Letters to the Editor

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Marshall Syndrome and a Defect at the COL11A1 Locus

To the Editor:

Accurate syndromic diagnosis is important in the provision of appropriate genetic counseling but is essential when the molecular basis of a syndrome is being evaluated. With this in mind, we read with interest Griffith et al.'s (1998) article on Marshall syndrome, which demonstrates a splice-donor site mutation, in the COL11A1 gene, that cosegregates with the abnormal phenotype in nine individuals in three generations with "characteristic features." Marshall syndrome overlaps with at least three other disorders of craniofacial development, including Stickler syndrome, which itself demonstrates phenotypic and genetic heterogeneity. Mutations in the genes encoding COL11A1, COL11A2, and COL2A1 have been reported (Spranger et al. 1994; Vikkula et al. 1995; Richards et al. 1996). In the family that they studied, Griffith et al. (1998) established linkage to the COL11A1 locus and concluded that their results demonstrate allelism of Marshall syndrome with the subset of Stickler syndrome families with COL11A1 mutations. We propose a different interpretation of their data.

We have reported a family in which six members in four generations are affected with Marshall syndrome (Shanske 1997). We also have reviewed the literature, in an attempt to clarify the debate about the existence of Marshall syndrome, as well as its overlap with three similar disorders—Stickler, Weissenbacher-Zweymuller, and Wagner syndromes. For example, ophthalmological abnormalities including high myopia, as well as midfacial hypoplasia, micrognathia with or without palatal clefting, and nonspecific skeletal abnormalities have been reported in both Marshall and Stickler syndromes. In spite of these overlaps, each of these disorders has distinctive features. Striking ocular hypertelorism and abnormalities of ectodermal derivatives have been reported only in Marshall syndrome. The distinctiveness of Marshall and Stickler syndromes is strongly supported by the work of Ayme and Preus (1984). It is significant that Marshall's (1958) article emphasized the finding of ectodermal dysplasia in seven members in three generations of a single family and that, thus far, the family that we studied represents the only other reported insatnce of ectodermal abnormalities. The phenotype described by Griffith includes only "mild" orbital hypertelorism and no evidence of ectodermal derivative abnormalities.

We suggest, therefore, that the family reported by Griffith et al. most likely does not have Marshall syndrome. Rather, the linkage with the COL11A1 locus and the demonstrated defect in the α1(XI) collagen polypeptide suggest that the mutation in this family may be allelic with the subset of Stickler syndrome families associated with COL11A1 mutations.

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