Electronic letter

Does Bardet-Biedl syndrome have a characteristic face?

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Bardet-Biedl syndrome (BBS) (MIM 209900) is an autosomal recessive disorder with a wide spectrum of clinical manifestations. The generally accepted features of the BBS as a sepa-

rate disorder from Laurence-Moon syndrome are retinal dystrophy, obesity, mental retardation, polydactyly, hypogenitalism, and renal anomalies.¹ Recently, Beales *et al*² presented

Figure 1 Facial appearance of adult patients with Bardet-Biedl syndrome. On front view, note the wide forehead, mild downward slanting palpebral fissures, large nose, a small mouth with a thin upper lip and slight everted lower lip, and a prominent mandible. On lateral view, however, clear rethronathia is shown. (A) RP-446-J, (B) RP-129-R, (C) RP-63-I, (D) RP-499-JL, (E) RP-357-D, (F) RP-129-JL, (G) RP-496-V.

the largest clinical survey of living patients with Bardet-Biedl syndrome. The study reviewed the prevalence of some of the principal manifestations of the syndrome and showed some previously undescribed features, including the presence of a typical facies. We have also observed this characteristic face in our study of BBS patients.

We studied a total of 18 affected subjects from 12 Spanish families, who were referred to our Centre because of their retinal dystrophy (RP). They were defined as having BBS if they had RP plus at least two more of the remaining cardinal features (obesity, polydactyly, hypogenitalism, mental retardation, and renal abnormalities). In the four families with two affected members, two cardinal signs were sufficient for the diagnosis of the second member. The patients were identified through the Spanish Retinitis Pigmentosa Register among a total of 600 RP families; 125 of them had syndromal forms of RP, including 87 families with Usher syndromes. They were invited to attend a new clinical investigation, which included physical and ophthalmological examination, biochemical and endocrinological analysis, renal ultrasonography, and karyotyping. The data from this new examination were completed by information from patients, relatives, doctors, and hospital records.

Consanguinity was confirmed in four families and presumed by inbreeding in four other families, which represents a probable consanguinity rate of 75%, higher than the last and previous reports.¹⁻³ Because of our method of identification, retinal dystrophy was present in 100% of the patients. The patients showed, however, a variable age of onset of the first symptoms with predominance of the first decade followed by rapid decrease of visual acuity and visual fields. These symptoms, in addition to the relatively high frequency of nystagmus and strabismus, are similar to those found by other authors⁴ and support the idea of a distinctive ocular phenotype in BBS. However, inter- and intrafamilial variability of some ocular features has been observed in all the reports, including the present one.

Obesity was present in all 18 cases (100%) from early childhood, although four cases have been corrected by diet in adulthood, suggesting that at least in some cases diet may help to control the obesity in BBS. Polydactyly, hypogenitalism, and mental retardation have been traditional cardinal features of BBS, but some studies have suggested that these features are not necessarily present.¹ This idea is also supported by our study, which found a polydactyly rate of 50% and only mild learning disabilities, speech deficits, and borderline intelligence among the majority of our patients, which allow them to become self supporting with independent work later in life. We did not, however, find the high prevalence of renal abnormalities observed by these authors.⁵ Our rate of 40% of the investigated patients is similar to that observed by Beales *et al.*²

Other clinical features found by us include situs inversus (1/18), Hirschsprung disease (1/18) (both patients have been previously reported⁶), hearing impairment (1/18), epilepsy (1/18), and multiple pigmented naevi (7/16). This high rate of naevi has also been observed in other previous studies,² and might be considered a secondary diagnostic criterion.

As reported by Beales *et al.*,² we had observed that our patients share a characteristic face with a wide forehead, mild downward slanting palpebral fissures owing to mild malar hypoplasia, a large nose, and a small mouth with a thin upper lip and slight everted lower lip. The mandible looks prominent on front view, but shows clear rethronathia on lateral view (fig 1).

Intrafamilial variation of the BBS phenotype was observed in the familial cases, particularly the polydactyly, but also the age of onset of retinal dystrophy. Previous studies have also reported inter- and intrafamilial variation of expression of some clinical features of BBS,⁷ which cannot be explained solely by the expression of the at least five different BBS gene loci reported to date.⁸

Bardet-Biedl syndrome has proven to be clinically and genetically heterogeneous, which can make diagnosis difficult. A more accurate definition of the diagnostic criteria, their prevalence, and the inclusion of new common features could improve the diagnosis. We agree with Beales *et al.*² that the prevalence of some of the generally accepted criteria for BBS might be lower than previously reported and their absence should not exclude the diagnosis. As reported by them, we had also observed a typical facies, which might be helpful in some cases. Finally, the high rate of multiple pigmented naevi found in this study and other previous studies² suggests that this might be considered a secondary feature for diagnosis.

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