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CASE REPORT

Twin pregnancy with chromosomal abnormalities mimicking a gestational trophoblastic disorder and coexistent foetus on ultrasound

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Case report

Gestational trophoblastic disorder with a coexistent foetus occurs in 1 in 20,000–100,000 pregnancies (Wee and Jauniaux 2005) and mostly involves a partial hydatidiform mole with a live foetus and rarely a twin pregnancy with a complete hydatidiform mole and co-twin foetus (Gupta et al. 2015). Most cases of partial hydatidiform mole have triploidy with multiple structural anomalies and result in first trimester miscarriage (Toufaily et al. 2016). However, their management is complicated because the coexistent foetus is occasionally a normal healthy diploid foetus. Furthermore, this condition is often accompanied by severe complications such as hyperemesis, preeclampsia or thromboembolic disease (Matsui et al. 2000; Sebire et al. 2002). Thus, the diagnosis and management of gestational trophoblastic diseases with coexistent foetus are clinically important.

A gravid 33-year-old woman (gravid 4, para 3) was referred to our hospital with vaginal bleeding from 9 weeks of gestation. She was noted on prenatal ultrasound to have a normal foetus with an abnormally thickened space in the placental region. At 11 gestational weeks, a snowstorm pattern was observed on ultrasound examination, but it was slightly different from the typical pattern for hydatidiform mole. Multivesicular areas were prominent, but the other areas appeared relatively normal (Figure 1(A)). At 13 gestational weeks, the snowstorm pattern persisted with a foetal growth retardation of a biparietal diameter of 22.3 mm (−1.9 SD). The serum β-human chorionic gonadotropin (β-hCG) level was alarmingly elevated at 369,065 mIU/ml at 14 gestational weeks, whereas alpha-fetoprotein (AFP) showed a normal level of 109.5 ng/ml. β-hCG was persistently high at 207,336 mIU/ml at 16 gestational weeks, whereas AFP was 159.8 ng/ml.

The couple decided to terminate the pregnancy after considering the risks because the possibility of hydatidiform mole and coexistent foetus could not be excluded. After the curettage, the woman was in good condition and the β-hCG level decreased to 4 mIU/ml. The delivered foetus had a median cleft lip and palate (Figure 1(B)). The placenta appeared to have patchy villous hydropic changes (Figure 1(C)). Histological examination revealed focal villous oedema. Trophoblast hyperplasia was not observed (Figure 1(D)). After receiving approval from the Ethical Review Board and obtaining written informed consent from the couple, we obtained samples from the foetal skin and from the oedematous and normal-seeming areas of the placenta.

Initial cytogenetic analysis by Giemsa staining indicated a normal karyotype (data not shown). Cytogenetic microarray of the foetus revealed three copies of an 8-Mb region at the terminus of 9p, but monosomy 2q and trisomy 4q in the placenta (Figure 1(E–G)). Although hydatidiform moles generally result from dispermic triploidy or diandric diploidy with the paternal genome only, there was no evidence of triploidy or uniparental disomy. The foetus was found to carry arr[hg19] 9p24.3p24.1(326,927–8,441,863)x3, which appeared to be mosaic with normal cells because the copy number (CN) state was 2.80. On the other hand, the placental tissue was found to carry arr[hg19] 2q37.3(237,337,625–242,408,074)x1, 4q25q35.2(113,816,349–190,957,.473)x3. These appeared to be in mosaicism because the CN state was 1.35 and 2.67, respectively. Approximately 65–67% of cells showed monosomy 2q and trisomy 4q, and it is likely that the same cells had monosomy 2q and trisomy 4q simultaneously. The placental tissue also showed 9p trisomy at CN state 2.33, suggesting that 33% of cells carried the 9p trisomy identified in the foetus. On the other hand, we did not detect monosomy 2q and trisomy 4q in foetal tissue at all.

Microsatellite analysis of the DXS0767 locus revealed that there was only a small level of maternal tissue contamination in placental tissue (2–3%, data not shown) and none in foetal tissue. The pattern of whole-genome SNP genotyping also excluded the chimeric pattern but indicated a single zygote origin, suggesting that all of the foetus and placenta were derived from a monozygotic twin or somatic

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Supplemental data for this article can be accessed here.

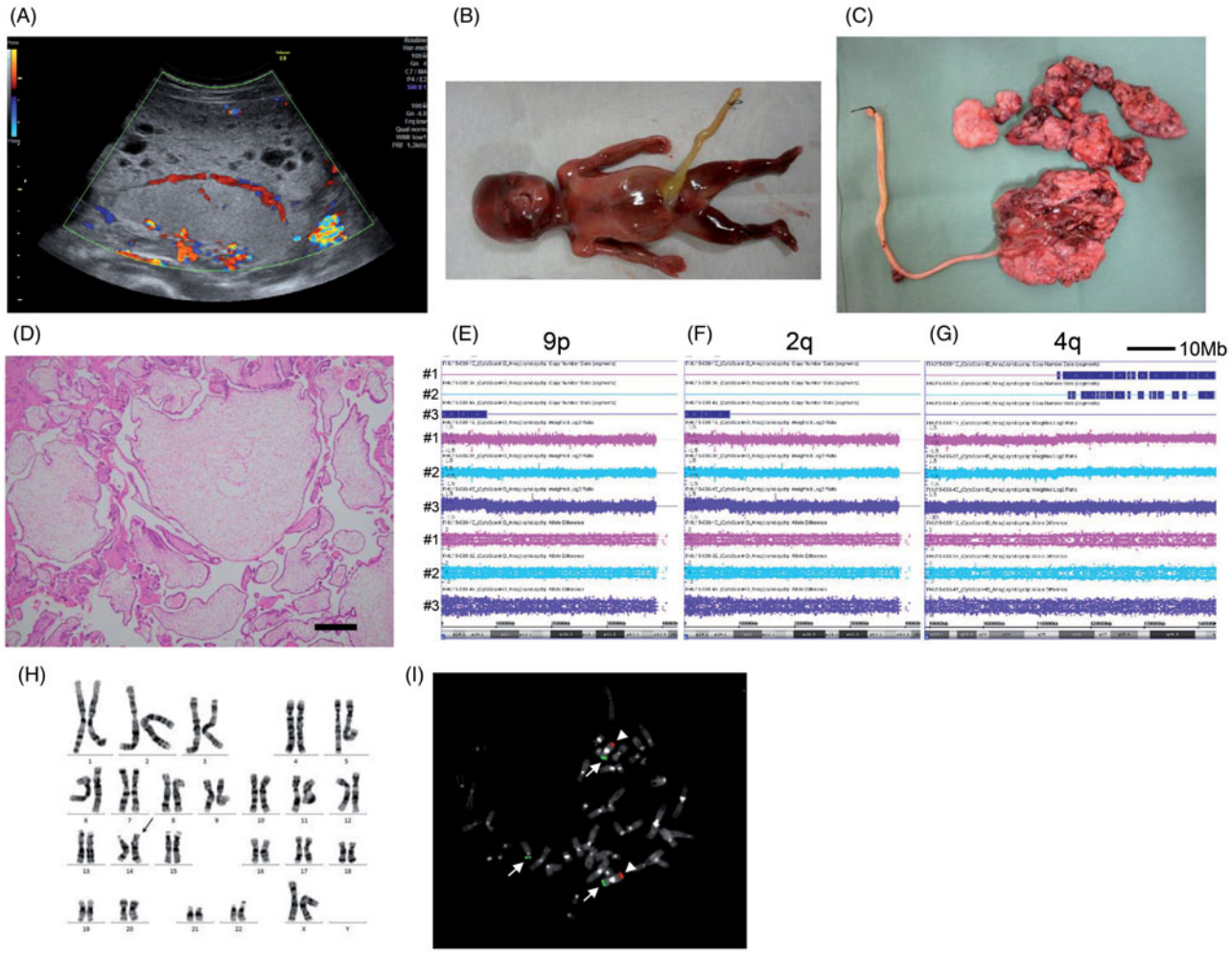

Figure 1. Clinical phenotypes and cytogenetic analysis of the foetus and placenta. Cytogenetic microarray was performed using CytoScan HD Array (Affymetrix). #1: placenta that appeared relatively normal; #2: placenta that included villous hydrops lesions; and #3: foetus. (A) Ultrasound examination at 11 weeks of gestation. Two separate areas – a vesicular area (upper area) and relatively normal area (lower area) – were observed, which are atypical for gestational trophoblastic disease. (B) Foetus. A median cleft lip and palate were observed. (C) Macroscopic analysis of the placenta. Patchy villous hydropic changes were observed. (D) Histological specimen for chorionic villi. Focal villous oedema was observed. Scale bars, 100 m. (E) 9p and 9q. (F), 2q. (G), 4q. Scale bars, 10 Mb. (H), Giemsa staining. Additional material was observed at the terminal region of 14p. (I) FISH. Subtelomeric probes (Vysis ToTelVision, Abbott Molecular) revealed the presence of der(14)t(9;14)(p24;p11.2) (arrow). White arrows: 9p; and white arrow heads: 9q.

mosaicism of a single zygote. As the CN state showed that the cell population with 9p and that with monosomy 2q and trisomy 4q were mutually exclusive, we concluded that they were likely from monozygotic twins (Supplementary Figure).

Reexamination of Giemsa staining of the foetal fibroblasts showed additional material at the terminal of 14p. Subtelomeric FISH was performed to further characterise the CN abnormalities. Trisomy 9p was found to originate from der(14)t(9;14)(p24; p11.2) in all of the 20 metaphases examined (Figure 1(H,I)). As the CN states of monosomy 2q and trisomy 4q are reciprocal, the monosomy 2q and trisomy 4q found in the placenta were likely to have originated from unbalanced t(2;4)(q37.3; q25) translocation. However, subtelomeric FISH did not detect the t(2;4) translocation in any of the foetal cells. We did not study the karyotype of the couple because they did not want to undergo the required examinations.

We recommend careful performance of the differential diagnosis of abnormal placenta with snowstorm pattern, particularly in cases with a coexistent foetus. A molecular cytogenetic study including zygosity test is necessary for differential diagnosis because it is possible that a chromosomal disorder might underlie placental abnormalities. The severities of the clinical symptoms in the foetus with such disorders vary widely. These disorders often result in lethality from multiple congenital anomalies, whereas cases with milder cytogenetic abnormalities can occasionally survive and live to a good age. Furthermore, confined placental mosaicism might affect the foetus to a lesser degree (Johnson and Wapner 1997; Lestou and Kalousek 1998). Thus, the results of the cytogenetic test might seriously affect the choice of treatment for the ultrasound findings.

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Disclosure statement

The authors report no conflicts of interest.

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