

LETTERS TO THE EDITOR

A familial X;autosome translocation associated with Becker type muscular dystrophy?

The molecular isolation of the Duchenne (DMD) and Becker (BMD) muscular dystrophy gene¹⁻³ has led to the characterisation of many of the mutations associated with these two allelic disorders. Internal deletions causing frameshift mutations are very common in DMD, whereas the reading frame is intact in most cases of BMD deletions.⁴⁻⁶ Some of the few in frame deletions associated with the DMD phenotype may be explained by the large size of the deletions but exceptions to this rule are known.⁶ Whatever the size, these deletions may all be inherited through normal carrier females.

However, truncation of the dystrophin gene by X;autosome translocations along with non-random X inactivation of the normal X chromosome have resulted in DMD, or in a minority BMD, in at least 20 females.^{7, 8} Cytogenetic and molecular characterisation of some of these translocations has shown great heterogeneity in the position of the breakpoints in the Xp21 region,^{7, 9} consistent with the large size of the dystrophin gene.⁶ So far, all published cases have been sporadic de novo mutations, and translocations have not been found in affected males. Since breakpoints in the region Xp21 would be outside the 'critical region' Xq13-q26 associated with ovarian dysfunction and impaired fertility in female X;autosome translocation carriers,^{10, 11} translocations in females with BMD should be transmissible if the clinical course permits it.

I wish to draw attention to a family described in the beginning of the era of DMD/BMD cytogenetics by Aguilar *et al*¹² with several features compatible with the presence of a familial reciprocal X;autosome translocation associated with BMD. Three generations were affected, including the mother and grandmother of the male proband, who had two other brothers with signs of BMD. The mother and grandmother of the proband were both fairly severely affected, and it was

discussed whether, by chance, the normal X chromosome was inactivated in more cells than in the usual non-manifesting heterozygote. A balanced X;autosome translocation would directly explain this type of non-random X inactivation in the female carriers.

Carriers of balanced reciprocal translocations are at risk of having chromosomally unbalanced offspring. According to the pedigree the mother had experienced three abortions (spontaneous?), and had had four other children, two girls and two boys, who died a few days after birth with an identical clinical picture, including congenital intestinal atresia. It was stated that the presence of the latter was probably a coincidental finding. This may not be so, assuming a similar, unbalanced karyotype in all four sibs. Chromosome analysis was not mentioned in the study and would shed light on this obvious possibility for identification of a translocation causing BMD in both males and females.

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- 1 Monaco AP, Neve RL, Coletti-Feener C, *et al*. Isolation of candidate cDNA for portions of the Duchenne muscular dystrophy gene. *Nature* 1986;323: 646-50.
- 2 Burghes AHM, Logan C, Hu V, Belfall B, Worton RG, Ray PN. A cDNA clone from the Duchenne/Becker muscular dystrophy gene. *Nature* 1987; 328:434-7.
- 3 Koenig M, Hoffman EP, Bertelson CJ, Monaco AP, Feener C, Kunkel LM. Complete cloning of the Duchenne muscular dystrophy (DMD) cDNA and preliminary genomic organization of the DMD gene in normal and affected individuals. *Cell* 1987;50: 509-17.
- 4 Malhotra SB, Hart KA, Klamut HJ, *et al*. Frame-shift deletions in patients with Duchenne and Becker muscular dystrophy. *Science* 1988;242:755-9.
- 5 Monaco AP, Bertelson CJ, Liechti-Gallati S, Moser H, Kunkel LM. An explanation for the phenotypic differences between patients bearing partial deletions of the DMD locus. *Genomics* 1988;2:90-5.
- 6 Den Dunnen JT, Grootsholten PM, Bakker E, *et al*. Topography of the Duchenne muscular dystrophy (DMD) gene: FIGE and cDNA analysis of 194 cases reveals 115 deletions and 13 duplications. *Am J Hum Genet* 1989; 45:835-47.
- 7 Boyd Y, Buckle V, Holt S, Munro E, Hunter D, Craig I. Muscular dystrophy in girls with X;autosome translocations. *J Med Genet* 1986;23:484-90.
- 8 Dubowitz V. X;autosome translocations

in females with Duchenne or Becker muscular dystrophy. *Nature* 1986;322: 291-2.

- 9 Boyd Y, Buckle VJ. Cytogenetic heterogeneity of translocations associated with Duchenne muscular dystrophy. *Clin Genet* 1986;29:108-15.
- 10 Sarto GE, Therman E, Patau K. X-inactivation in man: a woman with t(Xq-;12q+). *Am J Hum Genet* 1973; 25:262-70.
- 11 Forabosco A, Giorgi L, Formica A, Tarantino E, Dallapiccola B. Ovarian dysfunction in balanced X-autosome translocations. Report of two new cases involving band Xq21. *Ann Genet (Paris)* 1979;22:11-16.
- 12 Aguilar L, Lisker R, Ramos GG. Unusual inheritance of Becker type muscular dystrophy. *J Med Genet* 1978;15:116-8.

Facial measurements in the newborn

In a recent paper Dr Omotade concluded that for facial measurements in the newborn local values should be used in the evaluation of dysmorphic states.¹ For the last two decades the same idea has repeatedly been expressed on the basis of at least 50 studies on anthropometric measurements of newborn infants in relation to gestational age and birth weight; these parameters were disregarded by Dr Omotade. Eye measurements particularly have been the subject of a series of meticulous surveys.^{2, 3} Published reports have been summarised and ethnic/geographical variations have been discussed in comprehensive works from Israel and Hungary.⁴⁻⁶ Thus, in the form of charts and tables, normal values for many 'dysmorphic' and 'normal' variants are available from various countries of the world.

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- 1 Omotade OO. Facial measurements in the newborn (towards syndrome delineation). *J Med Genet* 1990;27: 358-62.
- 2 Sivan Y, Merlob P, Reisner SH. Eye measurements in preterm and term newborn infants. *J Craniofac Genet Dev Biol* 1982;2:239-42.
- 3 Demirkol M, Ertugrul T, Neyzi O. Ocular and periorbital anthropometry in the newborn. *Hum Biol* 1988;60: 11-21.
- 4 Merlob P, Sivan Y, Reisner SH. Anthropometric measurements of the newborn infant (27 to 41 gestational weeks). *Birth Defects* 1984;20(7):1-52.
- 5 Méhes K. *Minor malformations in the neonate*. Budapest: Akadémiai Kiadó, 1983:1-129.
- 6 Méhes K. *Informative morphogenetic variants in the newborn infant*. Budapest: Akadémiai Kiadó, 1988:1-228.