LETTERS TO THE EDITOR

Craniosynostosis and chromosome 22q11 deletion

In a recent article, Ryan et al reported some potentially very useful data for genetic counselling in chromosome 22q11 microdeletion. This was a questionnaire based, multicentre study, designed to find out from the various centres to try to minimise ascertainment bias. However, the authors admitted that this approach may have contributed some bias, but they highlighted the difficulty in obtaining consistence of clinical description between centres, and the associated variability in completeness of data with regard to the investigation and reporting of certain clinical features in different body systems. In discussing the occurrence of craniosynostosis with this deletion, we believe they intended to quote the small series of patients which two of us reported in 1995, although they have in fact referenced a different article written about cranial hemihyperplasia.1 In our series of seven patients from three families, one infant had bilateral coronal and sagittal craniosynostosis and broad thumbs, in addition to an interrupted aortic arch, thymic aplasia, hypocalcaemia, a bifid uvula, and a chromosome 22q11 deletion. His mother (also deleted) had brachycephaly and broad thumbs, but other adult family members without 22q11 deletion had some of these features, which is consistent with the hypothesis that this is a spectrum of clinical features associated with the deletion. However, the authors admitted that this disease was not considered as part of this clinical spectrum.

Spectrum of clinical features associated with interstitial chromosome 22q11 deletions

We read with great interest the paper "Spectrum of clinical features associated with interstitial deletion 22q11 deletions: a European collaborative study".1 Despite juvenile rheumatoid arthritis (JRA) being reported in many patients with 22q11 deletion, this disease was not considered as part of this clinical spectrum. We have recently diagnosed an additional patient with this association. She is a 4 year old girl, who was admitted to hospital in the first month of life because of velopharyngeal insufficiency and left multicystic kidney. At the age of 9 months she had hypocalcaemic seizures and at the age of 3½ years she developed polyarticular JRA, which responded poorly to treatment with non-steroidal anti-inflammatory drugs; she was therefore treated with steroids and methotrexate.

Immunological study showed IgA deficiency, high IgG, and normal IgM; T cell subset and lymphoproliferative response to mitogens were normal. FISH study with D22S75 (ONCOR) DNA probe showed deletion of chromosome 22 in the region 22q1.2 The number of cases reported published suggests that this deletion and polyarthropathy do not occur together by chance. Three of 80 patients enrolled in the chromosome 22q11 deletion syndrome cohort at the Children's Hospital of Philadelphia have developed JRA polyarthritis. Thus, the prevalence of polyarthritits in this cohort is 50 times that seen in the general population and 150 times that seen specifically for polyarticular JRA in the general population. This calculation is probably an underestimate because of the young age of patients in these series.1

Therefore, we propose enlarging the spectrum of 22q11 deletion syndrome to include polyarticular JRA and to follow with care all patients with this deletion for the possibility of developing an autoimmune disease.

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