LETTER TO THE EDITOR

Rapid Diagnosis of Trisomy 21 by Array Comparative Genomic Hybridization using Uncultured Amniocytes in a Pregnancy with Isolated Ventriculomegaly in the Fetus

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A 43-year-old, gravida 2, para 1, woman was referred for amniocentesis at 18 weeks of gestation because of advanced maternal age and fetal ventriculomegaly. Her husband was 45 years old. Prenatal ultrasound revealed a fetus with fetal biometry equivalent to 19 weeks and bilateral ventriculomegaly (Fig. 1). Other organs were unremarkable. About 28 mL amniotic fluid was aspirated, of which 10 mL was used for array comparative genomic hybridization (aCGH) analysis using uncultured amniocytes, and 16 mL for conventional cytogenetic analysis using cultured amniocytes. The aCGH investigation using whole-genome ISCA Plus Cytogenetic Array (Roche NimbleGen, Madison, WI, USA) on uncultured amniocytes showed the result of trisomy 21 [arr cgh 21p11.2q22.3 (10,538,318 – 48,129,895) × 3] (Fig. 2). Conventional cytogenetic analysis using cultured amniocytes revealed a karyotype of 47,XX,+21 (Fig. 3). The pregnancy was terminated at 21 weeks of gestation, and a 434-g female fetus was delivered with facial dysmorphisms of Down’s syndrome. Postnatal quantitative fluorescent polymerase chain reaction analysis revealed a heterologous duplication of chromosome 21 of maternal origin, consistent with the result of meiosis I nondisjunction (Fig. 4).

Rapid prenatal diagnosis of chromosomal abnormalities can be achieved by interphase aCGH quantitative fluorescent polymerase chain reaction, interphase fluorescence in situ hybridization and multiplex ligation-dependent probe amplification without the need for cell cultures[1–6]. The present case shows the usefulness of aCGH for rapid aneuploidy diagnosis in a pregnancy with fetal ventriculomegaly.

Prenatal diagnosis of ventriculomegaly should raise a suspicion of aneuploidy [7]. Ventriculomegaly occurs in...
5–25 out of 10,000 births and may be associated with aneuploidy, genetic disorders and syndromes, intrauterine hemorrhage, infections and neural tube defects [8]. Snijders et al [8] reported aneuploidy in 13% of the 690 fetuses with prenatally-detected ventriculomegaly including trisomy 21, trisomy 18, trisomy 13, triploidy and other rearrangements. The same authors [8] reported ventriculomegaly in 16% of fetuses with trisomy 21 (n = 155), 14% with trisomy 18 (n = 137), 9% with trisomy 13 (n = 54), 18% with triploidy (n = 50) and 2% with Turner syndrome (n = 65). They also found that the prevalence of aneuploidy in fetal ventriculomegaly was 2% for fetuses with no other detectable abnormalities and 17% for those with additional abnormalities. Our case represents an interesting instance of isolated ventriculomegaly associated with advanced maternal age and fetal trisomy 21.

Fig. 1  Prenatal ultrasound at 18 weeks of gestation shows: (A) an enlarged ventricle with a width of 1.12 cm; and (B) an enlarged contralateral ventricle with a width of 1.28 cm.

Chromosomal View

Fig. 2  Chromosomal view of array comparative genomic hybridization analysis on uncultured amniocytes showing the duplication of chromosome 21 (arrows), consistent with a diagnosis of trisomy 21.
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References


