

Electronic letter

J Med Genet 2000;37 (<http://jmedgenet.com/cgi/content/full/37/12/e46>)

Bardet-Biedl and Cohen syndromes: differential diagnostic criteria

EDITOR—Fig 1 in the paper by Beales *et al*¹ 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 retinal 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.^{1,2} The differences between the two are renal anomalies, male hypogenitalism, radiographic poly/syndactyly, and normal intelligence to mild intellectual disability in BBS.^{1,3} In CS, there are short, thin fingers and metacarpals, obesity localised to the abdomen, thin arms and legs, moderate to severe developmental delay, and characteristic facial features.² Granulocytopenia is almost always observed in CS when a series of blood smears are examined.^{4,5} There are dental malformations in both syndromes; CS shows large incisors and BBS has short roots.⁶

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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- 1 Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *J Med Genet* 1999;36:437-46.
- 2 Kivitiö-Kallio S, Eronen M, Lipsanen-Nyman M, Marttinen E, Norio R. Cohen syndrome: Evaluation of its cardiac, endocrine and radiological features. *Clin Genet* 1999;56:41-50.
- 3 Rudling O, Riise R, Tornqvist K, Jonsson K. Skeletal abnormalities of hands and feet in Laurence-Moon-Bardet-Biedl (LMBB) syndrome: a radiographic study. *Skeletal Radiol* 1996;25:655-60.
- 4 Kivitiö-Kallio S, Rajantie J, Juvonen E, Norio R. Granulocytopenia in Cohen syndrome. *Br J Haematol* 1997;98:308-11.
- 5 Warburg M, Pedersen SA, Hørlük H. The Cohen syndrome: retinal lesions and granulocytopenia. *Ophthalm Paediatr Genet* 1990;11:7-13.
- 6 Borgström MK, Riise R, Tornqvist K, Granath L. Anomalies in the permanent dentition and other oral findings in 29 individuals with Laurence-Moon-Bardet-Biedl syndrome. *J Oral Pathol Med* 1996;25:86-9.

This letter was shown to Dr Beales *et al*, who reply as follows.

The photograph of the subject in fig 1 (fourth down) from Beales *et al*¹ is in fact that of a boy taken when he was 13 years old. We concur that this photograph does illustrate the prominent incisors typical of the Cohen syndrome but disagree with the suggestion of microcephaly or short philtrum. Unfortunately, the quality of the photograph was somewhat diminished when this paper went to press.

This boy was born with postaxial polydactyly of both feet and hypogenitalism. 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 polydipsia and polyuria (in the absence of diabetes mellitus). He was delayed in reaching all major developmental milestones and had no speech or language until 3 years. Interestingly, he was diagnosed with BBS at 3½ 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 fundoscopy. The onset of night blindness and the time course of ensuing retinal degeneration appears to be quite consistent in BBS, whereas the chorioretinopathy (often with bull's eye macula) accompanying Cohen syndrome is less circumscribed.⁷ 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.⁸ In short, the subject in question fulfils all six of the cardinal features (and several of the minor features proposed by Beales *et al*¹) associated with BBS.⁹

We agree with Drs Warburg and Riise in that CS is an important differential diagnosis to consider, 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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