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Complete Molar Pregnancies with a Coexisting Fetus: Pregnancy Outcomes and Review of Literature

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Abstract

Objective The objective of the study was to review the obstetric outcomes of complete hydatidiform molar pregnancies with a coexisting fetus (CHMCF), a rare clinical entity that is not well described.

Materials and Methods We performed a retrospective case series with pathology-confirmed HMCF. The cases were collected via solicitation through a private maternal-fetal medicine physician group on social media. Each contributing institution from across the United States ($n = 9$) obtained written informed consent from the patients directly, obtained institutional data transfer agreements as required, and transmitted the data using a Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant modality. Data collected included maternal, fetal/genetic, placental, and delivery characteristics. For descriptive analysis, continuous variables were reported as median with standard deviation and range.

Results Nine institutions contributed to the 14 cases collected. Nine (64%) cases of CHMCF were a product of assisted reproductive technology and one case was

Keywords
- antenatal complications
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- molar pregnancy
- gestational trophoblastic neoplasia
- maternal morbidity

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trizygotic. The median gestational age at diagnosis was 12 weeks and 2 days (9 weeks–19 weeks and 4 days), and over half were diagnosed in the first trimester. The median human chorionic gonadotropin (hCG) at diagnosis was 355,494 mIU/mL (49,770–700,486 mIU/mL). Placental mass size universally enlarged over the surveillance period. When invasive testing was performed, insufficient sample or no growth was noted in 40% of the sampled cases. Antenatal complications occurred in all delivered patients, with postpartum hemorrhage (71%) and hypertensive disorders of pregnancy (29%) being the most frequent outcomes. Delivery outcomes were variable. Four patients developed gestational trophoblastic neoplasia.

Conclusion This series is the largest report of obstetric outcomes for CHMCF to date and highlights the need to counsel patients about the severe maternal and fetal complications in continuing pregnancies, including progression to gestational trophoblastic neoplastic disease.

Key Points

- CHMCF is a rare obstetric complication and may be associated with the use of assisted reproductive technology.
- Universally, patients with CHMCF who elected to manage expectantly developed antenatal complications.
- The risk of developing gestational trophoblastic neoplasia after CHMCF is high, and termination of the pregnancy did not decrease this risk.

Ultrasonographic evidence of an enlarged multicystic placenta with a normal-appearing fetus is an uncommon finding during routine surveillance of pregnancy. The differential diagnoses of these features include partial hydatidiform molar pregnancy with a coexisting fetus (HMCF) or complete HMCF (CHMCF), placental mesenchymal dysplasia (PMD), placental infarcts, chorioangioma, subchorionic hematoma, placental cysts, and placenta accreta spectrum (PAS) disorders. In the context of an otherwise normal-appearing fetus, the obstetrical course and postpartum follow-up of these conditions are vastly different (►**Table 1**).

In the case of a CHMCF, it is especially important to have an accurate diagnosis. This rare condition, affecting 20,000 to 100,000 pregnancies,[1,2] is fraught with potential maternal complications, such as hemorrhage, preeclampsia, and preterm delivery of the viable coexisting fetus. Persistent gestational trophoblastic neoplasia (GTN) is also seen more frequently in CHMCF, when compared with a single complete mole, and termination of the pregnancy has not been shown to decrease this risk.[1,3,4]

Although there have been large case series reported on CHMCF, they have focused mainly on outcomes as they relate to the GTN associated with this condition.[1,3,4] In these reports, the use of artificial reproductive technology (ART) was either not reported or, when reported, did not account for a majority of cases (13%). An increased use of ART over the past several decades may affect the prevalence of CHMCF and so obstetricians should be cognizant of this condition and its associated ante-, intra-, and postpartum risks. When an isolated complete molar pregnancy is noted, evacuation of the premalignant molar tissue is recommended. However, in the case of a CHMCF, a woman may elect to be managed expectantly to prolong the pregnancy. Here, we provide the first multicenter series of CHMCF reporting detailed accounts of the diagnosis, pregnancy outcomes, and postpartum follow-up, as well as a review of existing literature, to aid in the counseling of this at-risk cohort of pregnant women.

Materials and Methods

A retrospective analysis of women with CHMCF pregnancies was performed. The cases were collected via solicitation through a private maternal-fetal medicine physician group on social media. Each contributing institution from across the United States ($n = 9$) obtained written informed consent from the patient(s) directly, obtained institutional data transfer agreements as requested, and transmitted the data using a Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant modality.

Electronic records were reviewed and the following data were identified: maternal characteristics (age, gravidity, parity, prepregnancy body mass index, race, and prior maternal comorbidities); mode of conception; gestational age at diagnosis; human chorionic gonadotropin (hCG) at diagnosis; zygosity of the pregnancy; screening assessments (including laboratory and imaging); antenatal genetics (procedure type, results, and timing); and size of placental mass as measured by prenatal ultrasonography. Maternal complications including vaginal bleeding, hyperthyroidism, and hypertensive disorders of pregnancy were noted. The timing, mode, and indication for delivery, as well as the estimated blood loss or complications of delivery or procedure were recorded. Postnatal confirmation of genetics and

Table 1 Comparison of the clinical findings of placental mesenchymal dysplasia (PMD), complete hydatidiform mole (CHM), and partial hydatidiform mole (PHM)

	PMD	CHM	PHM
Ultrasound findings	Enlarged multicystic placenta with anechoic regions ("moth-eaten" appearance) Findings widely distributed, large edematous villi		
Fetus[18]	• Can be unremarkable • FGR (50%) • IUFD or neonatal death (43%) • Consider BWS findings: macroglossia, omphalocele, genitourinary abnormalities, overgrowth, polyhydramnios	• Coexisting fetus can be unremarkable	• May be structurally abnormal triploid fetus[19]
Pathology	• Enlarged stem villi with loose connective tissue and cisternlike formations • Absent trophoblastic changes	• Hydropic swelling of villi • Diffuse trophoblastic hyperplasia • Diffuse and marked trophoblastic atypia at the molar implantation site	• Focal trophoblastic hyperplasia • Marked variability in the size and degree of swelling, and cavitation of the villi • Marked scalloping and prominent stromal trophoblastic inclusion in the villi • Focal and mild trophoblastic atypia at molar implantation site
Associated maternal morbidities	None identified	• GTN • Preeclampsia • Choriocarcinoma	1. GTN 2. Preeclampsia 3. Choriocarcinoma
Cytogenetics	• Normal karyotype (89%) • 46 XX (78%), 46 XY (22%) • BWS: confirmed or suspected (23%)[20]	• 46 XX: haploid 23 X sperm duplicates its own chromosomes[21,22] • 46 XY: ova penetrated by 2 sperm (dispermy), 46 XY[23]	• Triploidy: extra haploid sperm[4]
Clinical presentation	No definitive clinical characteristics, but may be associated with preterm labor, secondary to amniotic fluid abnormalities	• Vaginal bleeding • Size greater than dates • Theca lutein cysts • Hyperemesis • Preeclampsia • Hyperthyroidism • Pulmonary edema • Respiratory distress	• Commonly diagnosed after missed or incomplete abortion, based on pathology

Abbreviations: BWS, Beckwith–Wiedemann syndrome; CHM, complete hydatidiform mole; FGR, fetal growth restriction; GTN, gestational trophoblastic neoplasia; IUFD, intrauterine fetal demise; PHM, partial hydatidiform mole; PMD, placental mesenchymal dysplasia.

pathology, postpartum follow-up, including hCG trend and time to nadir, diagnosis of GTN, and subsequent treatments were identified.

Fetal and neonatal outcomes recorded included any structural anomalies noted prenatally, intrauterine fetal growth restriction, intrauterine or neonatal fetal demise, and neonatal birthweight.

Statistical Analysis

For descriptive analysis, continuous variables were reported as median with standard deviation and range. Categorical variables were reported as proportions.

Results

After solicitation via social media, nine institutions were able to obtain patient consent and contributed 14 cases in total. Clinical characteristics of the patients are delineated in ►**Table 2**.

Of the cases presented here, 64% were the product of ART: 29% ovulation induction alone, 21% ovulation induction with intrauterine insemination, and 14% in vitro fertilization. Only five cases (36%) were due to spontaneous conception. The median gestational age at diagnosis was 12 weeks and 2 days (9 weeks–19 weeks and 4 days), with 64% ($n = 9$) diagnosed in the first trimester and the remaining diagnosed by 20 weeks of gestation. Upon either diagnosis or suspicion of diagnosis, all patients were referred to a maternal-fetal medicine specialist, who was involved in the remainder of the pregnancy. The median hCG at diagnosis was 355,494 mIU/mL (49,770–700,486 mIU/mL). The largest dimension of the placental mass at the time of diagnosis varied, ranging from 3.5 to 12 cm. The size of the placental mass universally enlarged over the antenatal surveillance period. Antenatal

Table 2 Patient characteristics and comorbidities

Case no.	Age (y)	G/P	Conception	BMI	Race/ethnicity	Comorbidities
1	30	2/1001	OI/GnTP/IUI	20.8	Caucasian	None
2	27	1/0	OI/CC	26.7	Caucasian	PCOS, seizure disorder on Lamictal
3	36	1/0	OI/CC/IUI	30.6	Caucasian	Lupus on Plaquenil
4	32	2/1001	Spontaneous	23.0	Caucasian	None
5	26	2/0010	Spontaneous	34.0	Caucasian/Asian	Anxiety, depression
6	29	2/1001	OI/GnTP	22.6	Caucasian	Chronic HTN
7	27	1/0	OI/CC	36.0	Caucasian	None
8	35	2/1001	Spontaneous	31.6	White	h/o Roux-en-Y, anemia, h/o gestational HTN
9	28	8/2052	OI/GnTP	28.2	White	Migraine, PCOS with infertility
10	28	3/1011	Spontaneous	19.4	Arab-American	h/o 2nd trimester IUFD (19 wk)
11	32	4/2012	Spontaneous	21.0	White	h/o bilateral PE, h/o 2nd trimester IUFD (16 wk)
12	38	2/1001	IVF	22.9	Asian	seizures on levetiracetam and lamotrigine
13	34	3/1011	COH/IUI	24.0	Caucasian	None
14	33	1/0	IVF	21.0	Asian	Asthma

Abbreviations: BMI, body mass index; CC, clomiphene citrate; COH, controlled ovarian hyperstimulation; GnTP, gonadotropin; h/o, history of; HTN, hypertension; IUI, intrauterine insemination; IUFD, intrauterine fetal demise; IVF, in vitro fertilization; OI, ovulation induction; PCOS, polycystic ovarian syndrome; PE, pulmonary embolism.

genetic analysis was performed in 10 of the 14 cases. Insufficient sample or no growth of the sample from either amniocentesis ($n = 5$) or chorionic villous sampling (CVS; $n = 5$) was a common finding, occurring in 40% of cases sampled ($n = 4$).

In the reported dizygotic CHMCF pregnancies, no malformations were identified. The one case of trizygotic CHMCF pregnancy had a complete mole, a coexisting structurally normal fetus, and a partial molar pregnancy with cystic hygroma and complex congenital heart defect.

Antenatal management and complications are described in ►**Table 3**. Universally, patients with CHMCF experienced some form of antenatal complication, including vaginal bleeding (10; 71%), hypertensive disorder of pregnancy (4; 28.9%), pulmonary edema (1; 0.7%), and hyperthyroidism (1; 0.7%). Of the patients with vaginal bleeding, 4 of 10 (40%) required admission and/or transfusion. The case of hyperthyroidism required medical treatment with antithyroid medications and ultimately resulted in termination of pregnancy.

The majority of patients opted for expectant management (64.3%, $n = 9$), and the average GA at delivery was 28 weeks and 3 days (16 weeks and 6 days to 34 weeks and 5 days). One patient developed an early-onset HELLP-like syndrome at 16 weeks and 6 days, which prompted treatment with dilation and evacuation (D&E). Another patient experienced persistent vaginal bleeding throughout the pregnancy, resulting in preterm labor and vaginal delivery at 20 weeks and 2 days. A third patient developed hemorrhage and chorioamnionitis and was delivered at 17 weeks and 5 days. Two patients who opted for expectant management also had postpartum hemorrhage, with one of these requiring a hysterectomy due to bleeding after emergent delivery at 24 weeks and 5 days. She subsequently required treatment for metastatic GTN (►**Table 3**).

None of the patients who opted for termination of pregnancy had complications from the procedure, including hemorrhage (►**Table 3**). One of the patients who underwent termination of pregnancy developed pulmonary edema at 20 weeks 0 days at the time of diagnosis.

GTN was diagnosed in 28.6% of patients ($n = 4$), with two (2/8; 25%) from the expectant management group and two (2/5; 40%) from the termination group. The two cases of GTN from the termination group were International Federation of Gynecology and Obstetrics (FIGO) stages 1 and 3, while the two cases from the expectant management were FIGO stages 3 and 4. All were treated with intravenous (IV) methotrexate. One patient also received leucovorin, and the patient with FIGO stage 4 disease also received IV dactinomycin. Two of these patients were also noted to have a nadir in their hCG levels by day 56 postdelivery/evacuation.

Discussion

In this series, we analyzed the patient characteristics, diagnosis, pregnancy complications, and resultant obstetric outcomes of 14 pregnancies complicated by CHMCF. Complete hydatidiform moles (CHM) are generally homozygous 46, XX and result from duplication of the haploid genome of a single sperm following fertilization of an ovum in which the maternal chromosomes are lost during meiosis, or due to postzygotic diploidization in a triploid conception.[5] A multizygotic pregnancy consisting of a partial or complete HMCF is a rare complication of pregnancy, and the available cases series to date focus on GTN risk, instead of obstetrical risk.[6] A multicystic placental mass on ultrasound imaging is

Table 3 Antenatal management and pregnancy outcomes

Case no.	Planned management	Complications	GA at delivery	Delivery type	EBL (mL)	Genetics prenatal	hCG trend	Subsequent Dx	Treatment
1	Expectant (initially declined termination) Serial growth ultrasounds Termination when HELLP	SAB of twin B at 14 wk HELLP at 16 wk	16 wk and 6 d	D&E	1,000	70 XXXY	Plateau at 8 wk PP	Metastatic GTN (FIGO stage 3) lung nodules	IV MTX
2	Expectant (declined termination) Serial growth ultrasounds	VB (admission) Anemia Preterm labor	20 wk and 2 d	SVD	300	None	Nadir by 12 wk PP	None	None
3	Expectant	VB Tachycardia Palpitations	13 wk and 3 d	D&E	200	T22	Nadir by 13 wk PP	None	None
4	Expectant (declined termination)	VB Hyperthyroidism (admission) Anemia/transfusion (2 U pRBC) PEC with severe features Hemorrhage with passage of molar tissue Intraoperative transfusion (3 U pRBC) Hysterectomy due to postpartum hemorrhage	24 wk and 5 d	Emergent classical CD	2,500	None	Nadir by 8 wk PP, then increased	Metastatic GTN FIGO stage 4	IV MTX then IV dactinomycin
5	Desired termination	Pulmonary edema	21 wk and 1 d	D&E	125	None	Nadir by 7 wk PP	None	None
6	Expectant Serial laboratories Serial growth ultrasounds	SAB of twin A VB Superimposed PEC with severe features	34 wk and 5 d	SVD	250	None	Nadir by 4 wk PP	None	None
7	Expectant Serial laboratories Serial growth ultrasounds	VB GHTN	34 wk and 2 d	Classical CD	1,000	None	Not available	None	None
8	Expectant Serial laboratories Serial growth ultrasounds	VB and anemia PTL Postpartum hemorrhage	32 wk and 2 d	Urgent classical CD due to funic presentation	1,500	None	Nadir by 7 wk PP	None	None
9	Expectant Serial laboratories Serial growth ultrasounds	VB PTL HTN Fever and tachycardia (unclear diagnosis)	28 wk and 3 d	SVD	350	None	Nadir by 10 wk PP	None	None
10	Desired termination	Abnormal TFTs with palpitations (started methimazole)	15 wk	D&E	250	None	Nadir by 4 wk PP then elevated	Metastatic GTN FIGO stage 3	IV MTX and leucovorin

Table 3 (*Continued*)

Case no.	Planned management	Complications	GA at delivery	Delivery type	EBL (mL)	Genetics prenatal	hCG trend	Subsequent Dx	Treatment
		Bilateral ovarian masses (largest $10 \times 9 \times 8$ cm)							
11	Expectant Serial laboratories Serial growth ultrasounds	VB PTL	34 wk and 2 d	SVD	300	None	Nadir by 6 wk PP	None	None
12	Desired termination	VB	16 wk and 6 d	D&E	250	None	Nadir by 12 wk PP	None	None
13	Desired termination	None	15 wk	D&C	50	None	Plateau at 2 wk PP	GTN FIGO stage 1	IV MTX
14	Expectant	Chorioamnionitis Postpartum hemorrhage	17 wk and 5 d	SVD	500	46 XX	Nadir by 12 wk PP	None	None

Abbreviations: CD, cesarean delivery; D&C, dilation and curettage; D&E, dilation and evacuation; FIGO, International Federation of Gynecology and Obstetrics; GA, gestational age; GTD, gestational trophoblastic disease; GTN, gestational hypertension; HELLP, hemolysis, elevated liver enzymes, low platelets; HTN, hypertension; IV, intravenous; MTX, methotrexate; PTL, preterm labor; PP, postpartum; SAB, spontaneous abortion; SVD, spontaneous vaginal delivery; VB, vaginal bleeding; PRBC, packed red blood cells.

typically seen in the first trimester (►**Figs. 1**–**4** and ►**Supplementary Video S1**) and should trigger a referral to a maternal-fetal medicine specialist for further imaging and potential diagnostic testing. With improved ultrasound technology and rising rates of ART,[7] HMCF diagnoses may be made earlier and more frequently, highlighting the importance of data accrual on the course and outcome of these pregnancies.[8]

The differential diagnosis of a multicystic placenta with a coexisting fetus can be broad, as a multicystic placenta can represent a hydropic abortus, chromosomal abnormalities, digynic triploid conceptions, PMD, or a molar pregnancy. These distinct diagnoses have varying complications, potential outcomes, and management strategies. The ability to differentiate between these diagnoses is key for optimal counseling and management. Pregnancies with these sonographic findings should be evaluated by and co-managed with a maternal-fetal medicine subspecialist. Maternal serum α-fetoprotein (MSAFP) measurements and β hCG measurements are helpful in confirming the diagnosis. The levels in our case series are comparable to previous case series with β hCG levels greater than 150,000 mIU/mL. Previous cases series have suggested a plateau of β hCG levels in the second trimester and that a failure to reach a plateau was associated with increased risk of adverse pregnancy outcomes.[7]

Ultrasound, β hCG, and MSAFP may not provide sufficient data to differentiate between possible diagnoses; thus, invasive diagnostic testing may be necessary for genetic analysis. Amniocentesis can be utilized to evaluate for a triploidy in the coexistent fetus or the placenta as this would be suggestive of a partial hydatidiform mole. Previous literature has suggested CVS of the suspected molar tissue as an alternative via molecular genotyping and segregation analysis of paternal and placental alleles, as absence of maternal alleles can confirm a diandrogenic complete mole.[9–11] Our series is the first to report common use of invasive testing in CHMCF, and to show that 40% of invasive procedures may yield no growth or insufficient sample in these cases. Preprocedural counseling regarding invasive testing should include this potential outcome of testing.

Furthermore, CHM is well recognized to have the potential for local invasion and distant spread. It has also been suggested that persistent trophoblastic disease and metastatic GTN are more pervasive with a multifetal gestation with concurrent mole, up to 30% increased risk.[12] β hCG and molar volumes have been used to predict malignant potential, although this is an area where more research is needed.[12]

The presence of a CHMCF creates complications for both the mother and the fetus with the clinical course frequently complicated by vaginal bleeding, preeclampsia, hyperemesis gravidarum, hyperthyroidism, and gestational trophoblastic disease.[10] Our case series describes the complication rates in a modern cohort, particularly highlighting the significance of morbid vaginal bleeding and hypertensive disorders of pregnancy in these women. A recent systemic review reported similar findings of a high rate of perinatal morbidities.[13]

Including the cases reported in this series, 16 reports of trizygotic pregnancy with two coexisting fetuses and a

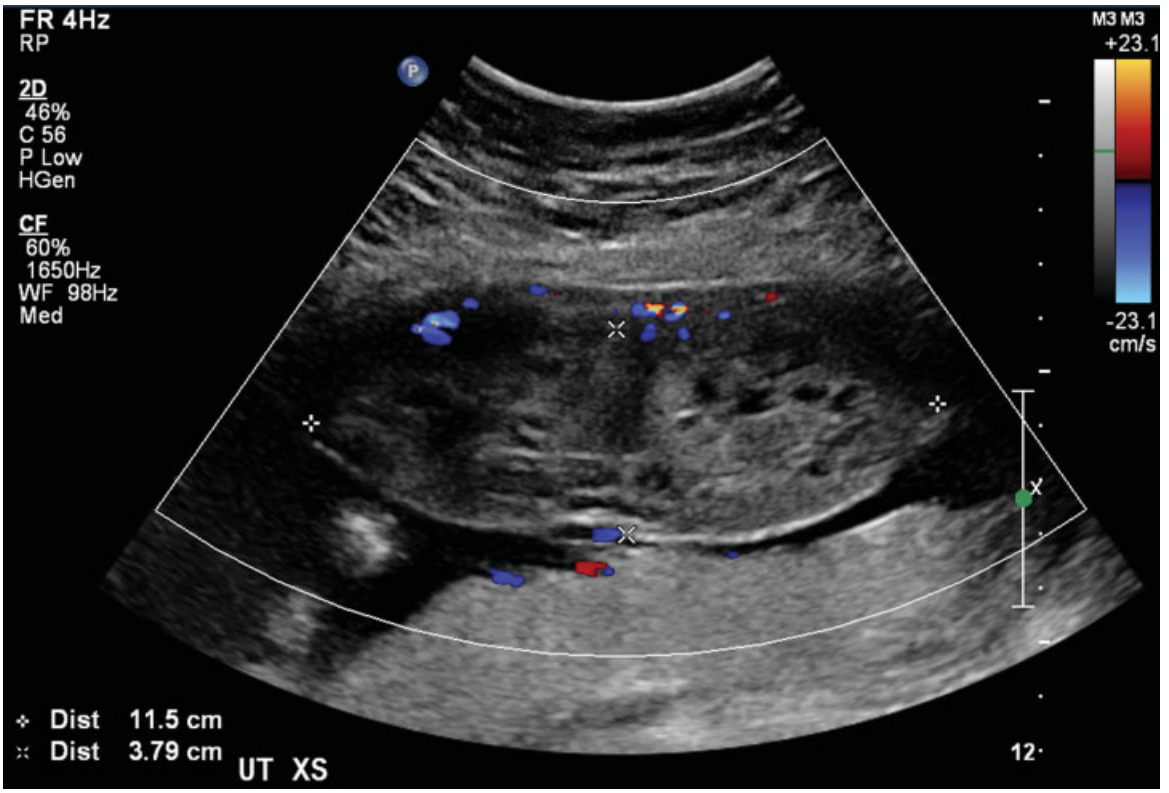

Fig. 1 Dizygotic pregnancy with large complete hydatidiform molar tissue and normal placenta.

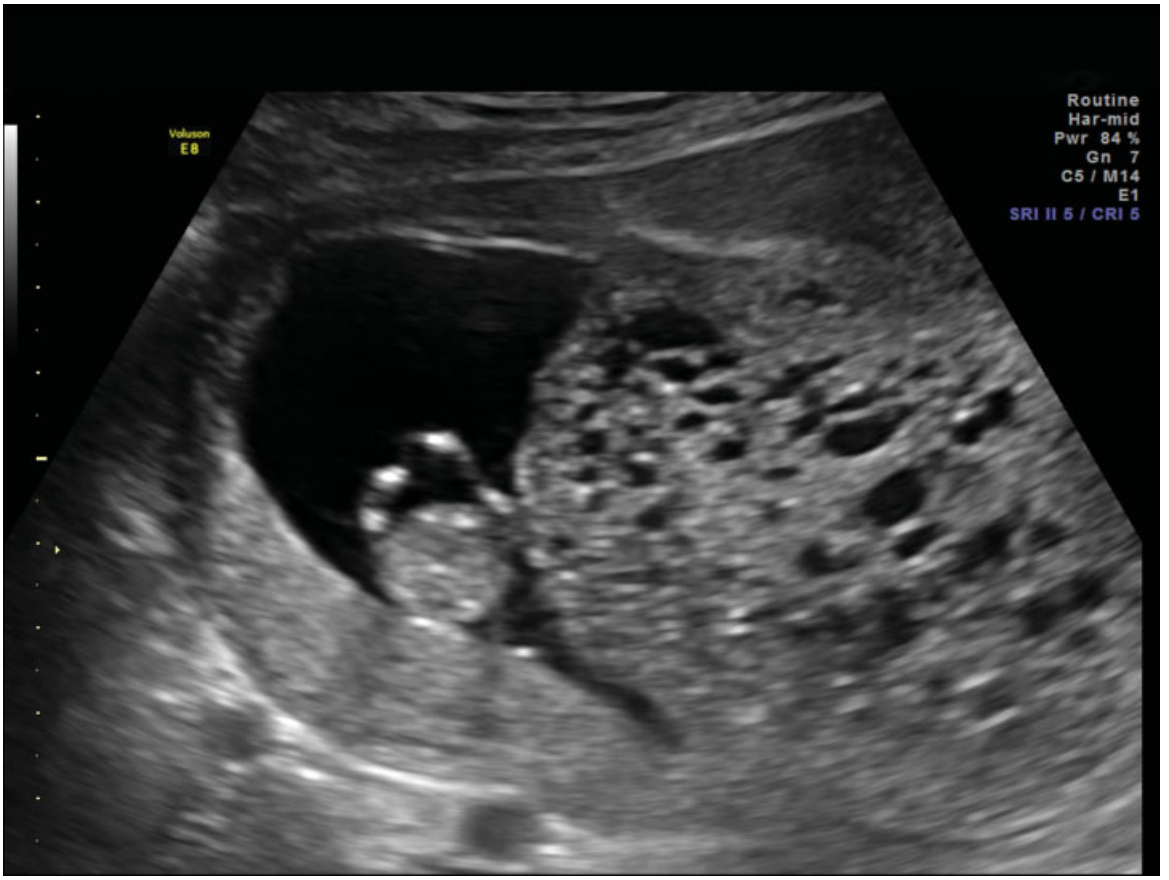

Fig. 2 Dizygotic pregnancy at 11 weeks and 4 days with complete hydatidiform molar tissue and viable fetus.

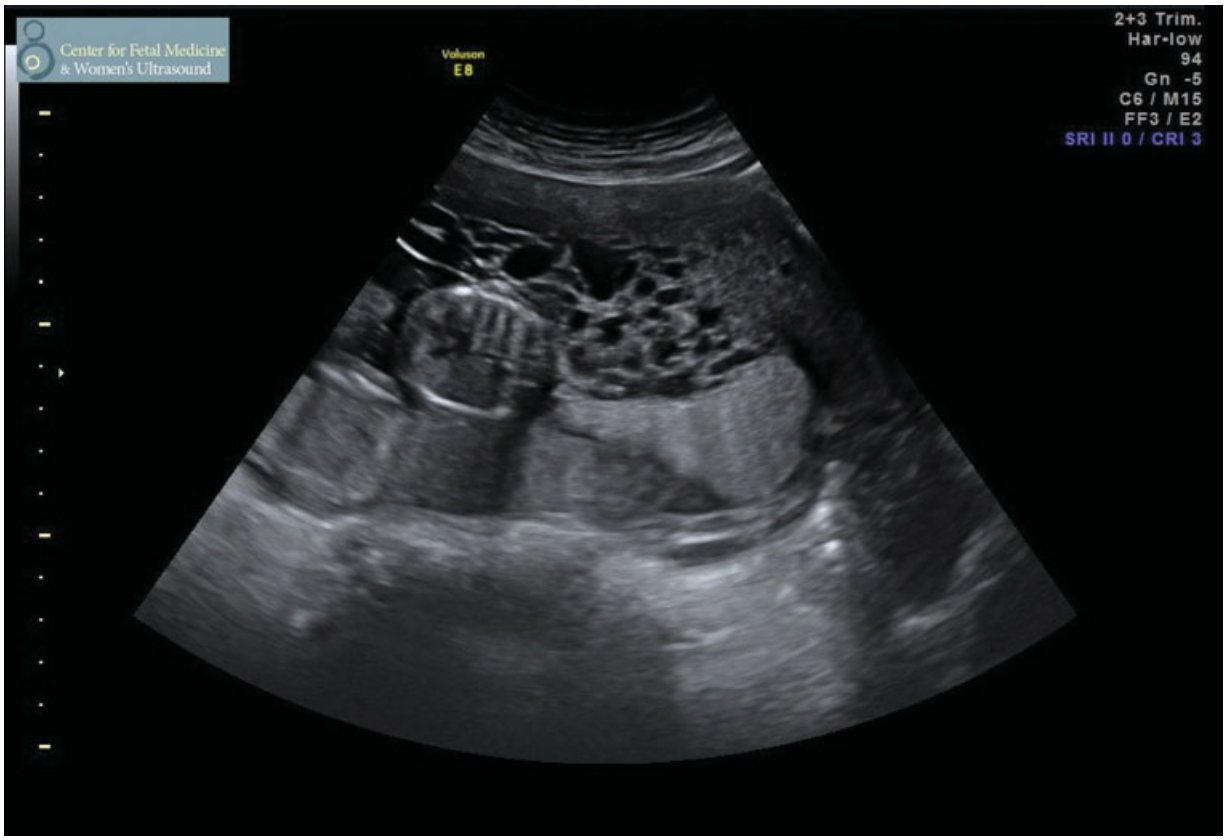

Fig. 3 Dizygotic pregnancy with complete hydatidiform molar tissue and abutting normal placenta from a viable fetus.

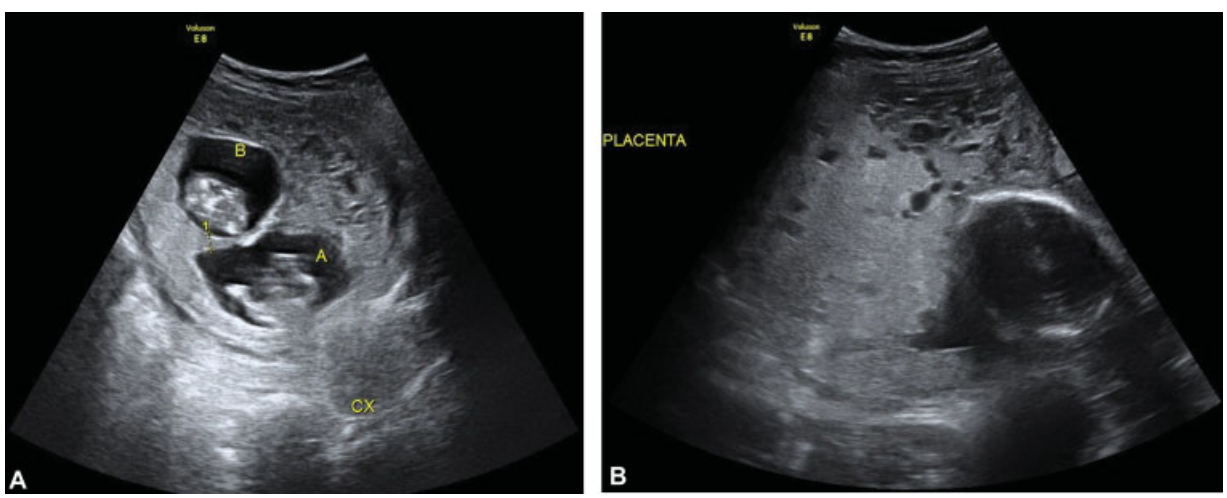

Fig. 4 Trizygotic pregnancy at (**A**) 11 weeks and 5 days with complete hydatidiform molar tissue and at (**B**) 24 weeks with the head of twin B and complete hydatidiform molar tissue.

complete mole have been reported (►**Table 4**).[5,9,10,14–16] Of the 16 cases, 87.5% have been pregnancies conceived with ovulation induction medications. The clinical course of these pregnancies shows that vaginal bleeding is very common, presenting in 59% of the cases reported to date.

The risk of GTN is higher in the presence of a complete mole compared with a partial mole (14–20% compared with 1–5%).[5] GTN can include invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. The series reported here suggests that the incidence of GTN may be higher in CHMCF than in other molar pregnancies, with 28.6% of patients in this series having GTN. Although the group who opted for termination had a high percentage of GTN, the FIGO stages appeared to be lower. This highlights the importance of counseling regarding the risk of distant metastatic disease with expectant management and need for close patient follow-up postdelivery of patients with CHMCF.

Table 4 Cases of trizygotic pregnancies consisting of complete mole and two co-existing twins

Study	Age (y)	Conception	GA at delivery (wk)	Maternal complications	Pregnancy outcome	GTD	Postpartum therapy	Confirmation of diagnosis
Sauerbrei et al[14]	23	Clomiphene	22	VB, PEC with severe features at 22 wk	Spontaneous abortion	No	MTX, ActD (5 cycles)	Postpartum by placental pathology and elevated hCG
Ohmichi et al[15]	34	hMG-hCG	17	VB	Spontaneous abortion	PTT	N/A	Postpartum by placental pathology and elevated hCG
Azuma et al[16]	24	hMG-hCG	19	VB	Spontaneous abortion	No	N/A	Postpartum by placental pathology
van de Geijn et al[24]	31	GIFT	24	VB	PTL, SVD, neonatal deaths of both twins	No	N/A	Antepartum US findings and elevated hCG Confirmed postpartum
Shahabi et al[25]	25	Clomiphene	17	Hyperthyroidism, hyperemesis	Induced abortion due to hyperemesis	Choriocarcinoma, pulmonary metastasis	MTX (2 cycles)	Antepartum US findings and elevated hCG Confirmed postpartum
Shozu et al[26]	31	IVF-ET	15	VB	Induced abortion due to VB	Invasive mole	MTX, ActD (6 cycles)	Postpartum by pathology and DNA polymorphisms in placental tissue
Higashino et al[27]	23	Clomiphene, hFSH-hCG	22	Hyperthyroidism, PEC with severe features, pulmonary edema	Induced abortion due to maternal status	Invasive mole	MTX (7 cycles), etoposide (2 cycles)	Antepartum US findings and elevated hCG Confirmed postpartum
Gray-Henry et al[28]	31	Metrodin, hCG	16	Massive VB	Induced abortion due to life-threatening hemorrhage	No	N/A	Antepartum US findings and elevated hCG Confirmed postpartum
Amr et al[29]	31	Clomiphene, hCG	30	None	PTL, SVD, neonatal death of 1 twin	No	N/A	Postpartum by placental pathology and elevated hCG
Rajesh et al[11]	29	Spontaneous	24	VB	PTL, SVD, neonatal death of both twins	No	N/A	Antepartum US findings and elevated hCG Confirmed postpartum

Table 4 (*Continued*)

Study	Age (y)	Conception	GA at delivery (wk)	Maternal complications	Pregnancy outcome	GTD	Postpartum therapy	Confirmation of diagnosis
Malhotra et al[12]	29	Spontaneous	21	VB	Spontaneous abortion	No	N/A	Antepartum US findings and elevated hCG Confirmed postpartum
Takagi et al[30]	37	hMG, hCG	28	Cerclage placed	PTL, CD for malpresentation, survival of both twins	Invasive mole, pulmonary metastases	MTX (6 cycles)	Antepartum US findings and elevated hCG Confirmed postpartum
Bovicelli et al[8]	32	ICSI	31	VB	Emergency CD for nonreassuring fetal testing, IUFD of one twin (fetomaternal hemorrhage)	No	N/A	Antepartum US findings and elevated hCG CVS c/w all paternal genotype Confirmed postpartum
Steigrad et al[31]	40	IVF	34	VB	CD due to VB, survival of both twins	Metastatic GTN, pulmonary metastases	MTX, FA (3 cycles)	Antepartum US findings and elevated hCG Confirmed postpartum
Ko et al[32]	36	IVF-ET, donor embryo	33	PEC with severe features	CD due to PEC, survival of both twins	No	N/A	Antepartum US findings and elevated hCG Confirmed postpartum
This study	30	GnTp, IUI	16	HELLP	SAB of twin B, then induced abortion of twin A due to maternal status	Metastatic GTN, pulmonary metastases	MTX	Antepartum US findings and elevated hCG Confirmed postpartum (twin A unremarkable, twin B partial mole)

Abbreviations: ActD, actinomycin D; CD, cesarean delivery; EMA-CO, etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine; ET, embryo transfer; FA, folinic acid; GA, gestational age; GIFT, gamete intrafallopian transfer; GTD, gestational trophoblastic disease; GTN, gestational trophoblastic neoplasia; hCG, human chorionic gonadotropin; HEELP, hemolysis elevated liver enzymes low platelets syndrome; hFSH, human follicle stimulating hormone; hMG, human menopausal gonadotropin; ICSI, intracytoplasmic spermatic injection; IUFD, intrauterine fetal demise; IUI, intrauterine injection; IVF, in vitro fertilization; MTX, methotrexate; PEC, preeclampsia; PT, preterm; PTL, preterm labor; SAB, spontaneous abortion; SVD, spontaneous vaginal delivery; VB, vaginal bleeding.

A recent meta-analysis by Albright et al states that the risk of GTN in patients with normalization of β HCG by day 56, or after 8 weeks, is 0.35% for complete mole and 0.03% for partial mole.[17] This is in contrast to our series, where 50% of CHMCF patients who developed GTN had a nadir of β hCG by day 56. More studies and collaborative efforts are warranted to further evaluate the possibility of additional risk of GTN. It is well known that CHMCF carries a much greater risk of pregnancy complication if expectant management is performed, with increased risk of vaginal bleeding, preeclampsia, and preterm labor, but the increased risk of CHMCF may also carry a significantly increased risk of GTN, and this may indicate a longer period of serial β hCG measurements and surveillance and should prompt extensive patient counseling.[1,3,4]

One of the greatest strengths of our study is that this is the largest series to date for obstetric data in CHMCF and includes a wide geographic region. Additionally, the use of social media to engage physicians from across the country is a novel approach to transmural collaborations, instead of individual reports of complex cases. Once connected, the physicians were able to use a standardized collection of data across institutions, giving more uniformity to the data for comparison. Although our study has many strengths, it is limited by the potential of selection bias, and given its retrospective recall of cases, the worst cases with the poorest outcomes could have been collected and reviewed. Furthermore, the observational nature of the study cannot truly compare the management protocols, as is often the case with rare disorders.

Conclusion

Overall, our findings demonstrate that it is possible to manage CHMCF expectantly but requires shared decision-making while factoring in maternal antepartum and peripartum risks, as well as increased risk of subsequent metastatic GTN. This case series can serve as a tool for engaging in full counseling of patients about the varied and potentially significant outcomes of CHMCF gestations, which are likely to be on the rise with the increasing use of ART.

Additionally, it is also important to consider innovative methods of extramural collaboration to amplify data accrual for rare disorders, such as CHMCF. This case series demonstrates a novel collaboration, as the idea was initiated in a private social media group of physicians and resulted in a wide collaborative effort from institutions across the United States. These same methods can be used with other rare complications to expand our knowledge base and lead to more meaningful observations from which to draw conclusions.

Supplementary Video S1

Dizygotic pregnancy with complete hydatidiform molar tissue and a viable fetus with normal placental tissue. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1678-3563.

Conflict of Interest
None declared.

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