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CORRESPONDENCE

Sir,

Bardet–Biedl syndrome associated with glaucoma

Bardet–Biedl syndrome (BBS) is a hereditary autosomal recessive disease characterized by mental retardation, obesity, retinal pigmentary dystrophy, polydactyly, and hypogenitalism.[1] Despite the fact that several forms of BBS are correlated with distinct loci on different chromosomes which have been identified, a diagnosis of this entity is still made on clinical data and is based on the aforementioned cardinal clinical signs.[2]

Glaucoma has been previously reported in two young patients with the Alstrom–Hallgren syndrome (AHS), a special variant of BBS.[1]

This paper reports the first description of glaucoma in a typical BBS patient, indicating the possibility of an infrequent association.

Case report

A 14-year-old black female patient, born from a consanguineous marriage (parents were second cousins) was referred to the Glaucoma Unit of Department of Ophthalmology, Fluminense Federal University, for evaluation of decreased visual acuity.

Anamnesis revealed that she was born by caesarean section, came to term, with a low birth weight. After 4 months of age she developed obesity. Intellectual deficit was noticed when she was 7 years old, which manifested as learning disorders.

Physical examination disclosed normal cranial conformity, atypical facies, ocular hyperthelorism, epicanthus, enlarged nasal base, small ears, mamilar hyperthelorism, trunk obesity, normal pulmonary and cardiovascular auscultation, umbilical hernia, braquidactyly, postaxial polydactyly of hands and feet, bilateral clinodactyly of fifth quirodactyly, and partial syndactyly between second and third pododactylys (Figure 1a, b). The following complementary examinations were done: abdominal ultrasound that showed discrete dilatation of left renal collecting system, normal pelvic ultrasound, normal renal function tests, plasma and urine amino acids chromatography with general aminoaciduria, normal gonadotropins, normal triglycerides, and total lipids.

The ophthalmic examination findings were: best corrected visual acuity in right eye (OD) 20/200 and in left eye (OS) 20/200, normal ocular motility, absence of nystagmus, corneas, sclera, and conjunctiva revealed no abnormalities, iris with normal crypts and configurations, posterior subcapsular opacification in the lenses of both eyes, and deep anterior chambers. The optic disc examination with Goldmann lens showed concentric cups in both eyes (OU), the cup–disc ratio in the right eye was 0.4 in the vertical and horizontal meridians, and 0.7 in the left eye in both meridians, nasal displacement of the retinal vessels and alpha peripapillar atrophy in OU. Fundoscopy also revealed granular paucipigmented aspect in the mid-periphery of the retina, with a bull's eye pattern of the macula, and attenuated retinal vessels (Figure 2a–d). The gonioscopy findings were similar in both eyes and showed open angle with flat iris insertion in the ciliary body band without iridian recess.

The initial intraocular pressure was 27 mmHg in OD and 29 mmHg in OS; these values were confirmed by separate measurements taken on different days, before beginning the medical therapy. All measurements were taken by Goldmann applanation tonometer. The central corneal thickness was 543 μm in OD and 537 μm in OS.

The electroretinogram (ERG) recorded in accordance with the International Society of Clinical Eletroctrophysiology of Vision (ISCEV) was extinct in both eyes; it was not possible to test the visual field because of the patient's intellectual deficit. Fluorescein angiography showed bull's eye maculopathy, optic disc hyperfluorescence, and window defect in all posterior pole and medium periphery, leading to the diagnosis of retinitis pigmentosa, paucipigmented form.

In order to decrease the intraocular pressure (IOP), the patient was treated with topical beta-adrenergic blocker (Timolol 0.5%) twice a day, and prostaglandins analog (latanoprost) once a day. Within 2 weeks, the IOP decreased to 15 mmHg OD and 16 mmHg in OS. The patient had regular follow-ups where the IOP levels remained inside normal limits.

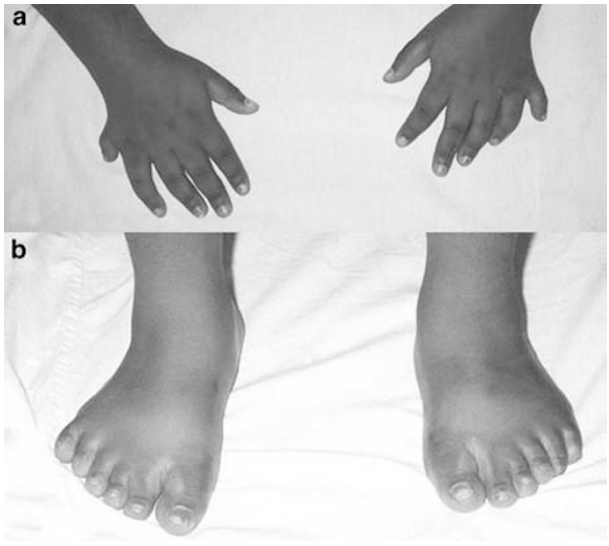

Figure 1 (a) Top: Braquidactyly and postaxial polydactyly of hands. (b) Bottom: Braquidactyly and postaxial polydactyly of feet.

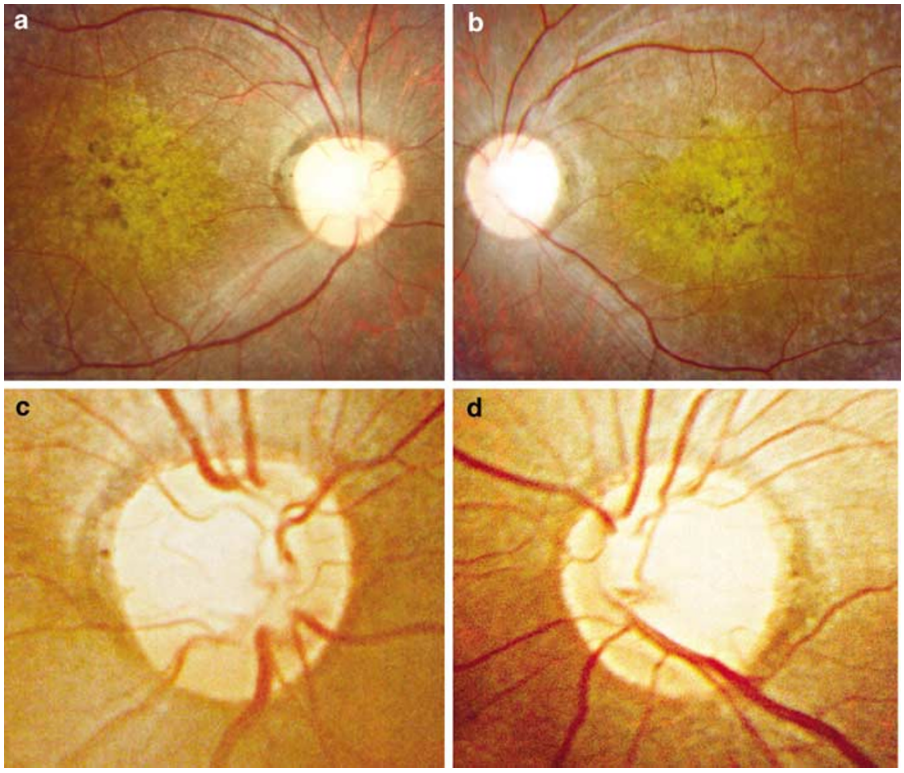

Figure 2 Fundus retinography showing bull's eye maculopathy in (a) right eye and (b) left eye. (c) Right eye — concentric cup–disc ratio 0.4 and nasal displacement of the retinal vessels and (d) left eye — concentric cup–disc ratio 0.7 and nasal displacement of the retinal vessels.

Discussion

In BBS patients, retinal dystrophy is the most frequently detected clinical feature.[3] In fact, various types of intraretinal pigmentary mobilization have been described in this entity ranging from changes apparently clinically indistinguishable from RP to salt and pepper type chorioretinopathy, diffuse pigmentation of the posterior pole, and fundus albipunctatus. It has been reported that the retinopathy in BBS affects central vision acuity early, unlike RP, and thus would be more correctly referred to as a 'cone-rod dystrophy'.[4] Our case presented typical alterations of RP and bull's eye maculopathy. The fluorescein angiography showed hyperfluorescence in areas of retinal pigment epithelium atrophy, leakage from macular capillaries and staining of the optic disc, without any evidence of cystoid macular oedema. In BBS patients, the ERG is very disturbed or even abolished as we observed in our case.[2]

Glaucoma has been described in two patients with the AHS, an autosomal recessive disorder that presents photoreceptor dystrophy, obesity, diabetes mellitus, and deafness.[1] In fact, AHS may be considered a variant of BBS and not a nosologically independent syndrome.[1] This is founded on the presence of two cardinal symptoms that are common to both syndromes: RP and obesity. Furthermore, deafness is found in approximately 5% of BBS patients, polydactyly may be seen in AHS patients and renal involvement, which is considered an important feature of BBS, may also be present in AHS, but generally it is diagnosed later in life (usually after 16 years of age).[1,5,6]

Unfortunately, in the paper of Klein and Ammann,[1] there was lack of information about the biomicroscopic and gonioscopic findings of the eyes of the two patients reported with the AHS–glaucoma association. These authors described the glaucoma as 'juvenile familial-type'. The diagnosis of glaucoma in our case was based on the high IOP associated with the following optic disc abnormalities: concentric cup enlargement, nasal displacement of retinal vessels and cup asymmetry between the eyes. The finding of flat iris insertion in this patient indicates the possibility of classifying this case as a late beginning developmental glaucoma, leading to the hypothesis of other malformations associated with BBS.[7] Considering the published literature, this case would be the first glaucoma description in a typical BBS patient, indicating the possibility of this association even in an infrequent way.

Furthermore, two studies demonstrated that BBS patients have significant worsening of visual function due to retinal degeneration and nearly 50% are legally

blind after 20 years of age.[3,8] Thus, it is important to investigate glaucoma in BBS patients in order to minimize the deleterious effects of this possible association in a syndrome with bad visual prognosis.

Acknowledgements

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Sir,

Corneal endothelial cell density in a normal Pakistani population

A healthy corneal endothelial cell count is vital for corneal clarity. The corneal endothelial cell density is known to decrease with age in normal populations. Corneal endothelial cell densities are important considering suitable corneal buttons for penetrating keratoplasties. These densities may also prove useful in identifying populations at risk of developing corneal decompensation following cataract extraction by phacoemulsification.

We collected data, by prospective data collection, from a Pakistani Punjabi population presenting in our outpatients department, with complaints ranging from decreased vision due to cataracts, refractive errors, and other pathological conditions unrelated to the anterior segment. Patients with corneal pathologies, dystrophies, dry eye states, ocular trauma, ocular surgery, contact lens wear, glaucoma or increased IOP, uveitis, and diabetes were excluded.

A total of 450 eyes of 225 Pakistani volunteer patients were included aged between 20 and 70 years and of both sexes. The mean age of the patients was 45.4 years. In all, 118 males and 107 females were included. Corneal endothelial cell densities were counted on Konan Non Con Robo SP6000 specular microscope by fixed frame method (Figure 1).

On average, our results showed a mean endothelial cell count of $2654 \pm 341/mm^2$ (1SD), with a range of 1960–3691 endothelial cells/mm^2. Detailed results are shown in Table 1.The breakdown of mean endothelial cell density by age clearly shows decreasing cell counts with increasing age (Figure 2). We compare the endothelial cell counts in our population to those previously published in the literature (Table 1).

Discussion

Age-related changes in the density of the human corneal endothelium are well described in literature.[1,2] Our figures for the corneal endothelial cell counts in a Pakistani Punjabi population closely resemble Indian and Caucasian eyes but show significant differences when compared to Japanese eyes.[3] However, the data published by Matsuda *et al*[4] considers smaller number of eyes when compared to the other two quoted figures.

The strength of our series is the large number of patients with apparently healthy corneas, prospective data collection, and relatively large number of patients in each patient subgroup.