

Research Letter

# Prenatal diagnosis of trisomy 8 mosaicism

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A 38-year-old, gravida 3 para 1, woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Cytogenetic analysis of cultured amniocytes revealed a karyotype of 47,XX,+8[1]/46,XX[24]. Of 25 colonies of cultured amniocytes, one colony had the karyotype 47,XX,+8, whereas the other 24 colonies had the karyotype of 46,XX (Fig. 1). The single colony with trisomy 8 had three metaphase cells, all with a karyotype of 47,XX,+8. The parental karyotypes were normal, and prenatal ultrasound findings were unremarkable.

Repeated amniocentesis was performed at 21 weeks of gestation. Array comparative genomic hybridization (aCGH) and interphase fluorescence *in situ* hybridization (FISH) were applied to uncultured amniocytes, and conventional cytogenetic analysis was applied to cultured amniocytes. The aCGH analysis of uncultured amniocytes revealed no genomic imbalance in chromosome 8. Interphase FISH analysis of uncultured amniocytes using an 8p11.1–q11.2-specific probe (Vysis CEP 8, D8Z2, green spectrum; Abbott Laboratories, Abbott Park, IL, USA) showed three green D8Z2 signals in 20% (10/50 cells) of uncultured amniocytes and two green signals in 80% (40/50 cells) of uncultured amniocytes (Fig. 2). Cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XX in 40 cultured colonies. Quantitative fluorescent polymerase chain reaction analysis of cultured amniocytes using chromosome 8-specific

microsatellite markers revealed a 1:1 biparental diallelic pattern for chromosome 8 and thus excluded uniparental disomy 8.

The woman underwent a third amniocentesis and simultaneous cord blood sampling at 23 weeks of gestation. Interphase FISH analysis of uncultured amniocytes using the CEP 8 (D8Z2) probe (green spectrum) showed three green D8Z2 signals in 15.8% (6/38 cells) of uncultured amniocytes and two green signals in 84.2% (32/38 cells) of uncultured amniocytes (Fig. 3). Cytogenetic analysis of cultured cord blood lymphocytes revealed a karyotype of 46,XX in 40 cells, and cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XX in 30 cultured colonies.

The parents elected to continue the pregnancy, and a healthy 3504-g female baby was delivered at term with no phenotypic abnormalities. Postnatal cytogenetic analysis of the blood revealed a karyotype of 46,XX in 40 cultured lymphocytes. The umbilical cord, placenta, and amnion had a normal 46,XX karyotype in 40 cultured cells. Interphase FISH analysis on uncultured urinary cells using the CEP 8 (D8Z2) probe (green spectrum) showed three green D8Z2 signals in 4.1% (4/98 cells) of uncultured urinary cells (Fig. 4). The neonate was normal in growth and psychomotor development at 6 months of age.

Trisomy 8 mosaicism has an estimated frequency of 1:25,000 to 1:50,000 births [1,2] and is more prevalent in males than females [3,4]. Trisomy 8 mosaicism has marked phenotypic and cytogenetic variability, and there appears to be little correlation between the level of mosaicism in the blood or skin and the severity and incidence of abnormal

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Fig. 1. A karyotype of 47,XX,+8.

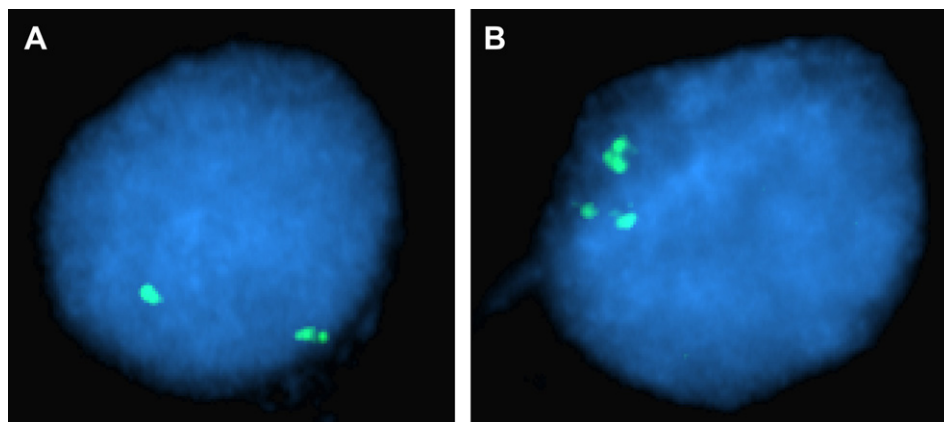


Fig. 2. Interphase fluorescence *in situ* hybridization analysis of uncultured amniocytes using the CEP 8 (D8Z2) probe (green spectrum) at the second amniocentesis shows (A) two green signals in an amniocyte with disomy 8, and (B) three green signals in an amniocyte with trisomy 8.

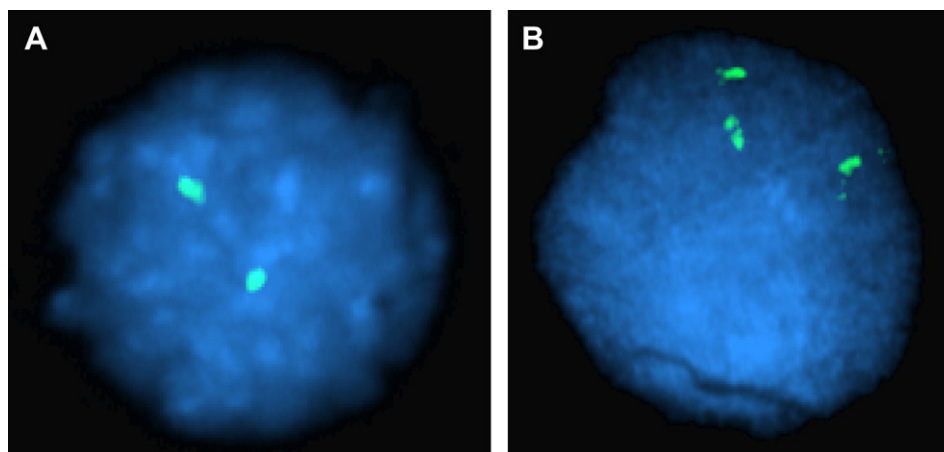


Fig. 3. Interphase fluorescence *in situ* hybridization analysis of uncultured amniocytes using the CEP 8 (D8Z2) probe (green spectrum) at the third amniocentesis shows (A) two green signals in an amniocyte with disomy 8, and (B) three green signals in an amniocyte with trisomy 8.

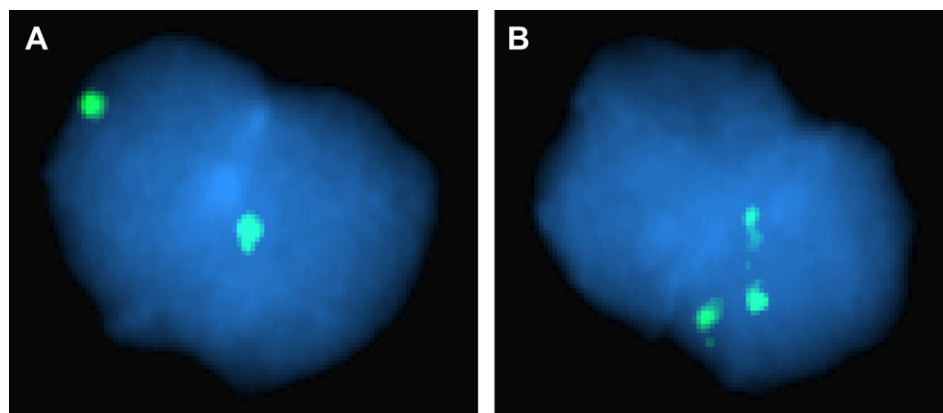


Fig. 4. Interphase fluorescence *in situ* hybridization analysis of uncultured urinary cells using the CEP 8 (D8Z2) probe (green spectrum) after birth shows (A) two green signals in a urinary cell with disomy 8, and (B) three green signals in a urinary cell with trisomy 8.

manifestations, malformations, and mental retardation [5]. The reported abnormalities associated with trisomy 8 mosaicism include moderate mental retardation, agenesis of the corpus callosum, congenital heart defects, renal anomalies, deep palmar and longitudinal plantar furrows, absent or hypoplastic patellae, camptodactyly, spinal deformity, limitation of joint motion, a long and slender trunk, narrow shoulders and pelvis, a short and webbed neck, and facial dysmorphisms of hypertelorism, a broad nasal root, a prominent forehead, a high arched palate, or facial clefts [1,2].

The present case provides evidence that interphase FISH on uncultured amniocytes is practical for rapid confirmation of low-level trisomy 8 mosaicism on amniocentesis. The present case also provides evidence that the abnormal trisomy 8 cell line in pregnancy with trisomy 8 mosaicism in amniotic fluid may disappear after culture of the amniocytes. Trisomy 8 mosaicism has been reported to be missed by conventional cytogenetic analysis using cultured amniocytes at amniocentesis in pregnancies with fetal trisomy 8 mosaicism [6–10]. Hulley et al [11] observed a selective growth advantage of normal cells versus a growth disadvantage of trisomy 8 cells in cases with trisomy 8 mosaicism. In our case, it is likely that the abnormal trisomy 8 cell line disappeared by selective growth disadvantage following the culture procedure.

Several reports have proposed that cordocentesis rather than repeated amniocentesis is preferably recommended for confirmation when trisomy 8 mosaicism is diagnosed at chorionic villus sampling [8,10]. However, recent studies have suggested that repeated amniocentesis using interphase FISH on uncultured amniocytes is useful for the confirmation of trisomy 8 mosaicism [4]. The present case additionally shows that the application of interphase FISH to uncultured amniocytes is better than cordocentesis in prenatal confirmation of trisomy 8 mosaicism.

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### References

- [1] Jordan MA, Marques I, Rosendorff J, de Ravel TJ. Trisomy 8 mosaicism: a further five cases illustrating marked clinical and cytogenetic variability. *Genet Couns* 1998;9:139–46.
- [2] Wiśniewska M, Mazurek M. Trisomy 8 mosaicism syndrome. *J Appl Genet* 2002;43:115–8.
- [3] Karadima G, Bugge M, Nicolaidis P, Vassilopoulos D, Avramopoulos D, Grigoriadou M, et al. Origin of nondisjunction in trisomy 8 and trisomy 8 mosaicism. *Eur J Hum Genet* 1998;6:432–8.
- [4] Chen C-P, Chen M, Pan Y-J, Su Y-N, Chern S-R, Tsai F-J, et al. Prenatal diagnosis of mosaic trisomy 8: clinical report and literature review. *Taiwan J Obstet Gynecol* 2011;50:331–8.
- [5] Schinzel A. Trisomy 8 mosaicism. In: Schinzel A, editor. *Catalogue of unbalanced chromosome aberrations in man*. 2nd ed. Berlin: Water de Gruyter; 2001. p. 384–91.
- [6] Klein J, Graham Jr JM, Platt LD, Schreck R. Trisomy 8 mosaicism in chorionic villus sampling: case report and counselling issues. *Prenat Diagn* 1994;14:451–4.
- [7] Schneider M, Klein-Vogler U, Tomiuk J, Schliephacke M, Leipoldt M, Enders H. Pitfall: amniocentesis fails to detect mosaic trisomy 8 in a male newborn. *Prenat Diagn* 1994;14:651–2.
- [8] Hanna JS, Neu RL, Barton JR. Difficulties in prenatal detection of mosaic trisomy 8. *Prenat Diagn* 1995;15:1196–7.
- [9] Southgate WM, Wagner CL, Shields SM, Cantú ES, Pai GS. Mosaic trisomy 8: a cautionary note regarding missed antenatal diagnosis. *J Perinatol* 1998;18:78–80.
- [10] van Haelst MM, Van Opstal D, Lindhout D, Los FJ. Management of prenatally detected trisomy 8 mosaicism. *Prenat Diagn* 2001;21:1075–8.
- [11] Hulley BJ, Hummel M, Cook LL, Boyd BK, Wenger SL. Trisomy 8 mosaicism: selective growth advantage of normal cells vs. growth disadvantage of trisomy 8 cells. *Am J Med Genet* 2003;116A:144–6.