Case reports

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Correspondence and requests for reprints to Dr J Burn, Department of Human Genetics, University of Newcastle upon Tyne, 19 Claremont Place, Newcastle upon Tyne NE2 4AA.

A de novo X;13 translocation with abnormal phenotype

SHIRLEY V HODGSON*, JOHN C K BARBER†, ALICIA DOWIE‡, AND VICTOR DUBOWITZ‡

*Paediatric Research Unit, Guy's Hospital Medical School, London SE1 9RT; †the Kennedy-Galton Centre for Clinical Genetics, Harpenden Hospital, Radlett, Herts WD7 9HQ; and ‡the Department of Paediatrics and Neonatal Medicine, Hammersmith Hospital, Duane Road, London W12 0HS.

SUMMARY We describe a female infant who presented with hypotonia and developmental delay. Her karyotype showed a de novo balanced translocation between the X chromosome and chromosome 13, with breakpoints at Xq13 and 13p11. The normal X was late replicating in all cells examined. The cause of this patient's abnormal phenotype is discussed.

Case report

The proband, a female, was born at term by normal delivery (birth weight 2.9 kg) to a 37 year old mother and 31 year old father. The parents were non-consanguineous, of normal intelligence, and had a normal son.

Neonatal examination revealed ligamentous laxity and marked hypotonia. She had hypertelorism, bilateral epicanthic folds, and a retroussé nose.

At 10 months of age, she was sitting with support (from 7 months) and reaching out for objects with an immature grasp. Her head control was poor and she had persistent hypotonia. She had smiled at 3 months and rolled over at 7 months. Investigations showed a normal CK level (163 IU/ml), a normal

EMG, and normal motor nerve conduction velocity (40 m/s).

Review at 18 months of age showed a height below the 3rd centile and head circumference on the 3rd centile. She could sit alone but fell forwards frequently and would not support her weight when held standing. Her speech was delayed, with vocalisations only, and one word ("Dad"). Examination of the eye for retinoblastoma was negative.

CYTOGENETIC FINDINGS

Peripheral blood lymphocytes from the proband and both parents were cultured for chromosome studies

FIGURE Basic fuchsin stained partial metaphase¹ showing the two derived chromosomes and their normal counterparts. From left to right: the normal chromosome 13; der(13) (13qter→cen→13p11::Xq13→Xqter); the normal late replicating X with its characteristic shadowed appearance; and der(X) (Xpter→cen→Xq13::13p11→13pter).

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using routine methods and analysed after trypsin G banding. In addition, lymphocytes were cultured with BrdU in order to demonstrate the late replicating X chromosome.

Both parents had normal karyotypes, but the proband's karyotype revealed an apparently balanced X;13 translocation: 46,X,t(X;13) (Xpter→Xq13::13p11→13pter;13qter→13p11::Xq13→Xqter) (figure). BrdU incorporation showed the normal X to be late labelling in all of 100 cells examined. As the normal X was late replicating in each cell, it was not possible to detect any spread of inactivation from the X to the 13 in the 100 cells examined.

Discussion

Although it is easy to see why unbalanced X;autosome translocations cause phenotypic abnormalities due to deletion or duplication of chromosomal material, carriers of balanced translocations are often phenotypically normal. However, there are several well established classes of abnormality found in association with X;autosome translocations. Firstly, ovarian dysgenesis is associated with breakpoints on the X within the region Xq13 and Xq26.² Secondly, evidence is accumulating that there can be mutation damage by gene disruption at the breakpoint on the X chromosome. Examples supporting this theory include the cases of Duchenne muscular dystrophy occurring in girls with de novo X;autosome translocations with breakpoints at or near Xp21 (listed in Hodgson and Bobrow³), corresponding to the position allocated to the DMD locus by linkage analysis.⁴

Thirdly, the position effect can cause phenotypic

abnormalities in balanced X;autosome translocations, due to dissociation of genes from regulator sites or the spread of inactivation from an area of heterochromatin to a portion of the neighbouring translocated chromosome which would not normally be inactivated.

Five of seven previously reported patients with X;autosome translocations with breakpoints at Xq13² were infertile, but none had other dysmorphic features. Of seven patients reported with deletions of Xq with breakpoints at Xq13, none had phenotypic abnormalities other than the Turner stigmata.⁵ Our patient is thus the first reported case of a balanced X;autosome translocation with a breakpoint at Xq13 and an abnormal phenotype, other than gonadal dysgenesis.

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Correspondence and requests for reprints to Dr S V Hodgson, Paediatric Research Unit, Guy's Hospital Medical School, Guy's Tower, London SE1 9RT.

Terminal deletion of the long arm of chromosome 10

HAZEL CURTIS*, R T HOWELL†, AND CELIA COPE†

*Royal Devon and Exeter Hospital, Wonford, Exeter EX2 5DW; and †SW Regional Cytogenetics Centre, Southmead Hospital, Bristol BS10 5NB.

SUMMARY A de novo chromosome abnormality interpreted as a terminal deletion of chromosome 10, del(10)(pter→q25·2:), was ascertained in a newborn female with multiple malformations. The clinical features observed at birth and on follow up at 10 months of age

are described and compared with previously reported cases.

Three patients with monosomy for the chromosome region 10q25→qter have been described previously, two with a de novo terminal deletion^{1 2} and one with an unbalanced familial translocation.³ In addition, five reports describe slightly more distal deletions with the breakpoint in band 10q26,⁴⁻⁸ and a single