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Gestational Trophoblastic Disease: A Case of Hydatidiform Mole Concurrent with Twin Pregnancy

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absent in CHM and potentially present in PHM [3]. Chromosomal

analysis of CHM reveals an apparently normal karyotype (46, XX

or 46, XY), but in its genesis, fertilization of an empty or nucleuslacking ovum occurs. Thus, there is no maternal genetic material, resulting in uniparental disomy, composed solely of paternal

genetic material. Conversely, PHM is caused by fertilization of a

normal ovum by two spermatozoa or by a diploid sperm, resulting in genetic material comprising two paternal haploid sets and one

maternal set, leading to triploidy (69 XXY) and, very rarely,

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ABSTRACT

Gestational Trophoblastic Disease (GTD) is a clinical entity characterized by abnormal cell proliferation affecting cells of trophoblastic tissue. Within the spectrum of the disease, Complete Hydatidiform Mole and Partial Hydatidiform Mole are the most common entities. However, cases of Hydatidiform Mole concurrent with twin pregnancy are rare.

The present report aims to describe a case of twin pregnancy in an 18-year-old patient, consisting of a normal fetus and placenta associated with a Partial Hydatidiform Mole, which progressed to miscarriage around the 17th week of gestation, covering from the moment of presentation at the Emergency Room to outpatient follow-up post-hospital discharge.

Keywords

Gestational Trophoblastic Disease, Twin Pregnancy, Partial Hydatidiform Mole.

Introduction

Gestational Trophoblastic Disease (GTD) is a clinical entity arising from abnormal proliferation of various types of trophoblastic tissue (villous cytotrophoblast, syncytiotrophoblast, and intermediate trophoblast). Clinically, it can manifest under the benign spectrum, encompassing Complete Hydatidiform Mole (CHM) and Partial Hydatidiform Mole (PHM), atypical placental site nodule, and exaggerated trophoblastic site; and under the malignant spectrum, known as gestational trophoblastic neoplasia (GTN), which includes subdivisions such as invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor [1].

Among the benign cases, differentiation between Complete and Partial Hydatidiform Mole can be achieved through macroscopic, histological, and karyotypic analyses [2]. These can be histologically differentiated based on the presence of fetal elements,

M) and Partial tetraploidy (92 XXXY) [4]. e nodule, and nant spectrum, Among the major risk factors for Gestational Trophoblastic Disease development, notable factors include maternal age over 35 or under 20 years (extremes of reproductive age) and a history of GTD in a previous pregnancy. Furthermore, the recurrence rate after a molar pregnancy is 1-2%, while after two molar pregnancies, the recurrence rate jumps to 16-28% [5,6].

Regarding incidence, an estimate suggests around 1 case per 1,000 pregnancies for CHM and 3 cases per 1,000 pregnancies for PHM [7]. Cases of Hydatidiform Mole associated with twin

pregnancy are even rarer, with an estimated incidence of 1 case per 22,000 to 100,000 pregnancies [8]. Suspicion arises in cases with significant vaginal bleeding, coupled with disproportionate elevation of human chorionic gonadotropin (β -hCG) levels relative to gestational age. Additionally, ultrasound imaging can play a crucial role in monitoring and determining the outcome of the case [9].

Case Report

An 18-year-old female patient, primigravida, with no known prior comorbidities and without any previous prenatal care, presented to the Gynecology Emergency Department referred from another facility due to vaginal bleeding and abdominal pain of one day's duration. An ultrasound examination was performed for further investigation (Figures 1 and 2), revealing an ongoing pregnancy with a single, viable fetus exhibiting fetal biometry consistent with 17 weeks and 4 days of gestation. However, signs of premature placental detachment were also noted. Additionally, a heterogeneous image without a clear cleavage plane was observed at the upper pole of the placenta, with hypoechoic areas resembling vesicles in between, suggesting the possibility of coexisting molar disease. Later on the same day, the patient experienced a miscarriage, expelling the fetus and placenta along with amorphous material filled with vesicles, which was brought to the consultation and can be seen in Figure 3.



Source: Ultrasound provided by the patient.

Figure 1: On the left, a single fetus is observed, with an anterior placental position and normal amniotic fluid. On the right, accelerated fetal heartbeats are evident (176 beats/min). Fetal biometry consistent with 17 weeks and 4 days of gestation.



Source: Ultrasound provided by the patient.

Figure 2: Anterior placental position, revealing a heterogeneous image with no clear cleavage plane at the upper pole, along with hypoechoic

areas resembling vesicles in between, measuring approximately 10.8 x 5.0 x 8.2 cm (volume 235.0 mL), suggesting the possibility of coexisting molar disease and premature placental detachment.



Source: Image authorized by the patient.

Figure 3: On the left, the placenta, fetus, and amorphous material filled with vesicles are observed, respectively; On the right: fetus.

On admission physical examination, the patient presented with a tender abdomen upon deep palpation in the hypogastric region, and the uterus was palpable 4 cm above the pubic symphysis, along with mild vaginal bleeding. She was subsequently admitted, and the expelled material was sent for histopathological study. Additional tests were requested, with a β -hCG result of 188,724.38, and a repeat transvaginal ultrasound revealed a anteverted, centered uterus with distinct and regular contours, measuring 135 x 82 x 105 mm, with a volume of 619 cm³. The myometrium displayed homogenous acoustic texture and a solid, echogenic image projecting toward the outer third of the myometrium in the isthmic region, showing intense vascular activity on color Doppler mapping, suggestive of residual trophoblastic material.

Due to the clinical presentation of ongoing vaginal bleeding and the results of these additional tests, the patient underwent and received Intrauterine Manual Aspiration (IUMA), resulting in the expulsion of a small amount of material suggestive of retained products of conception, which was also sent for histopathological examination. Following the procedure, the patient's vaginal bleeding improved, and her β -hCG levels regressed. She was discharged from the hospital and referred for outpatient follow-up. Histopathological examination of the initially expelled material revealed gestational trophoblastic disease, suggestive of partial hydatidiform mole (Figures 4, 5, and 6), along with a male fetus at a gestational

age consistent with 17 weeks of gestation. Additionally, mature second-trimester placental tissue was present, without significant associated histological changes. The material obtained from the IUMA showed extensively necrotic decidua remains, but no signs of trophoblastic disease in the sample.



Source: Pathology.

Figure 4: On the left, a villus is observed with trophoblast proliferation and intense atypia of trophoblastic tissue, 100X magnification; On the right, an enlarged, hyperchromatic, and irregular nucleus (arrow) indicating trophoblast atypia, 400X magnification.



Source: Pathology.

Figure 5: An enlarged villus is observed with intense villous edema and trophoblast inclusion, 100X magnification.



Figure 6: An avascular, hydropic, edematous villus is observed with the formation of a cistern (arrow) and trophoblast hyperplasia, 100X magnification. Source: Pathology.

The patient was monitored in a specialized gestational trophoblastic disease outpatient clinic for 17 months, with serial measurements of quantitative β -hCG. The monitoring initially occurred on a weekly basis, showing a continuous decline throughout, with only two minor elevations followed by subsequent decline, totaling 10 weeks until reaching a quantitative β -hCG level of 2.79 mIU/mL. After four consecutive values below 5 mIU/mL, the patient transitioned to monthly follow-up for an additional 7 months. The curve of β -hCG measurements can be observed in Graph 1.





Legend	
26/08/21	Hospitalization (red)
02/09/21	Post IUMA (blue)

The patient returned to the outpatient clinic in January 2023, 6 months after the last follow-up appointment, with a transvaginal ultrasound revealing a normally implanted gestational sac containing a single fetus, with a heart rate of 153 BPM, a present yolk sac with usual appearance, and the placenta developing in the posterior fundal region. The gestational age was consistent with 10 weeks and 6 days. The patient was referred for prenatal care.

Discussion

Gestational Trophoblastic Disease is a condition that affects cells of trophoblastic tissue, placental cytotrophoblast and syncytiotrophoblast, with varying prevalence among its different forms. This pathology can be divided into various entities based on histopathology, genetic characteristics, morphology, and progression. Its most common clinical form is Hydatidiform Mole, which despite having a potential benign nature, can progress to malignancy. Therefore, proper evaluation, monitoring, and appropriate management are necessary to prevent this outcome [10].

Regarding the histopathology of Hydatidiform Mole, differentiation between its forms is necessary, whether it be a Complete or Partial Hydatidiform Mole. In CHM, fetal elements are generally absent, with a pronounced and widespread proliferation of trophoblast and a higher frequency of atypia compared to PHM [11]. In the case of Partial Hydatidiform Mole, the presence of amnion and/or fetal tissue can be identified, even though these may display gross alterations. Structures like theca-lutein cysts can also be observed in some cases [1].

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As for the presented signs and symptoms, cases related to CHM are more commonly associated with increased uterine size and complications like preeclampsia, hyperthyroidism, and hyperemesis. In contrast, PHM may be accompanied by incomplete or missed abortion, with the diagnosis often made after histological evaluation of material collected during uterine curettage [4]. While most previous studies have shown that GTD is rarely accompanied by a viable pregnancy, it is important to note that the diagnosis of Mole can be challenging in the context of a twin pregnancy due to the concurrent presence of a normal fetus. Thus, it is crucial to differentially diagnose between Partial and Complete Hydatidiform Mole in one gestational sac and a normal pregnancy in the other. In the case of CHM, the fetus would exhibit malformations related to triploidy and result in fetal demise. Conversely, with PHM, the normal fetus may survive and, although presenting similar clinical symptoms, β -hCG levels are higher, and the incidence of gestational trophoblastic tumor (GTT) and preeclampsia is greater (20%) compared to 5% after partial mole, indicating a worse prognosis [12].

Therefore, in a molar pregnancy, it is important to recognize common signs and symptoms, which include hyperemesis, ovarian cysts, increased uterine size for gestational age, and genital bleeding. It should also be noted that with the advent of more accessible complementary tests, such as β -hCG measurements and, most importantly, ultrasound, early diagnosis is possible.

According to the literature, cases of CHM in twin pregnancies have not yet established well-defined management protocols for prenatal care. The termination of pregnancy is often prompted by clinical complications arising from the aggressive growth of trophoblast. Hence, several factors need to be considered to determine whether or not to terminate the pregnancy, including clinical progression, serial quantitative β -hCG measurements, presence of complications, fetal cytogenetic analysis, and patient decision [13].

This case report describes a patient with a twin pregnancy coexisting with a normal fetus and placenta alongside a PHM, resulting in a spontaneous miscarriage. This diagnosis was confirmed by histopathological examination. Immediate management included imaging studies, uterine cavity evacuation using the Intrauterine Manual Aspiration (IUMA) method, and assessment of the patient's laboratory parameters.

The subsequent course of the case involved outpatient followup, with serial quantitative β -hCG measurements until complete regression, which occurred three months after the patient's hospitalization, as shown in Graph 1. Concurrently, transvaginal ultrasounds were conducted to assess lesion regression. The last ultrasound, performed on the same date as the zero value of β -hCG (2.79 mIU/mL), revealed a uterus in midversion, centered, with distinct and regular contours and precise boundaries, measuring 77 x 42 x 58 mm, with a volume of 100 cm³. The endometrial echo was indistinct and heterogeneous, measuring 9.4 mm, and on color Doppler, vascularization was less evident in the anterior wall compared to previous exams.

The patient was monitored weekly until four consecutive β -hCG values reached zero, followed by monthly follow-up for seven months. At the last follow-up appointment, six months after the final monthly β -hCG measurement, the patient underwent a transvaginal ultrasound, which revealed an ongoing single, topical pregnancy of approximately 10 weeks and 6 days, prompting a referral for prenatal care.

Conclusion

Hydatidiform Mole is a pathology of significant importance, considering the potential consequences it can lead to, especially when dealing with its malignant forms. However, it can have favorable outcomes if diagnosed early and treated correctly. Thus, it is of fundamental importance to recognize and manage the case when confirmed, with periodic monitoring of the β -hCG curve after intervention being essential.

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