Research Letter

Rapid aneuploidy diagnosis of trisomy 18 by array comparative genomic hybridization using uncultured amniocytes in a pregnancy with fetal arachnoid cyst detected in late second trimester

Chih-Ping Chen a,b,c,d,e,f,g,* , Yi-Ning Su h , Shun-Long Weng i , Fuu-Jen Tsai e,j,k , Chen-Yu Chen b , Yu-Peng Liu l,m , Schu-Rern Chern c , Wen-Lin Chen b , Pei-Chen Wu b , Wayseen Wang c,n

a Department of Medicine, Mackay Medical College, New Taipei City, Taiwan
b Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan
c Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan
d Department of Biotechnology, Asia University, Taichung, Taiwan
e School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
f Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
g Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan
h Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Hsinchu, Taiwan
i Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
j Department of Medical Genetics, National Taiwan University Hospital, Hsinchu, Taiwan
k Department of Medical Genetics, China Medical University Hospital, Taichung, Taiwan
l Department of Medical Research, Mackay Memorial Hospital, Taichung, Taiwan
m Department of Radiology, Mackay Memorial Hospital Hsinchu Branch, Hsinchu, Taiwan
n Mackay Medicine, Nursing and Management College, Taipei, Taiwan

Accepted 31 October 2011

A 30-year-old gravida 2 para 1 (G2P1) woman was referred to the hospital at 22 weeks of gestation because of abnormal sonographic findings. The woman and her husband were non-consanguineous and healthy, and there was no family history of congenital heart or brain defects. Level II ultrasound revealed a singleton fetus with microcephaly (biparietal distance: 4.77 cm and head circumference: 18.35 cm, all less than 5th centile), rocker-bottom feet, a ventricular septal defect (VSD), and a 2.36 cm × 1.51 cm midline interhemispheric hypoechoic homogeneous lesion (Fig. 1). Prenatal magnetic resonance imaging (MRI) confirmed the diagnosis of an arachnoid cyst and hypogenesis of cerebellar vermis (Fig. 2). The corpus callosum and cerebral ventricles were normal. Amniocentesis was performed and 37 mL amniotic fluid was aspirated. About 20 mL of amniotic fluid was applied for array-comparative genomic hybridization (aCGH) using uncultured amniocytes, and 15 mL was applied for conventional cytogenetic analysis using cultured amniocytes. Within three days, bacterial artificial chromosome (BAC)-based aCGH showed the result of trisomy 18 [arr cgh 18p11.32q23 (RP11-1150C18 → RP11-87C15) × 3; Fig. 3A]. Fluorescence in situ hybridization (FISH) analysis of the cultured interphase amniocytes using a combination of BAC probes RP11-29G21 (18q12.3) (40,213,562-40,396,293 bp; spectrum

---

* Corresponding author. Department of Obstetrics and Gynecology, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

1028-4559/$ - see front matter Copyright © 2012, Taiwan Association of Obstetrics & Gynecology. Published by Elsevier Taiwan LLC. All rights reserved. http://dx.doi.org/10.1016/j.tjog.2012.07.036
Fig. 2. Magnetic resonance imaging (MRI) at 22 weeks of gestation shows an interhemispheric arachnoid cyst (black arrows), and hypogenesis of cerebellar vermis (white arrow) consistent with the diagnosis of Dandy-Walker variant. (A) Sagittal; (B) axial; and (C) coronal views of the MRI findings.

Fig. 3. (A) Bacterial artificial chromosome (BAC)-based array comparative genomic hybridization (aCGH) analysis using CMDX BAC aCGH CA3000 chips shows a duplication of chromosome 18 consistent with the diagnosis of trisomy 18; (B) Fluorescence in situ hybridization (FISH) analysis of interphase amniocytes using BAC probes RP11-29G21 (18q12.3; spectrum green) and RP11-98B6 (4q11-q12; spectrum red) shows three green signals and two red signals consistent with the diagnosis of trisomy 18.
The diagnosis of trisomy 18 at 22 weeks of gestation in a fetus was made in the second trimester or even in the newborns [5]. Prenatal ultrasound and MRI have led to the increased diagnosis of fetal arachnoid cysts mostly in the third trimester [6-8]. However, in a few cases, the diagnosis has been made in the second trimester or even in the first trimester [6,9]. Arachnoid cysts may progressively enlarge in utero causing ventriculomegaly and may be associated with corpus callosum dysgenesis. Prenatal MRI helps to demonstrate compression of the aqueduct, communication between the cyst and the ventricles, and corpus callosum dysgenesis.

We have presented a rare occurrence of second-trimester diagnosis of trisomy 18 in association with a midline interhemispheric fetal arachnoid cyst, microcephaly, a VSD and rocker-bottom feet. Pilu et al [10] first reported prenatal diagnosis of trisomy 18 at 22 weeks of gestation in a fetus with a small arachnoid cyst in ambient cistern in association with a double-outlet right ventricle and clenched hands. Fetal arachnoid cysts can be associated with various chromosomal abnormalities. Hogge et al [11] reported partial trisomy 9q (9q22→qter) and partial monosomy Xq (Xq22→qter) in a fetus with an intratentorial arachnoid cyst. The fetus postnatally manifested a prominent nose, micrognathia, overlapping of the fingers and a thin-walled cyst compressing the right cerebellar hemisphere. Souter et al [12] reported a subtelomeric deletion of the distal long arm of chromosome 14, or monosomy 14q (14q32.3→qter) in a fetus with tetralogy of Fallot, intrauterine growth restriction, and a midline intracraniar arachnoid cyst. The infant postnatally manifested facial dysmorphism, inguinal hernias, tetralogy of Fallot, a midline arachnoid cyst and marked global developmental delay. Elbers and Furness [13] reported the association of triploidy with a fetus with an arachnoid cyst. Stein et al [14] reported prenatal diagnosis of trisomy 20 mosaicism associated with an arachnoid cyst of basal cistern. We suggest that prenatal diagnosis of arachnoid cyst, especially in association with structural abnormalities, should alert aneuploidy and prompt a cytogenetic investigation.

**Acknowledgments**

This work was supported by research grants NSC-96-2314-B-195-008-MY3 and NSC-97-2314-B-195-006-MY3 from the National Science Council, and MMH-E-99004 from Mackay Memorial Hospital, Taipei, Taiwan.

**References**


