CASE REPORT: UNEVENTFUL AT TERM TWIN PREGNANCY STARTING THREE MONTHS AFTER COMPLETE HYDATIDIFORM MOLE DIAGNOSIS

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ABSTRACT

OBJECTIVE: To report an uneventful twin pregnancy begun only three months after evacuation of complete hydatidiform mole.

DESIGN: Case report.

SETTING: Department of obstetrics and gynecology of P.O. M. Melloni, Milan.

PATIENT: A 38 year-old woman, gravida, treated for complete hydatidiform mole with successive uterine cavity evacuation 85 days before her last menstrual period.

INTERVENTIONS: After being diagnosed with hydatidiform mole the patient was treated with uterine cavity evacuation. One undetectable hCG level was then obtained. With the occurrence of a new pregnancy, the patient underwent transvaginal ultrasound (US) that revealed a twin dichorial diamniotic pregnancy; she then underwent normal antenatal tests and care. Histological examination of the placentas was performed after delivery.

MAIN OUTCOME MEASURES AND RESULTS: The pregnancy progressed normally until the 38th week of gestation, when spontaneous rupture of membranes and uterine contractions occurred. Two healthy foeti were delivered vaginally.

CONCLUSIONS: Patients who conceive before the completion of the full 6-12 months hCG follow-up, albeit having one undetectable hCG value, should be encouraged to continue their pregnancy.

Key-words: hydatidiform mole, hCG, gestational trophoblastic disease surveillance, pregnancy outcome

RIASSUNTO

OBIETTIVI: riportare il caso di una gravidanza gemellare priva di complicanze insorta a soli 3 mesi dalla diagnosi di mola idatiforme completa

TIPO DI STUDIO: case-report

SEDE: Dipartimento di ostetricia e ginecologia; P.O. Melloni, Milano

PAZIENTE: una donna di anni 38, gravida, con revisione della cavità uterina in seguito a diagnosi di mola idatiforme completa in anamnesi solo 85 giorni prima della data dell'ultima mestruazione.

INTERVENTI: dopo la diagnosi di mola idatiforme la paziente è stata sottoposta a revisione della cavità uterina. E' stato ottenuto un solo dosaggio nullo di hCG prima della diagnosi di gravidanza. Durante la successiva gestazione la paziente è stata sottoposta ad ecografia transvaginale che rivelava una gravidanza gemellare bicoriale biamniotica; è stata poi sottoposta ai controlli standard dell'iter gravidico. Dopo il parto è stato eseguito l'esame istologico delle placente.

RISULTATI: la gravidanza è evoluta fisiologicamente fino alla 38° settimana gestazionale, quando è avvenuta la rottura spontanea delle membrane di parto e l'insorgenza del travaglio di parto. Due feti sani sono poi stati partoriti per via vaginale.

CONCLUSIONI: le pazienti che concepiscono prima di completare i 6-12 mesi di follow-up post diagnosi di mola idatiforme, anche se in possesso di un solo dosaggio nullo di hCG, dovrebbero essere esortate a proseguire la gravidanza.

Parole chiave: mola idatiforme, hCG, sorveglianza della malattia gestazionale trofoblastica, outcome gravidico

Gestational trophoblastic disease (GTD) includes a spectrum of interrelated but histologically distinct tumors including partial and complete hydatidiform mole. Both complete and partial moles may develop persistent gestational trophoblastic neoplasia (GTN) with local uterine invasion and dissemination[1,2,3]. The incidence of GTD is approximately 1 to 2 per 1.000 deliveries in the United States and Europe[4,5,6].

The disease occurs mostly in women under the age of 35; it is therefore necessary to consider the risks of successive pregnancies, especially the possibility of GTD recurrence[5,7].

There are no pathologic or clinical features at diagnosis that accurately predict which patients will ultimately develop GTN[8]. All GTDs produce human chorionic gonadotropin (hCG), which can be measured in both serum and urine. The serum hCG level is a sensitive indicator for disease progression, including response to treatment and detection of relapse. Pregnancies that occur during the monitoring period, and the resulting hCG production, can hinder detection of progression to GTN[9].

Normal practice is that, once undetectable hCG levels are obtained, follow-up measurements are

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made at 1-2 months intervals an additional 6-12 months[10]. After completing an exhaustive follow-up, the expectation of a normal future pregnancy is comparable to that of the general population, except for a somewhat higher risk of repeated mole occurrence[11].

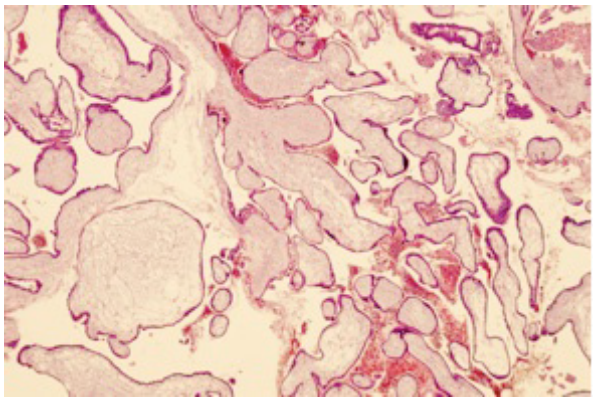
Some patients diagnosed with hydatidiform mole, however, get pregnant before completing the aforementioned follow-up, disregarding the physician's advice to hold-up conception [9-12]. Nevertheless, 42% to 63% of GTD patients fear the possibility of persistence of molar disease and the results of later pregnancies[13].

This article reports the successful outcome of a pregnancy in a patient previously treated for complete molar pregnancy who conceived before completing the hCG follow-up. To our knowledge, this is the first case that reports an uneventful twin pregnancy starting only three months after evacuation of complete hydatidiform mole.

CASE REPORT

A 38 year-old Italian woman, gravida 4, para 2, 1 hydatidiform complete mole came to our practice. She had been treated with uterine cavity evacuation for a molar pregnancy 85 days before last period. Histological exam was performed on the evacuation material and confirmed hydatidiform complete mole diagnosis. (Figure 1)

Figure 1
Histological finding of complete hydatidiform mole.



Forty days after evacuation, hCG levels were undetectable and a transvaginal ultrasound (US) scan revealed a normal uterine cavity. After this first undetectable hCG level, despite the physician's recommendations, the patient decided to disregard the planned follow-up. She undertook a pregnancy test as soon as the first pregnancy signs and symptoms appeared. Transvaginal US scan revealed a twin dichorial diamniotic pregnancy at 8 weeks + 4 days of gestation. The pregnancy had a monthly clinical and ultrasonographical follow-up and progressed normally until the 38th week of gestation, when spontaneous rupture of membranes and uterine contractions occurred. Twelve hours after rupture of membranes, two healthy foeti were delivered vaginally (male 2750g, female 2650g). Histological examination of the placenta showed a normal tissue, with some microinfarcted areas with calcium salt deposits.

DISCUSSION

GTD is relatively easy to diagnose by transvaginal (US) scan, human chorionic gonadotropin (hCG) level measurement and confirmed by histological analysis on uterine cavity evacuation material. It is known that GTD responds well to suction curettage and chemotherapy, and such modern therapy for molar pregnancy and GTN results in high cure rates and preservation of fertility[14].

Patients and their partners facing a future pregnancy after treatment for GTD express fear related to the risk of persistence of the disease affecting the outcome of subsequent pregnancies[15]. Follow-up is usually performed by testing hCG levels (having high sensibility and specificity), to ensure complete remission and the absence of any persistent postmolar tumor cells. GTN develops approximately in 15% to 20% of complete moles[16,17]. In contrast to this, GTN develops in only 2% to 4% of partial moles following evacuation[18,19]. Malignant transformation into metastatic choriocarcinoma occurs, but is fortunately exceedingly rare (0.1%)[20,21].

Ideally, serum hCG levels should be obtained within 48h of evacuation and every 1-2 weeks until undetectable; they should then be evaluated at monthly intervals for an additional 6-12 months. Use of contraception is usually recommended whilst hCG levels are monitored. After remission is documented for 6-12 months, women who desire a pregnancy may discontinue contraception[22].

The rationale for a 6-months interval of monitoring hCG levels after their normalization is to identify patients who develop malignant postmolar GTN. Indeed, although rare instances of long periods of latency have been reported, most episodes of malignant sequalae after hydatidiform moles occur within 6 months of evacuation[23,24].

Nevertheless poor compliance with the 6 months of monitoring has been reported,

especially among specific ethnic groups and indigent women. Furthermore when patients must travel long distances for the follow-up, the likelihood it not being completed increases significantly[25].

Actually, it is possible that the interval of hCG monitoring of patients with molar pregnancy may be shortened without compromising patient health and safety[23]. Once a patient with molar pregnancy achieves undetectable hCG values, the risk of gestational trophoblastic tumor relapse is extraordinary low. As recently reviewed by Sebire NJ et al.[26], the extended hCG level measurement beyond 6 months after the return of serum hCG level to normality provides minimal additional benefit, whilst having significant financial, healthcare and emotional cost; the authors suggest that this policy is no longer justified. It is possible that, given such a low risk of recurrence, a shorter post-evacuation screening could be acceptable for uncomplicated molar cases given that negative hCG levels are attained[27]. Prolonged hCG monitoring can be an economic, social and emotional burden for patients with molar pregnancy. A shorter follow-up period does not appear to negatively impact patient health or safety and certainly would improve percentages of follow-up completion. Resources would be best directed to encourage follow-up until the normalization of hCG levels[28].

Other recent literature reports that a single blood sample demonstrating an undetectable hCG level following molar evacuation is sufficient to exclude the possibility of progression to GTN. Patients could be then discharged safely from routine surveillance[27,23,19,17]. In accordance with these authors, in our case a single undetectable hCG value was associated with the remission of GTD, excluding any progression to GTN.

In addition, literature reports that conceptions occurring after molar pregnancy and started after only one undetectable hCG level, the gestational course is usually normal and leads to uneventful delivery of healthy babies. As reported in previous studies on hydatidiform mole[29,13,11,14], the rates of full term live birth, premature delivery, stillbirth delivery, spontaneous abortion, ectopic pregnancy and congenital anomalies in former GTD patients are similar to the overall average rates, and antepartum and postpartum complications and neonatal weight are similar to those of normal pregnancies[30].

Z. Selcuk Tuncer et al.[31] describe the outcome of pregnancies in 44 patients with previous molar pregnancy who conceived before completion of hCG follow-up, but after achievement of at least one undetectable hCG level: 22.7% had spontaneous abortion, 4.5% preterm delivery, 2.3% ectopic pregnancy, 70.5% term live birth. None of the live births had any detectable fetal anomaly. Equally, data from Garner E. et al.[32] concerning 1278 conceptions in patients with complete mole, show that the subsequent pregnancy experience is similar to that of the general population.

After having one molar pregnancy, the risk of molar disease in a future conception is higher than that of it naturally occurring, but still at a low rate of about 1%[33]. In the present case, the two foeti were healthy.

Once undetectable hCG levels are achieved, the risk of persistent tumor is low and reproductive outcome is favorable. Neither patients nor physicians need to fear a new pregnancy after molar disease; however, this is easier said than done.

To our knowledge, there are no data on incidence of twin pregnancies after recent hydatidiform mole diagnosis. However, we can assume that a period of ovarian hyper-stimulation by elevated hCG levels, as we observed in the course of the disease, can lead to increased incidence of twin pregnancies in the period immediately following its resolution.

Pregnancies occurring before the completion of hCG follow-up must be allowed to continue under careful surveillance. If the patient develops vaginal bleeding or any suspicious sign or symptom, she should be evaluated promptly and carefully. During the first trimester of a new pregnancy, an US transvaginal scan should be obtained to confirm normal gestational development. At the completion of any future pregnancy, the placenta or products of conception should undergo pathologic review, and hCG levels should be measured 6 weeks later to exclude occult persistent trophoblastic tumor.

In any case, our report gives evidence that patients who conceive before the completion of hCG level follow-up, having just one undetectable hCG level, should be encouraged to allow the physiological progression of pregnancy, even if it is a twin one.

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