

Our evolving understanding of 22q.11 deletion syndrome

A diagnosis of 22q.11 deletion syndrome (del22q.11) in a child brings with it a plethora of uncertainty in terms of developmental and neuropsychiatric prognosis. This relatively common genetic disorder has a highly variable phenotype with a multitude of potential physical features including palatal anomalies, congenital heart defects, facial dysmorphism, immunodeficiency, and hypoparathyroidism. As a result, patients may present in paediatric, cleft lip/palate, psychiatric, or antenatal clinics. It is necessary, therefore, that the multidisciplinary team are aware of this diagnosis. The overall clinical phenotype ranges from subtle isolated findings to severe multisystem involvement, even in the same family. The neurobehavioural phenotype is also highly variable. The spectrum of developmental delay, learning difficulties, behavioural problems, speech and language deficits, and psychiatric disorders seen in del22q.11 is well recognized. The implications for parents, medical professionals, educational staff and, indeed, the patients are significant. Thus, better understanding of the cognitive and behavioural problems could lead to the development of effective, targeted interventions and improved management.

The unpredictable variability of the condition makes genetic counselling difficult as some affected relatives may be mildly affected, whereas others may have significant problems. The cause of the psychiatric features found in this condition is unknown, but it has been reported that approximately 20 to 30% of patients with del22q.11 develop schizophrenia or schizoaffective disorder in adulthood.¹ This has led to the suggestion that people with schizophrenia and dysmorphic features could be screened for del22q.11.

Behavioural and neuropsychiatric features of del22q.11 are well documented. However, the developmental outcomes of the syndrome are less well described and warrant further studies. Gross motor delay, hypotonia and speech and language deficits were all reported in a group of patients with del22q.11 studied by Gerdes et al. (1999).² An assessment of motor development found that 79% of children were functioning in the significantly delayed performance range, 13% in the mildly delayed performance range, and only 2% in the average range. Hypotonia was present in more than half the children.² Oskarsdottir et al.³ and Swillen et al.⁴ also found that walking was delayed in children with del22q.11 and that hypotonia and impaired balance were common findings.

One of the two papers on del22q.11 in this issue, by Niklasson et al. (p 803), reports on a study carried out to examine the attention abilities of children with this particular microdeletion syndrome. Neuropsychiatric disorders, including attention-deficit-hyperactivity disorder (ADHD), autistic spectrum disorder, and learning difficulties were identified in more than half of the group of children with del22q.11. Ability

to sustain attention was impaired in all of them, regardless of their particular neuropsychiatric diagnosis. Appreciation of this specific impairment in these children is invaluable in planning educational and social management. The paper recommends assessment for ADHD in children with del22q.11, and it would also seem prudent to consider the diagnosis of del22q.11 in children with a compatible cognitive/behavioural profile. The spectrum of deficits can be broad and are not obviously related to the extent of the physical anomalies.⁵

The other paper by Swillen et al. (p 797) compares early motor development in infants (mean age 41mo) with del22.q11 and a congenital heart defect with a control group of infants (mean age 46mo) with a comparable congenital heart disease. Motor performance scores in the group with del22q.11 were significantly lower than in the control group. The authors conclude that this was not caused by congenital heart disease or behavioural features, but was possibly related to learning disability. However, if they are correct in this assertion, further research is required to establish the cause of the motor delay in these children. Rates of behavioural disturbances were generally similar in both groups but this could be due to the young age of the children in this series. This is because, as the previous paper and many other reports clearly document, behavioural problems in del22q.11 are well recognized.⁶

An evolving neurobehavioural phenotype with age in del22q.11 means that the approach to these children must encompass medical, genetic, behavioural, and neuropsychiatric aspects of this complex disorder.

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