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Case Report

Multiple metastatic gestational trophoblastic disease after a twin pregnancy with complete hydatidiform mole and coexisting fetus, following assisted reproductive technology: Case report and literature review

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ABSTRACT

Objective: Twin pregnancy with complete hydatidiform mole and coexisting fetus (CHMCF) is rare and associated with severe complications during pregnancy and subsequent gestational trophoblastic disease (GTD). We encountered a case of multiple metastatic GTD after a twin pregnancy with CHMCF, following conventional in vitro fertilization (IVF). Only one case of metastatic GTD after CHMCF due to assisted reproductive technology (ART) has been reported. Here, we present the clinical course and reveal the clinical features of CHMCF after ART through a literature review.

Case report: A 42-year-old primigravida woman had an abnormal pregnancy (i.e., CHMCF) by IVF. She had persisting severe vaginal bleeding, which led to termination of her pregnancy at 10 weeks of gestation. Pathohistological examination revealed that this was a case of CHMCF. Five weeks after the termination, the serum β-human chorionic gonadotropin level was still extremely high, and systemic contrast-enhanced computed tomography revealed a tumor in the uterine corpus and more than 30 lung nodules. After 11 cycles of combination chemotherapy with etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine (EMA/CO) to treat high-risk GTD, hysterectomy was needed as radical therapy.

Conclusion: Cases of CHMCF following ART may also have higher malignant potential and higher risk of GTD development and become more aggressive biologically. The clinical course of CHMCF after ART seems to be almost the same as that without ART based on the results of literature review.

Introduction

Twin pregnancy with complete hydatidiform mole and coexisting fetus (CHMCF) is rare, with the incidence ranging from 1 per 20,000 to 100,000 pregnancies [1]. These pregnancies are difficult to manage because they can be associated with severe complications (e.g., massive vaginal bleeding, hyperthyroidism, preterm delivery, preeclampsia, and/or fetal death) and subsequent gestational trophoblastic disease (GTD). Only a dozen cases of CHMCF after assisted reproductive technologies (ART) have been reported to date (Table 1) [2–16]. We encountered a case of multiple metastatic GTD after a twin pregnancy with CHMCF, following conventional in vitro fertilization (IVF) and embryo transfer (ET). Eleven cycles of combination chemotherapy, with etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine (EMA/CO), and hysterectomy were needed for radical therapy. To the best of our knowledge, only one case of metastatic GTD following CHMCF from ART has been reported [2]. Here, we present the patient's clinical course and reveal the clinical features of CHMCF after ART through literature review.

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Table 1
Literatures reported cases of complete hydatidiform mole coexisting with a fetus after assisted reproductive technologies.

Type of ART	Published Year	Authors [reference number]	Maternal age	Gravida/Para	Number of ET	Maximum serum β hCG (mIU/mL)	Delivery or termination (weeks)	Complications during pregnancy	Live neonate (birth weight)	GTD	Metastases	Chemotherapy (number of cycles)	Hysterectomy
IVF	1994	Jinno et al. [2]	35	0/0	2	1,024,000	31	hyperthyroidism, lung metastasis	yes (1,729g) but died #1	yes	lung	MA (6)	no
	1995	Cheng et al. [3]	29	0/0	3	501,808	29	preterm delivery	yes (986g)	no	no	no	no
	1999	Montes-de-Oca-Valero et al. [4]	41	1/0	3	840,000	27	preeclampsia, massive vaginal bleeding	yes (980g)	no	no	no	no
	2002	Kwon et al. [5]	35	5/2	NM	174 ng/mL	21	chorioamnionitis	no	yes	no	MTX (1)	no
	2005	Lin et al. [6]	39	NM	4	2,861	36	massive vaginal bleeding	yes (1960g) #2	yes	no	MTX (1)	no
	2005	Wu et al. [7]	36	1/0	4	685,000	24	massive vaginal bleeding, fetal death	no	no	no	no	no
	2008	Hsu et al. [8]	31	NM	1	NM	14	fetal death	no	no	no	no	no
		Present case	42	0/0	2	647,472	9	massive vaginal bleeding	no	yes	lung	EMA/CO (11)	yes
ICSI	2001	Petignat et al. [9]	29	NM	2 #3	191,437	15	preeclampsia (lung edema), massive vaginal bleeding	no	yes #4	no	no	no
	2006	Hamanoue et al. [10]	40	2/0	3	NM	33	preterm delivery	yes (1544g)	no #5	no	no	yes #5
	2008	Dodes st al. [11]	32	0/0	4	870,000	26	hyperthyroidism, preterm delivery	yes (720g) but died #6	no	no	no	no
	2008	Yamada et al. [12]	33	0/0	3 #7	774,840	15	preeclampsia (massive pleural effusion)	no	yes	no	MTX (2) → EMA/CO (8)	yes
	2008	Vandenhove et al. [13]	31	0/0	2	1,638,200	18	hyperthyroidism, massive vaginal bleeding	no	yes	no	MTX	no
	2009	Dolapcioglu et al. [14]	34	0/0	NM	198,000	29	pregnancy induced hypertension, massive vaginal bleeding	yes (1180g) #2	no	no	no	no
	2009	Kashani et al. [15]	29	1/0	NM	73,000	19	preeclampsia, fetal death	no	no	no	MTX #8	yes
	2012	Ferraz et al. [16]	39	2/0	2	1,402,565	13	none	no	yes	no	NM	NM

ART: assisted reproductive technologies, ET: embryo transfer, GTD: gestational trophoblastic disease, NM: not mentioned.
IVF: in−vitro fertilization, ICSI: intracytoplasmic sperm injection.
MA: methotrexate and actinomycin-D, MTX: methotrexate, EMA/CO: etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine.
#1: The infant was born with asphyxia and died 4 hours post partum, secondary to severe respiratory distress syndrome.
#2: Small for gestational age.
#3: One cleavage-stage embryo was obtained from a single pronucleus (1 PN). This 1 PN was at the origin of the hydatidiform mole.
#4: Repeat curettage was performed for the high concentration of β -humman chorionic gonadotropin, revealing decidual change without evidence of trophoblastic tissue on histopathology.
#5: Hysterectomy was performed at the time of cesarean section for the prevention of GTD.
#6: The infant died of extreme prematurity.
#7: Triplet pregnancy of complete hydatidiform mole with two coexsisting fetuses.
#8: Chemotheraphy was performed for the prevention of GTD.