Monozygotic twins with chromosome 22q11 deletion and discordant phenotype

I believe that the recent description by Goodship et al of discordance in monozygotic twins with a 22q11 deletion raises some interesting issues. The likelihood of a heart defect in a person with a constitutional 22q11 deletion cannot currently be estimated, as ascertainment of such patients is usually on the basis of the presence of a heart lesion. In addition, the true prevalence of 22q11 deletions is not known, although a low limit of 1:4000 has been quoted on the basis of children presenting with congenital heart defects. Thus, until prospective studies are carried out that allow complete ascertainment of subjects with a 22q11 deletion, irrespective of phenotype, this question cannot be answered. Variability of phenotypic expression among people with presumably identical deletions (that is, familial cases) strengthens the concept that a 22q11 deletion merely increases the likelihood of certain anomalies being present but does not guarantee them. It is clear, therefore, that the association of heart disease with this deletion is far from deterministic.

The discovery of monozygotic twins with a 22q11 deletion who are discordant for heart disease should, therefore, come as no surprise, although the role of “genetic background” could never be ignored. While it is clearly true that the phenotype in these twins could not have been predicted from a fetal ultrasound, the role of “genetic background” (that is, familial cases) strengthens the concept that a 22q11 deletion merely increases the likelihood of certain anomalies being present but does not guarantee them. It is clear, therefore, that the association of heart disease with this deletion is far from deterministic.

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