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RESEARCH LETTER

Rapid Aneuploidy Diagnosis by Array Comparative Genomic Hybridization Using Uncultured Amniocytes in a Pregnancy With Fetal Nuchal Edema and Mild Ascites

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A 37-year-old, Gravida 2 Para 0, woman was referred for genetic counseling at 14 weeks of gestation because of an increased nuchal thickness (Fig. 1). Prenatal ultrasound at 16 weeks of gestation showed nuchal edema and mild fetal ascites (Fig. 2). Amniocentesis was performed, and 28 mL amniotic fluid was aspired, of which 16 mL of amniotic fluid was applied for array comparative genomic hybridization (aCGH) using uncultured amniocytes, and 10 mL was applied for conventional cytogenetic analysis using cultured amniocytes. Within 1 week, oligonucleotide-based aCGH analysis using Oligo HD Scan (CMDX, Irvine, CA, USA) showed the result of trisomy 21 (arr cgh 21q11.2q22.3 [13,339,394-46,944,323]×3) (Fig. 3). Conventional cytogenetic analysis later revealed a karyotype of 47,XY,+21 (Fig. 4). The pregnancy was terminated at 18 weeks of gestation, and a 226-g edematous fetus was delivered.

Bacterial artificial chromosome (BAC)-based aCGH and oligonucleotide-based aCGH have been successfully applied for rapid aneuploidy diagnosis (RAD) of both partial aneuploidy [1] and full aneuploidy [2]. RAD refers to the applications of interphase fluorescence *in situ* hybridization, quantitative fluorescent polymerase chain reaction, multiplex ligation-dependent probe amplification, and aCGH for rapid prenatal diagnosis of aneuploidies [3]. The aCGH has the advantage of achieving a rapid genome-wide analysis without the need for cell culture. It has been shown that

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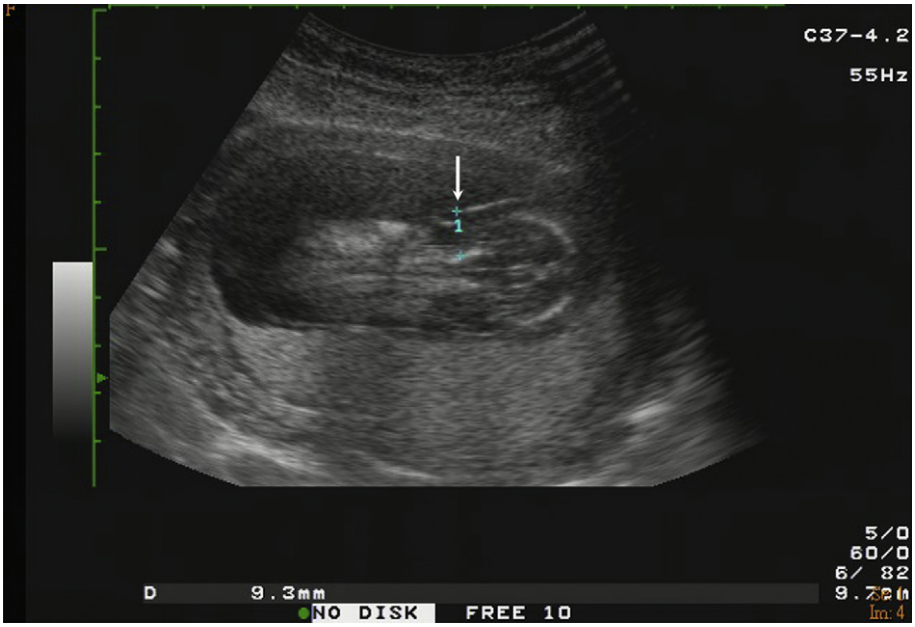

Fig. 1. Prenatal ultrasound at 14 weeks of gestation shows an increased nuchal thickness of 9.3 mm (arrow).

the results of aCGH can be available within an average of 6 days for uncultured cells [4]. However, aCGH has difficulty in detecting low-level mosaicism, balanced translocation, inversion, and polyploidy [5].

The present case was associated with Down syndrome, nuchal edema, and mild fetal ascites. Snijders et al [6] found that nuchal edema was diagnosed in 38% of fetuses with trisomy 21. About one-third of the fetuses with nuchal edema have chromosome abnormalities, mainly trisomies 21, 18, and 13 [7]. Snijders et al [6] found that hydrops fetalis was diagnosed in 20% of the fetuses with trisomy 21 ($n = 155$). Jauniaux et al [8] reported chromosome abnormalities in 15.7% (94/600) of the fetuses with nonimmune hydrops fetalis, and about 38.3% (36/94) of the aneuploid hydropic fetuses were diagnosed with trisomy 21.

In conclusion, prenatal diagnosis of fetal nuchal edema with mild ascites should alert one to the possibility of chromosomal abnormalities, and aCGH has the advantage of RAD.

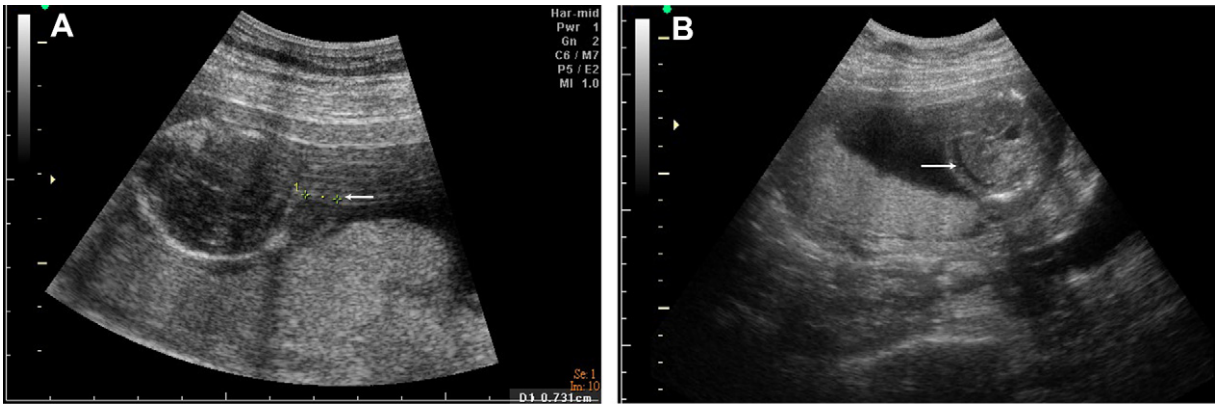

Fig. 2. Prenatal ultrasound at 16 weeks of gestation shows (A) nuchal edema (arrow) and (B) mild fetal ascites (arrow).

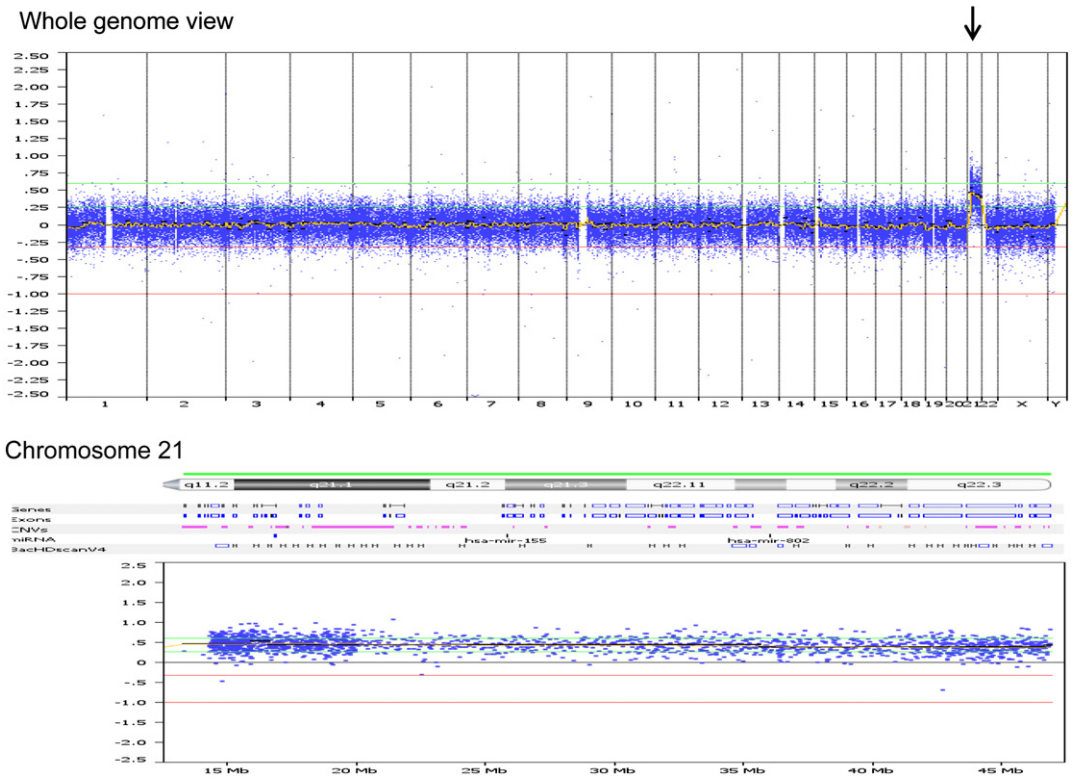

Fig. 3. Oligonucleotide-based array comparative genomic hybridization analysis using uncultured amniocytes shows a duplication of chromosome 21 (arrow) consistent with the diagnosis of trisomy 21.

Fig. 4. Conventional cytogenetic analysis using cultured amniocytes shows a karyotype of 47,*XY*,+21.

Acknowledgments

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