior segment showed bilateral

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posterior polar cataracts, clear corneas and round regular reactive pupils. Fundus examination showed mild pallor of the optic discs, bull's eye maculopathy and pigmentary retinopathy indicative of retinitis pigmentosa, see figures 2 and 3.

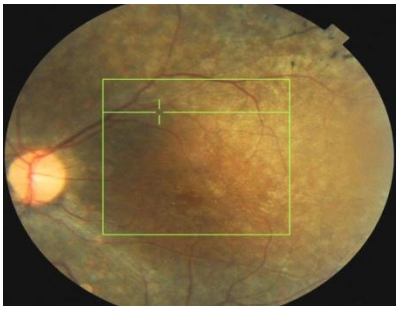

Figure 2: Colored Fundus Photo of the Left Eye Showing Pigmentary Changes (Bone Spicules) Characteristic of Retinitis Pigmentosa

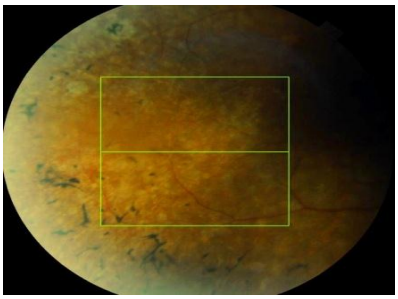

Figure 3: Colored Fundus Photo of the Right Eye Showing Peripheral Retina with Scattered Bone Spicules

CT abdomen showed bilateral multiple renal calculi, see figure 4. No cysts were detected. Creatinine was slightly elevated, other blood investigations were normal. Genetic study could not be performed because of the unavailability of the test.

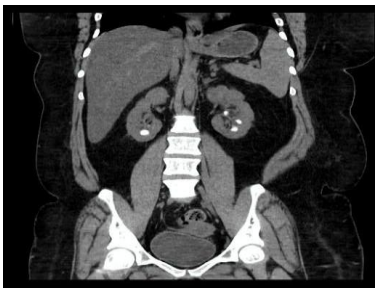

Figure 4: CT Abdomen Showing Bilateral Multiple Renal Stones

DISCUSSION

Bardet Biedl syndrome was first described in 1920 by Bardet GL, a French physician, and Biedl A, a Hungarian endocrinologist[3]. It was distinguished from Laurence-Moon syndrome by the presence of post axial polydactyly. Hence, the term Laurence-Moon-Bardet-Biedl syndrome is no longer used[4].

The incidence in North America and Europe is about 1 in 150,000, and 1 in 17,500 in Newfoundland[4]. It is even higher in some Arab populations, such as Kuwait (1 in 13,500) due to the high prevalence of marital consanguinity[5].

Diagnosis is usually made by the presence of four primary features or three primary features in addition to two secondary features, see table 1[6]. Most patients are diagnosed in late childhood or early adulthood, although polydactyly was present since birth. However, the feature that initiates the investigation of BBS is the development of retinal dystrophy. The retinal dystrophy usually starts with loss of rod photoreceptors followed by degeneration of cone receptors presenting as a typical retinitis pigmentosa with macular involvement[7]. Cataracts, refractive errors and strabismus might be present as well. Truncal obesity presents in more than 70% of cases. Renal abnormalities can be a major cause of morbidity and mortality. It classically manifests with cystic tubular disease and anatomical malformations and eventually leads to end-stage renal failure[8]. Hypogonadism may manifest as delayed puberty or hypogenitalism in males and genital anomalies in females. Involvement of other organ systems, such as, the heart and gastrointestinal system is also noted[1].

Table 1: Clinical Diagnostic Features of Bardet-Biedl Syndrome[6]

Primary Features	Secondary Features
• Rod-cone dystrophy	• Speech delay
• Polydactyly	• Developmental delay
• Obesity	• Diabetes mellitus
• Genital anomalies	• Dental anomalies
• Renal anomalies	• Congenital heart disease
• Learning difficulties	• Brachydactyly/Syndactyly
	• Ataxia/poor coordination
	• Anosmia/hyposmia

Although the classical features associated with BBS are well documented, other differential diagnoses should be considered; Laurence-Moon syndrome is usually differentiated from BBS by the presence of spastic paraparesis and absence of polydactyly; Alström syndrome characterized by hearing loss, but no polydactyly and learning difficulties; McKusick-Kaufman syndrome characterized by urogenital, cardiac and digits anomalies but normally lacks the rod-cone dystrophy, obesity and learning difficulties[4,9,10].

Diagnosis can be confirmed by molecular genetic testing. The first gene for BBS was discovered more than ten years ago and so far 16 disease-causing genes have been identified to be associated with BBS[1]. Electroretinography can be used in the first two years of life to detect early changes of retinal dystrophy[11].

BBS is a disease of immotile cilia. Immotile cilia are sensory organelle regulating the signal transduction pathways. Defects in immotile cilia present clinically with rod-cone dystrophy, situs inversus and cystic kidneys. Rod-cone dystrophy develops as a result of abnormal signaling across the defective cilia between the inner and outer photoreceptors leading to apoptosis[1].

The management of this condition is multidisciplinary. Blood pressure should be measured regularly if there is an evidence of hypertension. Ophthalmologic assessment is required including electroretinogram to determine the onset and severity of rod-cone dystrophy. Low visual aids can significantly improve the quality of life for those who are visually impaired. Every individual with BBS should be examined by a nephrologist. They should be assessed by endocrinologist for the possibility of developing diabetes mellitus and for effective weight management. Regular developmental and educational assessment is important to ensure that the patients benefit maximally from their learning environment[1,3,4].

Prognosis is usually poor due to renal failure. Genetic counseling and preconception genotyping of family members may be worthwhile. In high risk families, a second trimester sonography can be offered to detect post-axial polydactyly and renal anomalies[1,3,4].

CONCLUSION

A case of Bardet-Biedl syndrome in a twenty-nine year old lady was presented. Bardet-Biedl syndrome is a rare autosomal recessive cilliopathic disorder that manifests with rod-cone dystrophy, polydactyly, obesity and renal dysfunction. In this paper, we are presenting the third case diagnosed in Bahrain.

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