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Complete molar pregnancy with transformation to choriocarcinoma of the liver: A case report

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ABSTRACT

Objective: Highlight a complete molar pregnancy with possible complications and pertinent clinical information to aid doctors in recognizing the disease quickly to provide treatment to limit adverse outcomes.
Context: Complete molar pregnancy is rare and compromises 1:500–1:2000 pregnancies [1-4]. As technology has improved, the presentation of complete molar pregnancy has changed [1,5-6].
Summary: A 19-year old African American female presented to the emergency room (ER) three times within 14 days for abdominal pain. A pregnancy test was positive and on the third visit quantitative β-human chorionic gonadotropin (HCG) was elevated without signs of an intrauterine pregnancy (IUP). Dilation and curettage (D&C) was done with small perforation of the uterus. Pathology report indicated a complete molar pregnancy. The patient failed to follow-up and returned to ER 22 days later where an abdominal mass was found prompting surgery. Hematomas and abdominal adhesions were removed and again pathology showed a complete molar pregnancy. Follow-up HCG levels failed to decrease appropriately so the patient was referred to oncology where metastatic choriocarcinoma of the liver was diagnosed. Chemotherapy was initiated and HCG monitored. Patient was readmitted for infections and complications, but did eventually have her HCG return to zero.
Data sources: Clinical Key, Purdue Library, and UpToDate were used to search for literature.
Conclusion: Prompt recognition of a complete mole may lead to a less extensive disease process. Presentation has recently changed so it is important to know signs. Patient compliance likely results in fewer complications and costs.

1. Introduction

This case report highlights a complete molar pregnancy with some possible complications and its pertinent clinical information to aide obstetrics and gynecology (OB/GYN) doctors in appropriately recognizing the disease early in order to quickly provide treatment to prevent adverse outcomes. Current literature on a complete molar pregnancy is reviewed with the case. A molar pregnancy is one in which an extra set of paternal chromosomes fertilize an egg with no genetic material or also called an empty egg [1–3]. Two variations of molar pregnancy are known; complete (diploid) and partial (triploid) [1–2,4]. This case study describes a complete molar pregnancy, how it may present, the diagnosis, the treatment, and why it is important for the early identification of this condition.

1.1. Incidence and Epidemiology

Complete molar pregnancies are thought to occur in 1:500–1:2000 pregnancies [1–4]. The majority of them, 90%, are from a single male sperm with a diploid genome (46XX) [3,7]. Once the empty egg is activated by the sperm, no zygote forms. Instead, colonic villi turn into grape like vesicles [3,6]. The exact cause is not known, but the incidence appears to have a bimodal age distribution for those in their teens and those between 40 and 50 years old [1,3]. African American females have a higher chance of having a complete molar pregnancy and mortality from it [8]. Previous molar pregnancy increases incidence 20–40× as does intermarriage [2–3]. A diagnosis of complete mole gives 15–28% chance of developing persistent disease and need for chemotherapy, but this decreases to 1.1% if HCG reaches 50 IU/L any time after evacuation of the pregnancy [4,9].

1.2. Signs and Symptoms and Diagnosis

Technology such as the ultrasound (US) and turnaround time on lab tests have changed how one presents with a complete molar pregnancy [5]. Whereas enlarged uterus, anemia, preeclampsia, hyperthyroidism,

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and hyperemesis used to be the most common way to present, now it seems to be vaginal bleeding in as many as 84% of cases [5–6]. In the 1960s–70s, 97% of patients would experience vaginal bleeding, 54% anemia, 51% enlarged uterus, 27% pre-eclampsia, 26% hyperemesis, with virtually all patients experiencing some symptoms [1,5–6]. In 1996–2006, 81% of patients experienced vaginal bleeding, 13.9% anemia, 33.9% enlarged uterus, 2.2% pre-eclampsia, 30% hyperemesis, with 19.1% being completely asymptomatic [1,5–6]. An US can be ordered if a pregnant women has any signs or symptoms that may cause concern [3,6]. A complete mole may appear as a "snow storm" pattern on US due to the villi which appear like vesicles [1,3,6]. In addition, serum HCG should be measured and number compared to the standard values for weeks of gestation as it is really the best test for diagnosing and following a complete mole [10]. If an HCG continues to increase past 14 weeks and at any time reaches a level of one million, this should cause concern for a complete molar pregnancy [3]. The higher the HCG, the higher the chance for more severe disease [6,9–10].

1.3. Treatment and Follow-up

If a molar pregnancy is suspected, a D&C should take place as soon as possible and the HCG followed to prevent a major adverse outcome, choriocarcinoma [1,3]. Choriocarcinoma is rare, occurring in only one in 20,000–40,000 with 50% of those in a molar pregnancy [1,3,8]. It commonly metastasizes to lungs, liver, brain, kidney, and gastrointestinal tract [1]. The goal is to have a zero HCG within 8–12 weeks following D&C [3]. In order to ensure this, it is recommend that HCG be followed every one to two weeks until it reaches zero and then every one to two months for six to twelve months for a total of six months after it has gone to zero [3,10–12]. Several studies have questioned the necessity to have the HCG followed so strictly and if it is even necessary for HCG to reach zero [4,9]. If the HCG decreases to zero then no treatment is needed and the patient is considered cured, but one should avoid pregnancy for a year [4,10]. If a patient does become pregnant before a year after having the HCG return to zero from a molar pregnancy, it can continue with close follow-up [12]. If the HCG does not decrease to zero, then chemotherapy is warranted [8]. Chemotherapy regimens and protocols vary depending on physician preference, but some of the common drugs used either alone or together include methotrexate, dactinomycin, etoposide, vincristine, and cyclophosphamide [1]. Treatment success rate is generally high and the condition is easier to eliminate if found early [10,13].

2. Methods

A literature search was performed using Clinical Key, Purdue University Online Library, PubMed, and UpToDate. A total of 13 articles were obtained from 1994 to 2013. Terms used for the search included "complete molar pregnancy," "choriocarcinoma," and its corresponding clinical features, as well as the presentation of the patient in the case study. The most relevant articles were selected upon reading full article.

3. Presentation of Case

A 19-year old African American female, with past medical history of only genital herpes, presented to the emergency room (ER) multiple times within six weeks for abdominal pain. During the first visit on 12/12/13, she had 8/10 abdominal pain and a distended abdomen. A pregnancy test was found to be positive, but the patient declined an ultrasound (US) and no β-human chorionic gonadotropin (HCG) level was obtained. She was diagnosed with constipation and pregnancy with an unknown last menstrual period date. On the second ER visit ten days later, she was found to have a HCG level of 60,638 IU/L. The patient was discharged again without an US. Three days later, on 12/25/13, she again returned to the ER for the pain and allowed for an US which did not show any IUP even though her HCG level was 100,606 IU/L. She was told to follow up with her obstetrician/gynecologist (OB/GYN) doctor because of a likely abnormal pregnancy. She followed up with her OB/GYN doctor the next day and again an US showed no intrauterine pregnancy (IUP). A dilation and curettage (D&C) was scheduled for the next day, 12/27/13, and a HCG of 115,795 IU/L was found prior to the procedure. A D&C was performed using suction with no major complications, but there was a small perforation of the posterior uterus. Pathology showed a complete hydatidiform mole. The patient failed to show for a 2-week follow-up and returned to ER 1/18/14 with abdominal pain. An abdominal mass was found on US that prompted emergency surgery. Several hematomas and abdominal adhesions were found and a drain was placed. Following surgery, a chest x-ray was found to be negative. When the pathology returned several days later it showed the hematoma mimicked the D&C pathology, a complete mole. Post-op HCG values (Table 1) originally started to decrease, and then started to increase again so the patient was referred to oncology for further assessment and the possibility of metastatic choriocarcinoma.

When the patient arrived to her first appointment with the oncologist four days later, she had a computed tomography (CT) of the abdomen and pelvis and was given a prescription for contraceptive pills. The CT scan showed liver metastasis and confirmed the patient did have metastatic choriocarcinoma. On follow-up for her CT scan results she appeared sick so was admitted to the hospital. She had severe right upper quadrant pain with nausea and vomiting, but denied any other symptoms. On admission to the hospital (laparoscopy post-op day 12), she had hemoglobin 8.6 g/dL, hematocrit 0.263 proportion of 1.0, platelets 323×10^9/L, basic metabolic panel (BMP) was unremarkable except for glucose of 7.83 mmol/L, white blood cell count (WBC) 12.4×10^9/L, and HCG of 40,610 (see table 5 for normal values). She had a negative abdominal X-ray, and magnetic resonance imaging (MRI) showed liver metastasis. Due to concern for pelvic abscesses and sepsis, blood cultures were taken (negative) and the patient was started on antibiotics (clindamycin and piperacillin-tazobactam), as well as oxycodone, and IV fluids normal saline 0.9%. On the second hospital day, the patient reported feeling weak and lightheaded. The patient was found to be orthostatic and labs showed hemoglobin 4.3 g/dL, hematocrit 0.129 proportion of 1.0, and platelets 84×10^9/L. The patient was rushed to the ICU to be stabilized and transfused. She had another CT scan which revealed fluid in the pelvis that was thought to be due to a bleed. She underwent emergency surgery where it was discovered she was hemorrhaging from her liver at segment VIII and diaphragm. The segment was debulked, and the patient was coagulated with packing, continued on the antibiotics and had several transfusions (six units of packed red blood cells, two units of fresh frozen plasma, and two units of platelets). On the third hospital day, she was started on multiagent chemotherapy (MAC) consisting of methotrexate, dactinomycin, and cyclophosphamide for five days.

She successfully completed 1 cycle of MAC as an inpatient with no infections so antibiotics were stopped and a port was placed so that she could have MAC as an outpatient. She was discharged eight days after being admitted to the hospital with a hemoglobin 9.2 g/dL, platelets 141×10^9/L, and liver function tests ranging from 200 to 300. She was injected with Depo-Provera, to prevent pregnancy as she had not yet started her oral contraceptive pills. She was discharged with hydrocodone bitartrate/acetaminophen, ibuprofen, docusate, and ferrous sulfate as well as instructions when to seek immediate medical attention, and a follow-up appointment.

Nine days later on 2/3/14, the patient presented to the ER with a fever > 38.8 °C, a runny nose, lower back pain, and right inguinal pain. She denied any other symptoms and stated her family was sick with a similar illness and that she had not received the flu shot for the year. She was admitted and had labs drawn (Table 2), chest X-ray (negative), urine analysis (showed a trace of blood), blood cultures (negative), and started on piperacillin/tazobactam, potassium, as well as filgrastim for her low white blood cell count. She stayed in the hospital for fifteen days where she was followed with labs to monitor infection and HCG

Table 1
HCG levels in IU/L.

12/12/13	60,638
12/25/13	100,606
12/27/13 (prior to D&C)	115,795
1/19/13 (day 1 post op laparoscopy)	47,365
1/20/14	32,085
1/21/14	22,660
1/23/14	24,491
1/26/14	38,250
1/30/14	40,610
2/07/14	40,610
2/17/14 9 (Post op liver surgery and start of MAC)	2764
2/23/14	1817
3/3/14	1702
3/8/14	182

Table 2
Admission labs and vitals on 2/3/14.

Labs		Vitals
WBC	1.6×10^9	Temperature 38.6 °C
ANC	288×10^6	Heart rate 130 beats per minute
Hb	10.1	Blood pressure 140/80 mm Hg
Hct	0.295	Oxygen saturation 98% on room air
PLT	98	
K	3.3	

levels (Table 3). Her fever disappeared on day seven of her admission so her antibiotic was discontinued. During her stay, she had nausea, vomiting, diarrhea, and intermittent atrial fibrillation due her refusing potassium supplements. She also underwent her second round of chemotherapy with MAC and was then discharged with plans to follow-up in three days and to continue future chemotherapy treatments as an outpatient.

On follow-up the patient had stomatitis of the mouth and felt weak. Oxycodone and Magic mouthwash were given for her pain and a follow-up appointment was scheduled in a week. Five days later, on 3/8/14, at the scheduled appointment, the patient presented for MAC round three and was found to be tachycardic (with a heart rate of 140 beats per min (BPM)). She was sent to the ER where her heart rate decreased to 118 BPM and labs were drawn (Table 4). She was admitted to have her potassium replaced and to be given filgrastim for her low white blood cell count and was then found to have a fever > 39.4 °C, likely due to neutropenia. She was discharged after four days and told to follow-up the next day. Prior to discharge the HCG was found to be 182 IU/L and the patient was told that chemotherapy would have to continue for three rounds after the HCG reached zero. The patient successfully had her HCG return to zero following a total of seven rounds of MAC treatment.

4. Discussion

The patient in this case study represents the common age, race, and socioeconomic status in which complete mole occurs and subsequent choriocarcinoma develops [1,8,13]. Approximately 70% of minority women fail to comply with post-molar surveillance despite being counseled on possible mortality [10]. Living >20 miles from the doctor's location is considered a main culprit to making and keeping appointments [10]. Because of the noncompliance rate, the Depo-Provera shot is recommended for post-molar contraception in this population [6]. Even though the incidence of choriocarcinoma has decreased since the 1970s, it is still a possible outcome of complete molar pregnancy so it is important to continue to inform the patient of this possibility [8]. The patient in this case study did not follow-up after her D&C, which confirms what past research has shown based on her race and socioeconomic status [1,8,13]. It is possible that if caught earlier this patient would not have had metastasis to her liver or that it would not have spread as much leading to a shorter duration of chemotherapy although a molar pregnancy can metastasize both before and after evacuation [1].

Further research is needed to determine if a uterine perforation during D&C causes an increased incidence of metastatic choriocarcinoma since studies in this area are lacking. In addition, research into how to get a higher rate of compliance in patients with low socioeconomic status is needed.

Table 3
Labs during 2/3–2/28/14 hospital admission.

HCG	2764 on 2/17/14
	1817 on 2/23/14
ANC	2.7×10^{10} on 2/19/14

Table 4
Admission labs for 3/8/14 admission.

WBC	2.4
Hb	9.5
Hct	0.274
PLT	81
ANC	288
Na	134
K	2.7
Cl	101
BUN	0.09
Cr	0.006
Ca	0.09
ALT	46
AST	15
Total Bili	0.018
Alk Phos	171

5. Conclusion

Complete molar pregnancy is quite rare, but due to the adverse outcomes that can occur, it is vital that it be found as early as possible. Doctors must realize that the patient may not present with the symptoms typically expected (large uterus, hyperthyroidism, etc.). If at any time there are any signs that cause concern, especially in early pregnancy before a normal viable pregnancy has been confirmed, an US and HCG level should be performed. It is vital that once a complete molar pregnancy is confirmed that it is removed and the patient is monitored to ensure no subsequent complications. Any ensuing problems must be

Table 5
Normal lab values with abbreviations.

Lab name	Normal value/range
White blood cell (WBC)	$3.7–10.6 \times 10^9$/L
Hemoglobin (Hb)	110–140.9 g/L
Hematocrit (Hct)	0.36–0.46 proportion of 1.0
Absolute neutrophil count (ANC)	$>2000 \times 10^6$/L
Platelet (PLT)	$141–359 \times 10^9$/L
Alanine aminotransferase (ALT)	0–32 IU/L
Aspartate aminotransferase (AST)	0–40 IU/L
Bilirubin total	0–0.012 g/L
Alkaline phosphatase (Alk Phos)	25–150 IU/L
Sodium (Na)	134–144 mmol/L
Potassium (K)	3.5–5.2 mmol/L
Chloride (Cl)	97–108 mmol/L
Calcium (Ca)	0.087–0.102 g/L
Blood urea nitrogen (BUN)	0.06–0.20 g/L
Creatinine (Cr)	0.0057–0.01 g/L
Glucose	3.9–6.1 mmol/L
β-Human chorionic gonadotropin (HCG)	0 non-pregnant IU/L

promptly treated. Further research in complete molar pregnancies is still needed.

Disclosure Statement

The authors of this paper have no conflicts of interest to report.

References

[1] Seckl MJ, Sebrie NJ, Fisher RA, Golfier F, Massuger L, Sessa C. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2013 Sept;24(6):vi39–50.
[2] Seoud M, Khalil A, Frangieh A, Zahed L, Azar G, Nuwayri-Salti N. Recurrent molar pregnancies in a family with extensive intermarriage: review of the literature. Obstetrics & Gynecology 1995 Oct;86(4):692–5.
[3] Robinson B. Intraoperative molar pregnancy crisis. AORN J 1994 Aug;60(2):193–201.
[4] Wolfberg AJ, Berkowitz RS, Goldstein DP, Feltmate C, Lieberman E. Low risk of relapse after achieving undetectable hCG levels in women with complete molar pregnancy. Obstetrics & Gynecology 2004 Sept;104(3):551–4.
[5] Bahasadri S, Kashanian M. Clinical presentation of molar pregnancy at a teaching Hospital in Iran, 1996–2006. International Journal of Gynecology and Obstetrics 2011 Nov;115(2):194–5.
[6] Soto-Wright V, Bernstein M, Goldstein DP, Berkowitz RS. The changing clinical presentation of complete molar pregnancy. Obstetrics & Gynecology 1995 Nov;86(5):775–9.
[7] Murphy K, McConnell T, Hafez M, Vang R, Ronnett B. Molecular genotyping of hydatidiform moles: analytic validation of a multiplex short tandem repeat assay. Journal of Molecular Diagnostics 2009 Nov;11(6):598–605.
[8] Smith H, Qualls C, Prairie B, Padilla RW, Key C. Trends in gestational choriocarcinoma: A 27 year perspective. Obstetrics & Gynecology 2003 Nov;102(5):978–87.
[9] Wolfberg AJ, Berkowitz RS, Goldstein DP, Feltmate C, Lieberman E. Postevacuation hCG levels and risk of gestational trophoblastic neoplasia in women with complete molar pregnancy. Obstetrics & Gynecology 2005 Sept;106(3):548–53.
[10] Feltmate C, Batorif J, Fulop V, Goldstein D, Doszpod J, Berkowitz R. Human chorionic gonadotropin follow-up in patients with molar pregnancy: a time for reevaluation. Obstetrics & Gynecology 2003 April;101(4):732–6.
[11] Juan C. Fallopian tube invasive molar disease. International Journal of Gynecology and Obstetrics 2013 August;122(2):161–2.
[12] Tuncer ZS, Bernstein MR, Goldstein DP, Lu KH, Berkowitz RS. Outcome of pregnancies occurring within one year of hydatidiform mole. Obstetrics & Gynecology 1999 April;94:588–90.
[13] Massad L, Abu-Rustum N, Lee S, Renta V. Poor compliance with postmolar surveillance and treatment protocols by indigent women. Obstetrics & Gynecology 2000 Dec;96:940–4.