The Prader-Willi-like phenotype in fragile X patients: a designation facilitating clinical (and molecular) differential diagnosis

We thank Gillessen-Kaebach and Horsthemke for their comment on our paper “Clinical and molecular studies in fragile (X) patients with a Prader-Willi-like phenotype” in the March 1994 issue. The use of “like” syndromic designations generally invokes discussion. We nevertheless chose to describe this rare phenotype of the fragile (X) syndrome in direct comparison with the Prader-Willi syndrome (PWS). The eight fragile (X) patients described in our paper showed a special subtype consisting of mental retardation, a full, round face, truncal obesity, hypogonadism, small, broad hands and feet (all prominent PWS symptoms) and regional skin hyperpigmentation. Moreover, they lacked major features of the Martin-Bell phenotype described in the majority of fragile (X) patients: a long face with large everted ears and megalotestes. Therefore the suggestion by Gillessen-Kaebach and Horsthemke that these eight patients are just obese fragile (X) patients would be an insufficient clinical description of this special phenotype. Considering the erroneous clinical diagnosis of PWS in two patients, the (partial) resemblance to classical PWS, and the necessity for a recognisable name for this special subtype we suggested the name “Prader-Willi-like”. We hope that this will make clinicians aware of the need for performing DNA analysis for both chromosome 15q abnormalities and the FMR-1 gene mutations in the mentally retarded patients presenting with either the Prader-Willi syndrome or the Prader-Willi-like subtype of the fragile (X) syndrome.

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Arthrogryposis multiplex congenita, renal dysfunction, and cholestasis syndrome

We read with interest the article by Horslen et al. “Liver histology in the arthrogryposis multiplex congenita, renal dysfunction, and cholestasis (ARC) syndrome: report of three new cases and review.” We would like to comment on the possibility of variation of histological findings in the liver within a single syndrome of arthrogryposis multiplex congenita, cholestatic liver disease, and renal impairment, or the existence of two separate conditions. Whenever paucity of intrahepatic bile ducts was seen on hepatic histology, patients died between the ages of 3 months 2 weeks and 7 months. However, when lipofuscin deposition was present without paucity of intrahepatic bile ducts, patients always died before they were 3 months 2 weeks old. It is unlikely that paucity of intrahepatic bile ducts could resolve, and as lipofuscin deposition only, whenever present, was always seen at the time of death, the possibility that the two histological features are different stages in the evolution of the disease can be discarded. However, the different hepatic histologies may be two non-specific changes resulting from the same insult, as was suggested by the presence of features compatible with both groups in one patient.

We propose that the lipofuscin deposition occurs only when the liver is more severely affected and this would imply a worse prognosis. As there are two sibships where the first patients died when they were more than 4 months old and the younger affected brothers when they were less than 3 months old, we would suggest that the former had paucity of intrahepatic bile ducts and the latter had lipofuscin deposition. Unfortunately, in only one of the four patients were hepatic histological features studied but the result agrees with our hypothesis.

If the different clinical outcomes in the same sibship result from different hepatic histology, this would support the suggestion that different histological findings are nothing more than variation within a single syndrome. However, this remains an open question until the two are reported in the same sibship.

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