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LETTER TO THE EDITOR

Rapid Diagnosis of Monosomy X using Uncultured Amniocytes in Amniotic Fluid and Cultured Lymphocytes in Cystic Fluid in a Pregnancy with Fetal Cystic Hygroma and Hydrops

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A 40-year-old, primigravid woman was referred for amniocentesis at 17 weeks' gestation because of nuchal edema. Prenatal ultrasound at 17 weeks of gestation showed cystic hygroma, pleural effusion and hydrops fetalis (Fig. 1). About 26 mL amniotic fluid were aspirated, of which 10 mL was used for array comparative genomic hybridization (aCGH) using uncultured amniocytes, and 16 mL for conventional cytogenetic analysis using cultured amniocytes. About 10 mL cystic fluid were aspirated from the cystic hygroma, and conventional cytogenetic analysis was made using cultured lymphocytes in the cystic fluid. The aCGH investigation using whole-genome ISCA Plus Cytogenetic array (Roche NimbleGen, Madison, WI, USA) on uncultured amniocytes revealed monosomy X and absence of Y chromosome (Fig. 2). Conventional cytogenetic analysis using cultured lymphocytes in the cystic fluid of cystic hygroma revealed a karyotype of 45,X (Fig. 3). The cultured amniocytes also showed a karyotype of 45,X. Quantitative fluorescent polymerase chain reaction (QF-PCR) assays revealed presence of the X chromosome of maternal origin and absence of the X chromosome of paternal origin (Fig. 4). The pregnancy was terminated at 19 weeks of gestation, and a 370-g hydropic fetus was delivered with cystic hygroma and hydrops fetalis (Fig. 5).

Rapid aneuploidy diagnosis (RAD) refers to the application of molecular cytogenetic technologies such as interphase fluorescence *in situ* hybridization, QF-PCR, multiplex ligation-dependent probe amplification and aCGH for rapid prenatal diagnosis of aneuploidy without the need of cell culture [1—3]. In the present case, aCGH using uncultured amniocytes is useful for RAD in a pregnancy with fetal major malformations. The present case also shows that the lymphocytes in the cystic fluid of cystic hygroma are as useful as cord blood lymphocytes for rapid cytogenetic analysis.

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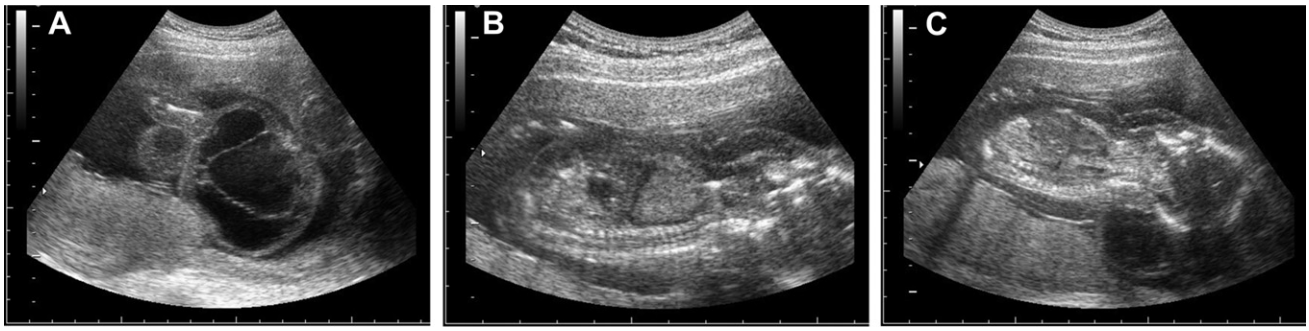

Fig. 1 Prenatal ultrasound at 17 weeks of gestation shows (A) cystic hygroma, (B) pleural effusion and (C) hydrops fetalis.

About 75% of second-trimester fetuses with cystic hygroma have chromosomal abnormalities of which 80% are 45,X [4]. Azar et al [4] found that among 44 second-trimester fetuses with cystic hygroma, 33 cases had aneuploidy including Turner syndrome ($n = 31$), trisomy 18 ($n = 1$) and trisomy 21 ($n = 1$). Snijders et al [5] found that

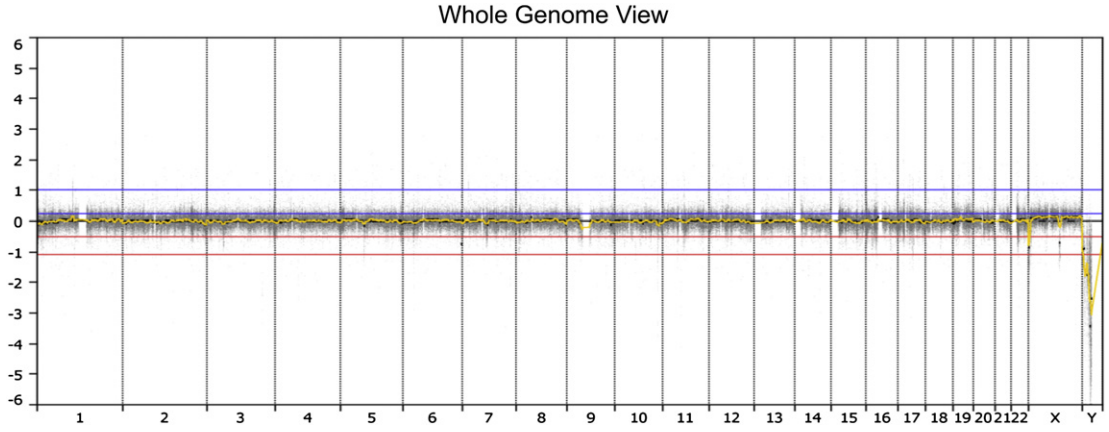

Fig. 2 Array comparative genomic hybridization analysis on uncultured amniocytes shows monosomy X and absence of Y chromosome.

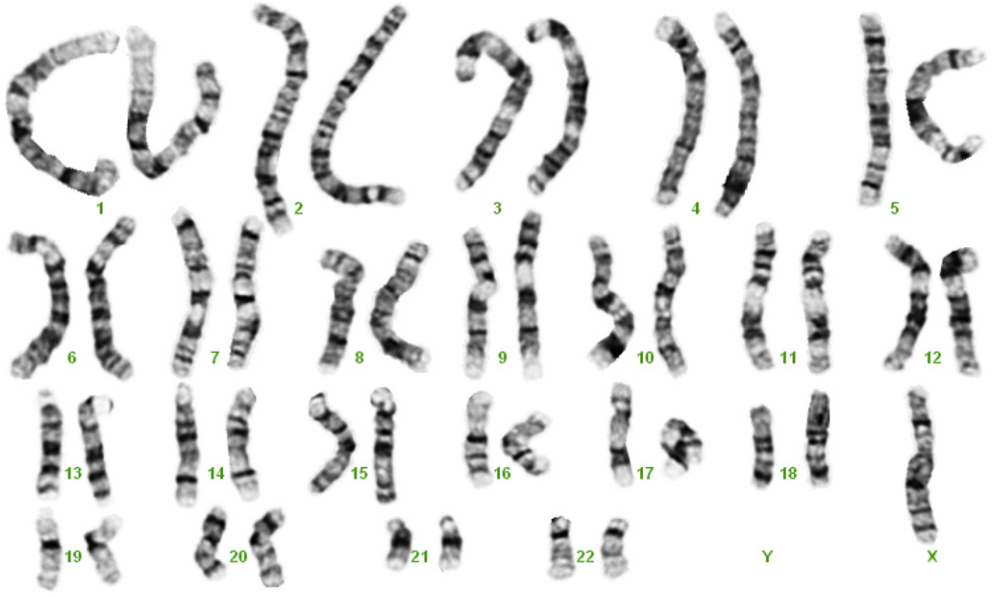

Fig. 3 Cytogenetic analysis of cultured lymphocytes in the cystic fluid of cystic hygroma shows a karyotype of 45,X.

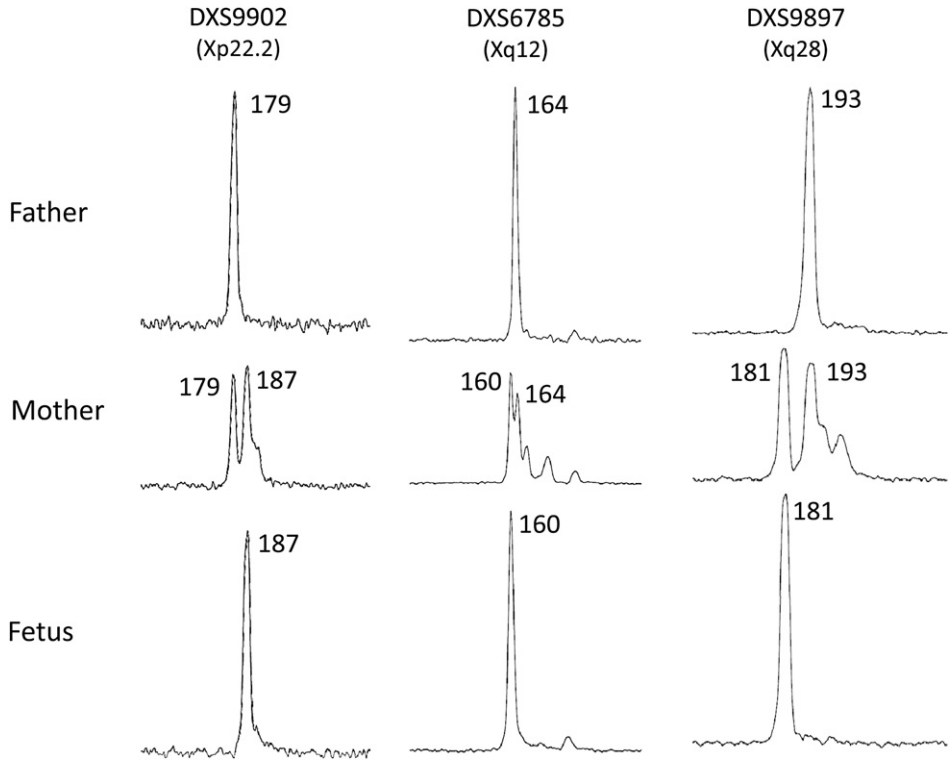

Fig. 4 Representative electrophoretograms of polymorphic DNA markers specific for chromosome X show that the fetus inherits only the maternal allele, indicating a paternal origin of absence of one X chromosome in the fetus.

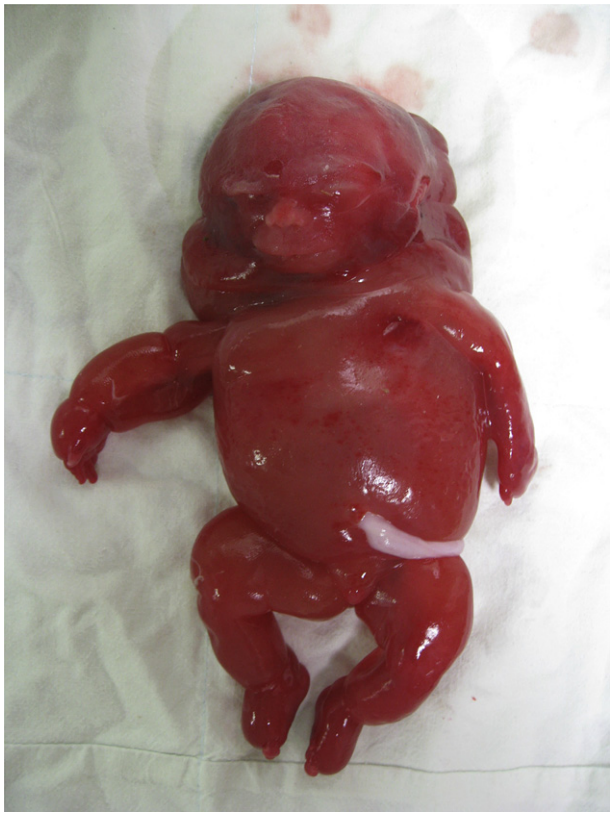

Fig. 5 The fetus at termination.

among 276 fetuses with cystic hygroma, about 77% of the cases had aneuploidy, including 45,X ($n = 163$), trisomy 21 ($n = 26$), trisomy 18 ($n = 13$) and other rearrangements ($n = 11$). Snijders et al [5] also found that cystic hygroma appeared in 88% of fetal Turner syndrome ($n = 65$), 2% of fetal trisomy 18 ($n = 137$) and 1% of fetal trisomy 21 ($n = 38$).

In conclusion, prenatal diagnosis of cystic hygroma should raise a suspicion of aneuploidy. We suggest that aCGH using uncultured amniocytes is useful for RAD, and aspiration of cystic fluid is as useful as cordocentesis for rapid cytogenetic analysis.

Acknowledgments

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References

[1] Chen CP, Su YN, Tsai FJ, et al. Rapid genome-wide aneuploidy diagnosis using uncultured amniocytes and array comparative genomic hybridization in pregnancy with abnormal ultrasound findings detected in late second and third trimesters. Taiwan J Obstet Gynecol 2010;49:120—3.

[2] Chen CP, Su YN, Lin SY, et al. Rapid aneuploidy diagnosis by multiplex ligation-dependent probe amplification and array

comparative genomic hybridization in pregnancy with major congenital malformations. Taiwan J Obstet Gynecol 2011;50: 85—94.
[3] Chen CP, Su YN, Wu PC, et al. Rapid aneuploidy diagnosis by array comparative genomic hybridization using uncultured amniocytes in a pregnancy with fetal nuchal edema and mild ascites. J Med Ultrasound 2011;19:64—7.
[4] Azar GB, Snijders RJ, Gosden C, et al. Fetal nuchal cystic hygromata: associated malformations and chromosomal defects. Fetal Diagn Ther 1991;6:46—57.
[5] Snijders RJM, Farrias M, von Kaisenberg C, et al. Fetal abnormalities. In: Snijders RJM, Nicolaides KH, editors. Ultrasound markers for fetal chromosomal defects. New York: Parthenon Publishing Group; 1996. p. 1—62.