Taiwanese Journal of Obstetrics & Gynecology 53 (2014) 572–578

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Short Communication

First-trimester molecular diagnosis of complete hydatidiform mole associated with dizygotic twin pregnancy conceived by intrauterine insemination

Chih-Ping Chen [a, b, c, d, e, f, *], Tsang-Ming Ko [g], Chen-Yu Chen [a], Tao-Yeuan Wang [h, i, j], Schu-Rern Chern [b], Yu-Ling Kuo [k], Wayseen Wang [b, l]

[a] Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan
[b] Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan
[c] Department of Biotechnology, Asia University, Taichung, Taiwan
[d] School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
[e] Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
[f] Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan
[g] Genephile Bioscience Laboratory, Ko's Obstetrics and Gynecology, Taipei, Taiwan
[h] Department of Pathology, Mackay Memorial Hospital, Taipei, Taiwan
[i] Department of Medicine, Mackay Medical College, New Taipei City, Taiwan
[j] Mackay Junior College of Medicine, Nursing, and Management, Taipei, Taiwan
[k] Department of Obstetrics and Gynecology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
[l] Department of Bioengineering, Tatung University, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 3 October 2014

Keywords:
complete hydatidiform mole
dizygotic twin
intrauterine insemination
microsatellite genotyping
prenatal diagnosis

ABSTRACT

Objective: To present first-trimester molecular diagnosis of complete hydatidiform mole (CHM) associated with dizygotic twin pregnancy conceived by intrauterine insemination.
Materials and methods: A 32-year-old woman presented to the hospital with a huge complex cystic mass measuring about 8.5 cm × 4.1 cm in the uterine cavity and a living co-existing fetus with fetal biometry equivalent to 9 weeks. She underwent chorionic villus sampling at 13 weeks of gestation, and microsatellite genotyping for molar pregnancy test was applied. A molar pregnancy test was performed by a short tandem repeat (STR) identifier polymerase chain reaction (PCR) polymorphic marker analysis. The pregnancy was terminated at 14 weeks of gestation. Postnatal polymorphic DNA marker analysis of the placenta by quantitative fluorescent PCR (QF-PCR) was performed. Analysis of maternal blood total β-human chorionic gonadotropin revealed a high level of 551,600 mIU/mL at 10 weeks of gestation and a level of 1.0 mIU/mL at 15 weeks postpartum. The woman was doing well at 4 months after delivery.
Results: The results of STR identifier PCR polymorphic marker analysis showed androgenic conception in the complex cystic mass and biparental conception in the living fetus. Pathological analysis of the cystic mass confirmed the diagnosis of CHM. The results of QF-PCR showed biparental inheritance in the normal fetus and complete paternal homozygosity in the CHM of the abnormal fetus in all STRs, indicating dizygotic twinning and CHM of monospermy.
Conclusion: Prenatal sonographic diagnosis of placentomegaly with many grape-like vesicles should include a differential diagnosis of CHM, partial hydatidiform mole (PHM), placental mesenchymal dysplasia (PMD), and recurrent hydatidiform mole. Microsatellite genotyping for molar pregnancy testing and zygosity testing is useful in cases of prenatal diagnosis of placentomegaly associated with many grape-like vesicles and a twin pregnancy with a living fetus in the first trimester.

* 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).

http://dx.doi.org/10.1016/j.tjog.2014.10.001

Introduction

Complete hydatidiform mole (CHM) associated with twin pregnancy and a normal fetus is very rare, and has an estimated incidence from 1 in 20,000 to 1 in 100,000 pregnancies [1,2]. CHM with twin pregnancy and a normal co-existing fetus can be associated with fetomaternal complications such as persistent gestational trophoblastic disease, vaginal bleeding, thromboembolic disease, hyperemesis, intrauterine fetal death, and even uterine rupture [1,3–6]. CHM has been associated with advanced maternal age and assisted reproductive technology such as *in vitro* fertilization and intracytoplasmic sperm injection [4,7–15]. Shazly et al [16] previously reported a case of twin pregnancy with CHM and co-existing fetus following ovulation with a non-prescribed clomiphene citrate. Here, we present our experience of first-trimester molecular diagnosis of CHM associated with dizygotic twin pregnancy conceived by intrauterine insemination.

Materials and methods

Clinical description

A 32-year-old, gravida 2, para 1, woman presented to the hospital at 9 weeks of gestation with a huge complex cystic mass measuring about 8.5 cm × 4.1 cm in the uterine cavity and a living co-existing fetus with fetal biometry equivalent to 9 weeks (Fig. 1). Her husband was 37 years of age. The woman had a 4-year-old healthy son, and this pregnancy was conceived by intrauterine insemination. She underwent chorionic villus sampling at 13 weeks of gestation, and microsatellite genotyping for molar pregnancy test was applied. A molar pregnancy test was performed by a short tandem repeat (STR) identifier polymerase chain reaction (PCR) polymorphic marker analysis. The results were consistent with the diagnosis of CHM associated with dizygotic twin pregnancy. The pregnancy was terminated at 14 weeks of gestation. The living female fetus was normal. Pathological analysis of the cystic mass confirmed the diagnosis of CHM. Postnatal polymorphic DNA marker analysis of the placenta by quantitative fluorescent PCR (QF-PCR) confirmed the prenatal diagnosis. Analysis of maternal blood total β-human chorionic gonadotropin revealed a high level of 551,600 mIU/mL at 10 weeks of gestation (normal: 10,000–100,000 mIU/mL at 8–12 weeks), a level of 99,563 mIU/mL on the day after delivery of the placenta, a level of 1986 mIU/mL at 1 week postpartum, a level of 357.5 mIU/mL at 2 weeks postpartum, a level of 140.4 mIU/mL at 3 weeks postpartum, a level of 21.8 mIU/mL at 7 weeks postpartum, a level of 5.5 mIU/mL at 11 weeks postpartum, and a level of 1.0 mIU/mL at 15 weeks postpartum. The woman was doing well at 4 months after delivery.

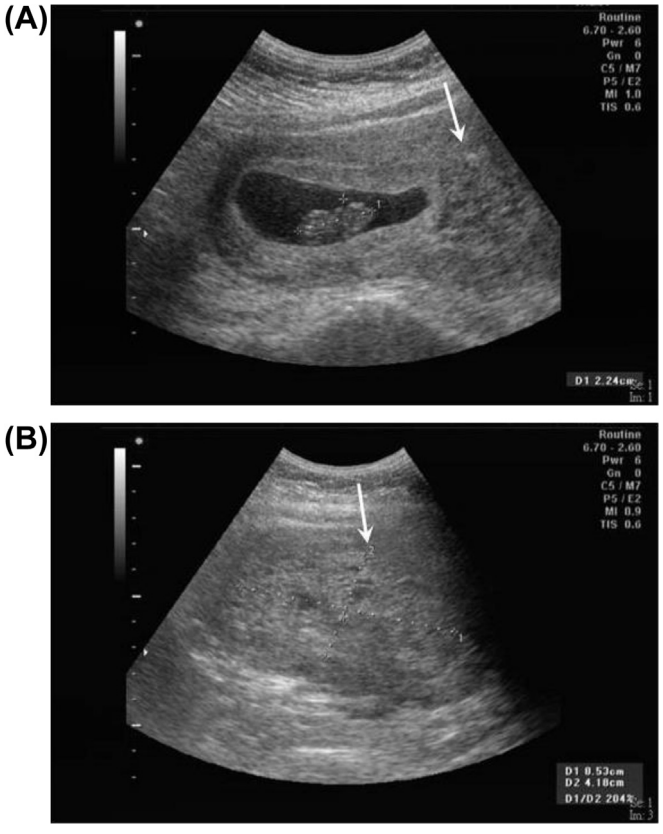

Fig. 1. Prenatal ultrasound at 9 weeks of gestation shows a huge complex cystic mass (arrow) and a living co-existing fetus.

STR identifier PCR polymorphic marker analysis

STR identifier PCR polymorphic marker analysis was performed on the DNA extracted from the placental tissues obtained prenatally by chorionic villus sampling. This analysis contains fluorescently labeled primers for sex determination marker or amelogenin and 15 STR markers of D21S1437 (21q21.1), D22S683 (22q12.3), D8S1110 (8q11.23), D10S2325 (10p13), D12S1090 (12q13.3), D17S1294 (17q11.2), Penta D (21q22.3), D3S1744 (3q24), D14S608 (14q12), D20S470 (20p12.1), Penta E (15q26.2), D4S2366 (4p16.1), D18S536 (18q12.1), D13S765 (13q14.11), and D6S474 (6q21).

QF-PCR analysis

QF-PCR analysis was performed on the DNA extracted from the placental tissues obtained postnatally by placental samplings. This analysis contains uncultured fluorescently labeled STR markers of D13S768 (13q21.1), D18S877 (18q12.1), and D21S2049 (21q22.11).

Table 1
Microsatellite genotyping using amelogenin and 15 small tandem repeat (STR) markers.[a]

Marker	Location	Father	Mother	Mole (abnormal fetus)	Normal fetus
D21S1437	21q21.1	14/14	14/16	14	14/14
D22S683	22q12.3	14.2/20.2	13/15.2	14.2	13/14.2
D8S1110	8q11.23	26/27	26/26	27	26/26
D10S2325	10p13	11/13	11/11	13	11/13
D12S1090	12q13.3	6/12	9/13	6	6/9
D17S1294	17q11.2	15/15	14/15	15	14/15
Penta D	21q22.3	9/9	9/11	9	9/11
D3S1744	3q24	14/19	17/20	19	14/20
D14S608	14q12	7/10	6/12	10	7/12
D20S470	20p12.1	14/17	10/16	14	16/17
Penta E	15q26.2	10/21	11/16	10	10/11
D4S2366	4p16.1	11/12	9/12	11	9/11
D18S536	18q12.1	11/12	11/12	11	11/11
D13S765	13q14.11	8/9	9/9	8	9/9
D6S474	6q21	13/14	13/13	14	13/14

[a] Each algebraic number represents a specific allele with a specific base pair size in a specific STR marker.