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Case Report

Prenatal Confirmation of the Translocation between Chromosome 15 and Y-Chromosome by Fluorescence in situ Hybridization

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Fukada, Y., Yasumizu, T., Amemiya, A., Kohno, K., Takizawa, M. and Hoshi, K. *Prenatal Confirmation of the Translocation between Chromosome 15 and Y-Chromosome by Fluorescence in situ Hybridization*. Tohoku J. Exp. Med., 1999, **187** (3), 285-289 —— A 30-year-old woman and her husband visited our hospital with habitual abortion as the complaint. Chromosome examination revealed a normal 46, XX for her and 46, XY, -15, der (15) t (Y; 15) (q12; p12) for him. After her pregnancy amniocentesis was performed. The karyotype was 46, XX, -15, der (15) t (Y; 15) (q12; p12) pat. ish der (15) (DYZ1+). A female baby was delivered. The growth of the baby was normal at 12 months of age. ———— chromosome 15 and Y translocation; fluorescence in situ hybridization (FISH); uncultured amniotic fluid cells; prenatal diagnosis

Fluorescence in situ hybridization (FISH) is a recently developed technique that enables a rapid identification of fetal chromosomal abnormalities. FISH has become one of the standard tools for perinatal diagnosis, because established cell culture is not required for this technique. We report a case of rare translocation between the chromosome 15 and Y-chromosome confirmed prenatally by FISH analysis of amniotic fluid cells. The translocation was inherited from the father, and the baby was phenotypically normal and showed normal development.

Case Report

A 30-year-old woman, gravida 4, para 1 and her husband visited our hospital with habitual abortion as the complaint. She had three spontaneous abortions before 12 weeks of gestation after one normal delivery. She and her husband

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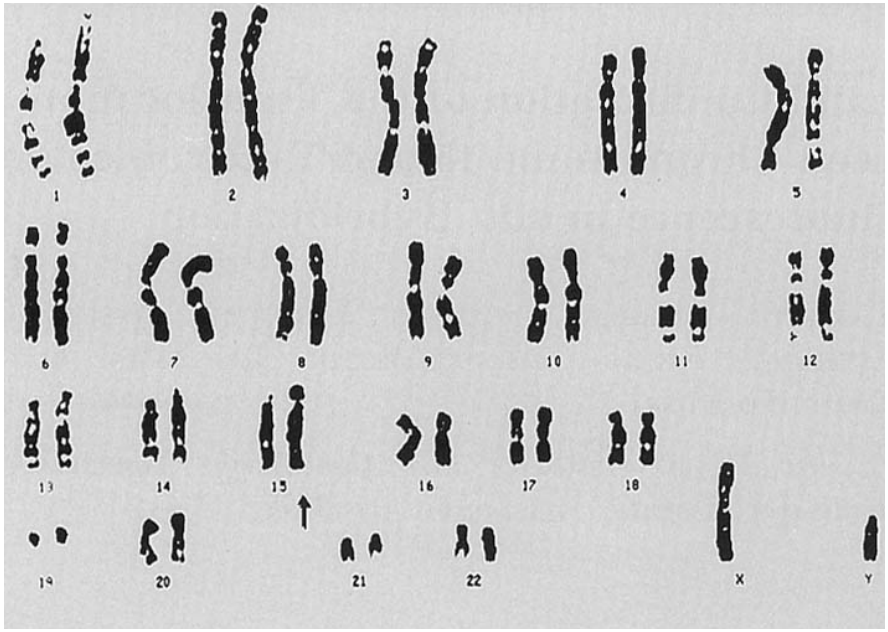

Fig. 1. Orcein-stained chromosomes from the father.

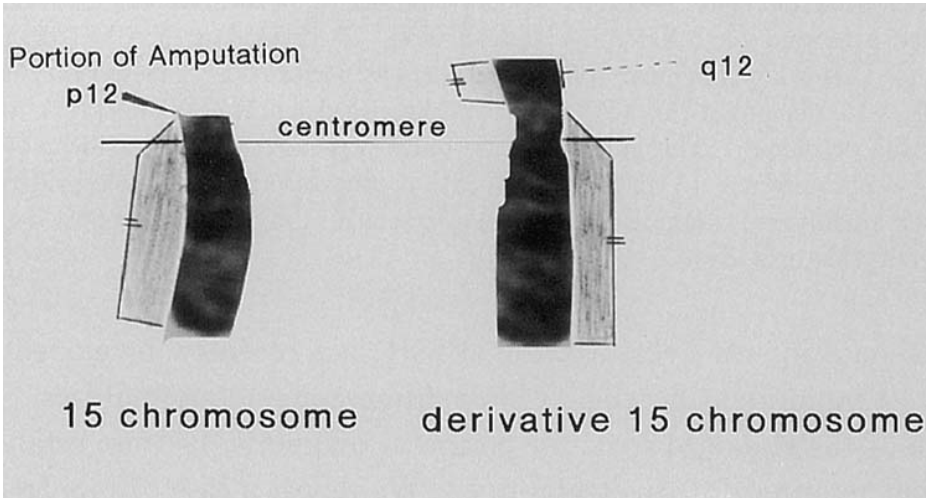

Fig. 2. Orcein-stained normal 15 and derivative 15 chromosome from the father.

were Japanese, non-consanguineous, and healthy. Chromosome examination using 72-hours routine cultures of peripheral blood cells revealed a normal 46, XX chromosome complement for her and the karyotype 46, XY, -15, der (15) t (Y; 15) (q12; p12) for him (Figs. 1 and 2). Since they showed no abnormal findings in other laboratory results, we judged that no medical intervention was necessary for the habitual abortion.

Six months after she visited our hospital again at 12 weeks of gestation. At that time her pregnancy was uneventful and the fetus had no abnormal ultrasound findings.

Amniocentesis was performed at 14 weeks of gestation in accordance with parents' wishes and 18 ml of clear fluid was collected. Standard cytogenetic

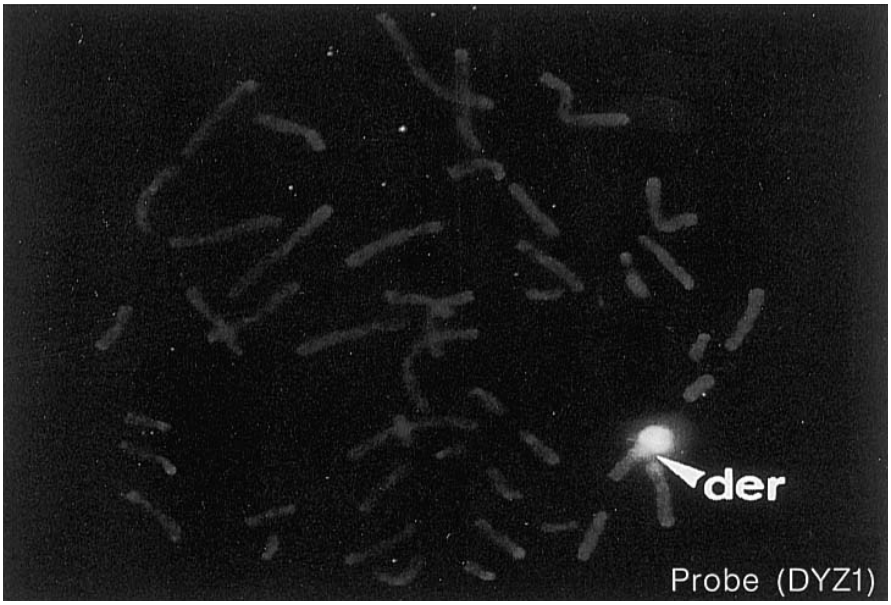

Fig. 3. Orcein-stained chromosomes from amniotic fluid cells.

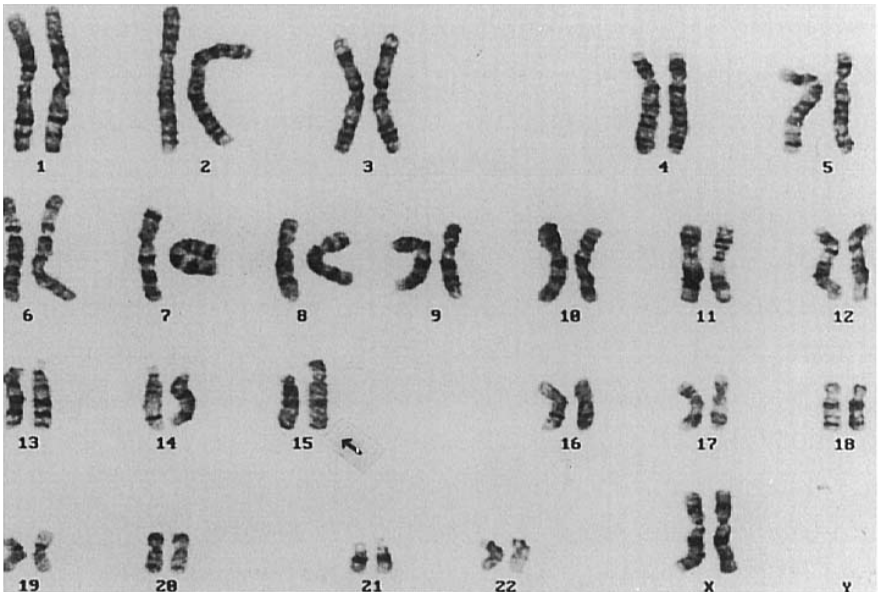

Fig. 4. FISH with a DYZ1 probe showing positive Y signal (arrowed) in uncultured amniotic fluid cell. der; paternal derivative chromosome.

analysis of 15 colonies showed an unbalanced karyotype with additional on the short arm of a chromosome 15; 46, XX, add (15) (p12). Fluorescence in situ hybridization analysis of metaphase chromosomes with a DYZ1 probe showed the 15p insertion to be derived from Yq12 heterochromatin (Fig. 3). The method used for FISH analysis was the same as that described previous report (Verlinsky et al. 1995). Therefore, the karyotype was 46, XX, -15, der (15) t (Y; 15) (q12; p12) pat. ish der (15) (DYZ1+) (Fig. 4).

Since the chromosome 15 is acrocentric, loss of 15p probably does not affect phenotypes. Furthermore, some genes have been detected recently in the Y

chromosome, but the distal portion of Yq, which involves DYZ1 loci, is heterochromatin. This point also suggests that the aberranted chromosome 15 probably induces no abnormal phenotypes. After above-mentioned counseling, the couple opted for continuation of the pregnancy.

The pregnancy had been uneventful and repeated ultrasonographic examinations of the fetus showed no abnormal findings. A phenotypically healthy normal female baby weighing 2740 g was delivered at 38 weeks of gestation. The growth of the baby was normal at 12 months of age.

Discussion

Previously a case of translocation between the chromosome 15 and Y-chromosome reported in an idiopathic case that was not used FISH (Alitalo et al. 1988).

Fluorescence in situ hybridization was used in uncultured amniocytes first for common aneuploidies in prenatal diagnosis (Julien et al. 1986). Standard cytogenetic analysis of cultured amniocytes is necessary to confirm an accurate diagnosis and avoid a misdiagnosis of aneuploidies. The clinical utility of FISH is generally accepted as a technique to rapidly identify additional (trisomies) or missing (deletions) chromosomal material.

Existence of extra Yp signals affects the phenotypes, which is inconsistent with the result of karyotype as in this case with the translocation between chromosomes 15 and Y. Our case demonstrated that the FISH technique in combination with the standard karyotyping is useful for the detection of rare chromosome rearrangement involving the Y-chromosome as mentioned in several reports (Neumann et al. 1992; Verlinsky et al. 1998). In the genes mapped on Y-chromosome, the abnormality in the SRY region has been reported to induce abnormal phenotypes. SRY regions are mapped on the short arm of Y-chromosome. Therefore, insertion to the long arm of Y-chromosome in females is not considered to affect the gonadal, physical and mental development. Our case also confirmed this hypothesis same as several reports (Alitalo et al. 1988; Neumann et al. 1992; Verlinsky et al. 1998).

References

1) Alitalo, T., Tiihonen, J., Hakola, P. & de la Chapelle, A. (1988) Molecular characterization of a Y; 15 translocation segregating in a family. *Hum. Genet.*, **79**, 319–329.
2) Julien, C., Bazin, A., Cynyot, B., Forestier, F. & Daffos, F. (1986) Rapid prenatal diagnosis of Down syndrome with in situ hybridization of fluorescent DNA probes. *Lancet*, **2**, 863–864.
3) Neumann, A.A., Robson, L.G. & Smith, A. (1992) A15p+ variant shown to be a t (Y; 15) with fluorescence in situ hybridization. *Ann. Genet.*, **35**, 227–230.
4) Verlinsky, Y., Ginsberg, N., Chmura, M., White, M. & Kuliev, A. (1995) Cross-hybridization of the chromosome 13/21 alpha-satellite DNA probe to chromosome 22 in the prenatal screening of common chromosomal aneuploidies by FISH. *Prenat. Diagn.*, **15**, 831–834.

5) Verlinsky, Y., Ginsberg, N., Chmura, M., White, M., Strom, C. & Kuliev, A. (1998) Detection of translocations involving the Y-chromosome in prospective prenatal screening of common chromosomal aneuploidies by FISH. *Prenat. Diagn.*, **18**, 390–392.