Bardet-Biedl and Cohen syndromes: differential diagnostic criteria

EDITOR—Fig 1 in the paper by Beales et al shows portraits of six patients with the Bardet-Biedl syndrome (BBS). Number 4, the lower left picture, has the facial appearance of the Cohen syndrome (CS) with apparent microcephaly, thick hair, coarse eyebrows, short philtrum, and prominent incisors. Since she is presented as a case of the BBS, she should have a rod-cone dystrophy and other signs of BBS.

The differential diagnosis between BBS and CS is so far a clinical one. Both disorders present rod-cone dystrophy from an early age, obesity, and often speech disorders/delay. The differences between the two are: BBS has agenesis of the corpus callosum, whereas CS does not; BBS has more severe malformations in the skeletal system, whereas CS is associated with congenital heart defects; and BBS has hypogonadism, whereas CS has hypergonadism.

In a study of BBS based on questionnaires, there is a risk of underestimating the number of patients with CS. To avoid this risk we suggest that the above mentioned diagnostic features of CS should be included as differential diagnostic criteria.

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This boy was born with postaxial polydactyly of both feet and congenital hypogonadism. He has brachydactyly (as opposed to tapering fingers), partial 2nd and 3rd toe syndactyly, and wide hands and feet. Within his first year he gained weight rapidly and developed polydactyly and polyuria (in the absence of diabetes mellitus). He was diagnosed with BBS at 31⁄2 years of age by a paediatrician in the absence of any retinal dysfunction. He later developed night blindness at around 6 years and was legally registered blind by 9 years with typical electroretinographic findings and evidence of early bone spicule-like pigmentation on funduscopy. The onset of night blindness and the time course of ensuing retinal degeneration appears to be quite consistent in BBS, whereas the choriotereinopathy (often with bull’s eye macula) accompanying Cohen syndrome is less circumscribed. He struggles with his weight to this day (now 17 years old), which remains generally distributed throughout, in sharp contrast to the more localised truncal obesity associated with CS. In early adolescence, he developed urinary tract problems owing to a ureterocele and bladder outflow obstruction. Although renal function continues to be normal, there is evidence of persistent fetal lobulation on ultrasound, a common nephrological feature of BBS. In short, the subject in question fulfills all six of the cardinal features (and several of the minor features proposed by Beales et al) associated with BBS.

We agree with Drs Warburg and Riise in that CS is an important differential diagnostic consideration, as is Alstrom syndrome, Biemond II syndrome, Edwards syndrome, and Laurence-Moon syndrome. In particular it would be important to exclude a relative neutropenia (associated with CS) during the initial investigation of a patient suspected of having BBS. However, we felt that the detailed nature of the questionnaire used in the study and the follow up process described provided maximal safeguards against such misdiagnoses.

The accuracy with which diagnoses of this group of retinopathy-obesity syndromes are made remains a problem and at present is based on clinical signs alone. We may have to wait for the advent of a molecular breakthrough before any of these issues can be definitively resolved.

Incidentally, the patient cited in this letter is the son of one of the authors of the paper in question.

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