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IMAGES IN ENDOCRINOLOGY

Retinal Findings in Bardet-Biedl Syndrome

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Abstract

We report three cases of Bardet-Biedl syndrome (BBS) among which a young female and two siblings from a separate family, presented with common features of obesity, postaxial (ulnar) polydactyly, speech delay, developmental delay with learning difficulties and progressive deterioration of vision. Fundus examination revealed maculopathy and other remarkable findings in these patients. In this image of endocrinology, we describe the BBS phenotypes of these cases highlighting the fundus photography features with a plan for close follow up on obesity and endocrine complications.

Key words: polydactyly, obesity, maculopathy, Bardet-Biedl syndrome.

A 22-year-old female (patient A) (Fig.1)(Fig.2) born from non-consanguineous marriage and two siblings from a separate family, 10-year-old boy (patient B) (Fig.3) and 15-year- old girl (patient C) (Fig.3), born from consanguineous marriage had common features of weight gain, postaxial (ulnar) polydactyly, speech delay, developmental delay with learning difficulties and progressive deterioration of vision since early childhood.

Figure 1. Photograph of patient A showing an overweight female.

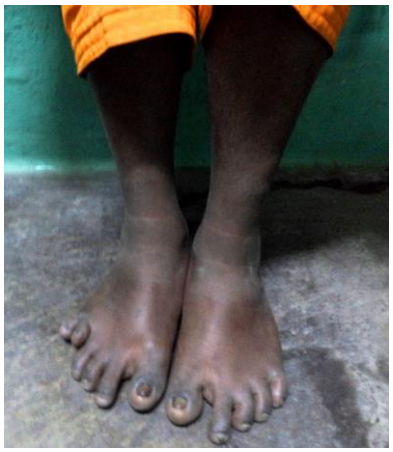

Figure 2. Postaxial polydactyly in patient A.

Figure 3. Photograph showing the two overweight siblings (patients B and C) with postaxial polydactyly.

The boy (patient B) had ataxia; body mass index (BMI) of 23.5 kg/m^2 (>95th centile) with phallic length of 5 cm and testis measuring 3 cc bilaterally. Both girls (patients A and C) also had higher BMI [first patient:

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27.4 kg/m^2 and third patient: 26.8 kg/m^2 (>95th centile)]; regular menstrual cycles and normal secondary sexual characteristics.

Fundus examination: Patient A: mild pallor of the disc, attenuation of retinal arterioles; cellophane maculopathy; few isolated bony spicules along the terminal blood vessels (Fig.4)(Fig.5).

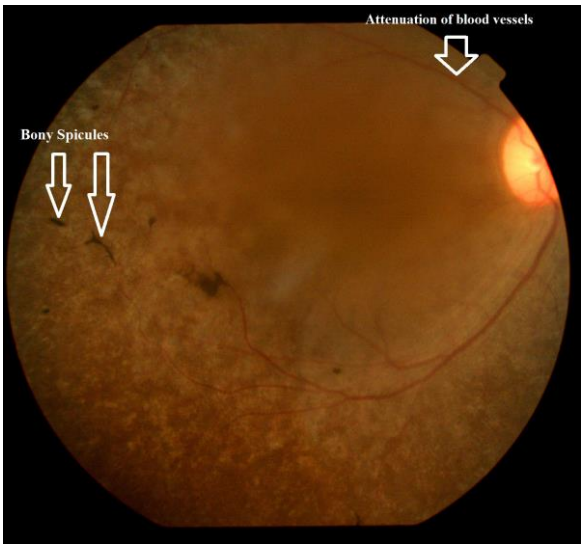

Figure 4. Fundus photograph of the right eye (patient A).

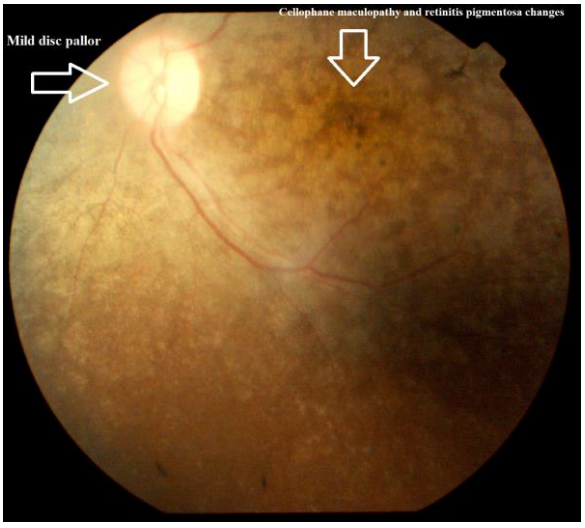

Figure 5. Fundus photograph of the left eye (patient A).

Patient B: mild pallor of the disc; presence of internal limiting membrane folds surrounding the fovea; retinal pigment epithelial atrophy around the foveal and peri-foveal zone resembling Bull's eye maculopathy (Fig.6)(Fig.7).

Patient C: mild pallor of the disc; attenuation of retinal arterioles; cellophane maculopathy with pigment clumps around the macula (Fig.8)(Fig.9). Biochemical investigations including correlated hormonal and lipid profile, ultrasound (USG) abdomen and echocardiography were non-contributory. Electroretinography and further investigations were refused by the patients' families.

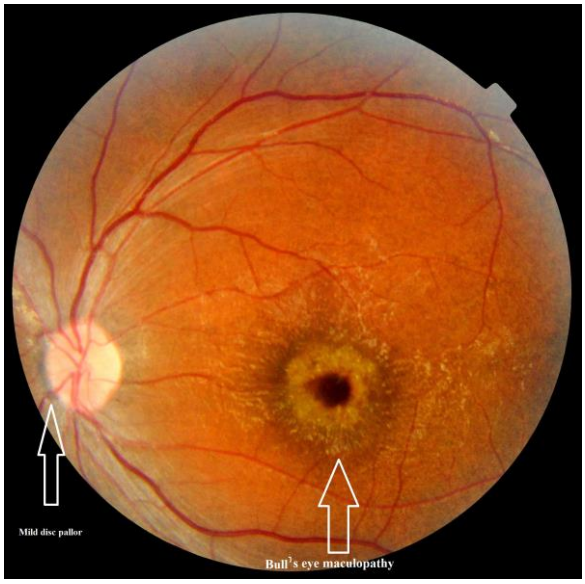

Figure 6. Fundus photograph of the left eye (patient B).

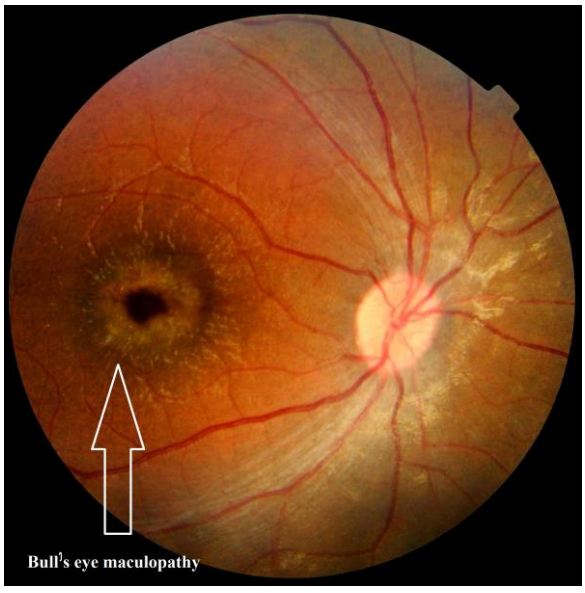

Figure 7. Fundus photograph of the right eye (patient B).

Based on the manifestations, the following differential diagnoses of syndromes associated with obesity were considered: Weiss syndrome, Biemond II syndrome, McKusick–Kauffman syndrome, Alstrom syndrome and Bardet-Biedl syndrome.[1,2]

With characteristic clinical features, Bardet-Biedl syndrome (BBS) was diagnosed in our patients as per modified diagnostic criteria by Beales et al., (Table 1)[3,4] and other possibilities were ruled out. The inheritance of BBS is usually considered autosomal recessive

although this was absent in our first case. The diagnosis can be made based on clinical features and phenotype evolves variably in different patients.

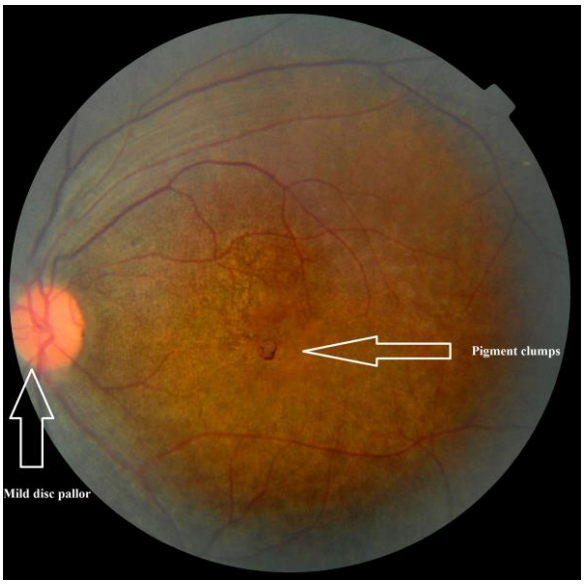

Figure 8. Fundus photograph of the left eye (patient C).

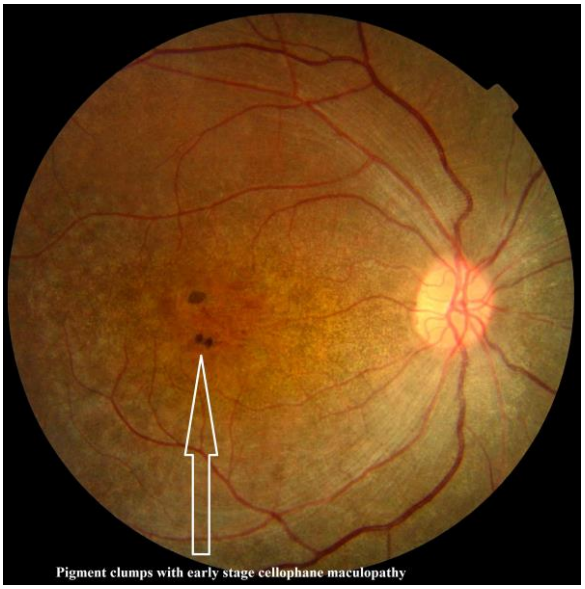

Figure 9. Fundus photograph of the right eye (patient C).

Hypogonadism in BBS patients may manifest as delayed puberty or hypogenitalism in males and genital abnormalities in female;[3,5,6] although this was absent in our cases at the time of presentation.

Table 1. Diagnostic features (Four primary features or three primary features and two secondary features are required for a clinical diagnosis of BBS).[3,4]

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

Bardet-Biedl syndrome is also a genetic form of obesity probably caused by mutations in any of at least 12 genes with increased risk of diabetes, and it is distinct from nonsyndromic obesity.[3-6] Feuillan et al., found that patients with BBS had higher leptin than expected for their degree of adiposity, consistent with the notion that ciliopathy-induced leptin signaling dysfunction is associated with leptin resistance. These BBS patients also had predisposition for metabolic complications, including hypertension and hypertriglyceridemia.[7] Apart from obesity, our cases (diagnosed in late childhood to adolescence) are probably still in the evolving phase of other metabolic and endocrine complications which we will follow up and manage accordingly. The ocular phenotypes in BBS2, BBS3 and BBS4 genotypes were reported to be early and severe.[8] However, in our cases, fundus findings varied even within the same family. This spectrum of findings may further elucidate the evolving pathogenesis of BBS.

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