A de novo translocation $t(3;17)(q26.3;q23.1)$ in a child with Cornelia de Lange syndrome

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Abstract

A female infant with Cornelia de Lange syndrome and severe limb reduction defects is described. Chromosome analysis showed a de novo translocation with breakpoints at 3q26.3 and 17q23.1. This is the first reported case of a de novo translocation associated with this syndrome.

Cornelia de Lange syndrome, first described in 1933, is characterised by mental handicap, retardation of growth, distinctive facial features, and reduction abnormalities of the limbs.¹ The spectrum of limb abnormalities ranges from micromelia to phocomelia. Since the advent of banding no significant chromosomal abnormality has been reported.

Case report

The proband was the second child of healthy, unrelated European parents aged 29 and 30 years. Her mother booked for antenatal care at 20 weeks' gestation. An ultrasound scan at that time confirmed the gestation, but was unable to show either upper limb. In addition to this, a minor discrepancy in cardiac chamber size was noted. Fetal echocardiography showed no abnormality, but confirmed the absence of upper limbs. A further scan at 27 weeks' gestation indicated a short right upper limb which ended at the elbow. Pregnancy continued uneventfully to 36 weeks' gestation when maternal weight gain was noted to be poor and the fetus small on palpation. A further scan confirmed the intrauterine growth retardation and labour was induced. The proband was

born vaginally with good Apgar scores and weighed 1620 g (<3rd centile). At birth she was noted to be dysmorphic with severe limb reduction abnormalities (fig 1). She was microbrachycephalic with a head circumference of 28.8 cm (<3rd centile). Her neck was short with a low posterior hairline and her orbital ridges and zygomatic arches were poorly developed. Her eyebrows were low set and formed a well defined arch which fanned out laterally. In addition, she had synophrys, long curled eyelashes, and a hirsute forehead. Her nose was small with a depressed bridge and anteverted nostrils. There was a long philtrum, thin lips, crescent shaped mouth, and micrognathia. Examination of her mouth showed a high arched but intact palate. Her ears were posteriorly rotated and low set. She had bilateral phocomelia, above the elbow on the right and below the elbow on the left. It was not possible to

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Figure 1 The proband aged 4 weeks

extend her elbow from which protruded a single, normally developed finger. She had hypoplastic nipples but no other cutaneous features. Both feet were micromelic with bilateral partial syndactyly of the second and third toes.

CHROMOSOME ANALYSIS

Chromosome analysis of trypsin G banded blood preparations from the proband showed an apparently balanced translocation: 46,XX,t(3;17)(q26.3;q23.1) (fig 2). The parental karyotypes were normal.

Discussion

This infant has the classic features of Cornelia de Lange syndrome. The highly characteristic phenotype in this disorder has led many to speculate on a genetic basis, but almost all cases are sporadic.

Figure 2 Chromosome pairs 3 and 17 from the proband showing the apparently balanced reciprocal translocation with breakpoints in bands 3q26.3 and 17q23.1. The abnormal chromosome is on the right of each pair.

Reports of affected sib pairs are rare² and several are open to question on diagnostic grounds.

The likely significance of the de novo translocation reported here is enhanced by the involvement of the long arm of chromosome 3. Extensive studies have, to date, failed to identify a chromosome abnormality in de Lange syndrome,³ with the exception of a probable balanced translocation reported in 1965⁴ involving chromosome 2 and a C group chromosome. Cornelia de Lange syndrome shows considerable phenotypic overlap with partial trisomy 3q⁵ and, although there are distinguishing features, a genetic defect involving 3q is considered likely. Several deletions of 3q have been reported but only one involved 3q26.⁶ That case did not have features of de Lange syndrome, but review of the published karyotype suggests that band q26.1 was the distal limit of the deletion. To our knowledge, the only report of a deletion of the region of 17q involved in the present case was an infant with monosomy 17q23.1→17qter resulting from a maternal translocation. This case showed none of the features of de Lange syndrome.⁷ We propose, therefore, that the gene for Cornelia de Lange syndrome is located at 3q26.3.

- 1 Berg JM, McCreay BD, Ridler MAC, Smith GF. *The de Lange syndrome*. New York: Pergamon Press, 1970.
- 2 Fryns JP, Dereymaeker AM, Hoefnagels M, et al. The Brachmann-de Lange syndrome in two siblings of normal parents. *Clin Genet* 1987;31:413-5.
- 3 Beck B, Mikkelsen M. Chromosomes in the Cornelia de Lange syndrome. *Hum Genet* 1981;59:271-6.
- 4 Craig AP, Luzatti L. Translocation in de Lange's syndrome? *Lancet* 1965; ii: 445-6.
- 5 Steinbach P, Adkins WN, Caspar H, et al. The dup(3q) syndrome: report of eight cases and review of the literature. *Am J Med Genet* 1981;10:159-77.
- 6 Franceschini P, Cirillo Silengo M, Davi G, Bianco R, Biagioli M. Interstitial deletion of the long arm of chromosome 3 in a patient with mental retardation and congenital anomalies. *Hum Genet* 1983;64:97.
- 7 Bridge J, Sanger W, Mosher G, et al. Partial deletion of distal 17q. *Am J Med Genet* 1985;21:225-9.