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Sad fetus syndrome: A case report

Alan O. Kintanar III[1], Darleen SJ Estuart[1], Lynette L. Lasala[1]

Abstract:

Sad fetus syndrome is a rare gestational trophoblastic disease wherein a hydatidiform mole coexists with a live fetus. We report a case of a 40-year-old G4P2 (2012) with 29 weeks gestational age who came in with vaginal bleeding and labor pains. A previous ultrasound done at 16 weeks of gestation showed a live fetus, a normal placenta, and a focal multicystic uterine mass. The beta-human chorionic gonadotropin level was 1,500,000 mIU/mL. She delivered a live preterm female fetus weighing 900 g by partial breech extraction. The placenta was grossly normal. Postpartum hemorrhage secondary to uterine atony was encountered and a total hysterectomy with bilateral salpingectomy was performed. Cut section of the specimen revealed molar tissue at the anterofundal area with evidence of gross myometrial invasion. The histopathologic finding was consistent with a diagnosis of partial hydatidiform mole. This paper describes the incidence, pathology, clinical presentation, diagnosis, treatment, and postpartum course of this rare condition.

Keywords:

Hydatidiform mole, partial mole, sad fetus syndrome, twin molar pregnancy

Introduction

Hydatidiform mole belongs to a group of gestational trophoblastic diseases characterized by an abnormal proliferation of trophoblasts. The prevalence is 1–2 in 1000 pregnancies in Western countries, one in 500 pregnancies in Asia, and one in 250 pregnancies in the Philippines.[1]

Hydatidiform moles are categorized as either complete hydatidiform moles or partial hydatidiform moles based on the gross morphology, histopathology, and karyotype. Complete hydatidiform moles display generalized hydatidiform swelling with diffusely scattered trophoblastic hyperplasia with no fetal tissue or amnion. Complete hydatidiform moles demonstrate a 46XX karyotype with the chromosomes entirely paternal in origin. This is due to the fertilization of an empty ovum either by a haploid sperm duplicating its chromosomes or by two sperm cells. Partial hydatidiform moles only displays focal hydatidiform swelling with chorionic villi of varying sizes, and an identifiable fetal or embryonic tissue with a triploidy karyotype of 69 chromosomes. This is due the extra haploid set of chromosomes derived from the father. The coexisting fetus rarely develops or survives beyond the first trimester due to the congenital anomalies related to triploidy.[2]

Case Report

A 40-year-old gravida 4 para 2 (2012) on her 29 1/7 weeks age of gestation came in for labor pains associated with profuse vaginal bleeding.

She is a public school teacher with unremarkable medical, family, and social history.

She has regular menstrual cycles with normal duration and flow.

Her first two pregnancies were livebirths delivered vaginally and without complications. Her third pregnancy was a complete spontaneous abortion at 9 weeks age of gestation.

[1]*Department of Obstetrics and Gynecology, Brokenshire Medical Center, Davao City, Davao del Sur, Pilippines*

Address for correspondence:
Dr. Alan O. Kintanar III, Department of Obstetrics and Gynecology, Brokenshire Medical Center, A. Pichon St, Armau, Davao City, 80203 Davao del Sur, Philippines.
E-mail: mykindacoach@gmail.com

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On her fourth pregnancy, she came to our institution at 16 weeks age of gestation due to vaginal spotting. Ultrasonography revealed a live fetus with a possible partial hydatidiform mole [Figure 1]. She was advised to see a trophoblastic disease specialist but she was not able to comply due to financial constraints.

At 18 weeks gestation, she developed persistent nausea and vomiting associated with body malaise and was subsequently admitted. On admission, her blood pressure was elevated at 200/100 mmHg.

The following blood levels were abnormal: Hemoglobin 97 g/L, platelet count 119 × 10^9/L, lactate dehydrogenase (LDH) 363 U/L, alanine aminotransferase (ALT) 56 U/L, thyroid stimulating hormone (TSH) <0.05 mIU/L, and FT4 39.99 pmol/L. The serum beta-human chorionic gonadotropin (β-hCG) level was extremely high at >1,500,000 mIU/ml in 1:100 dilution.

The impression was threatened abortion 18 weeks AOG, G4P2 (2012); twin molar pregnancy; preeclampsia with hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome; hyperthyroidism-uncontrolled. She was given antihypertensives, propylthiouracil, and isoxuprine. She was discharged improved on the 10th hospital day. She was counseled on the possibility of recurrence of these pregnancy complications and the possibility of pregnancy loss. The necessity for regular weekly prenatal check-up, ultrasound scan, and laboratory tests was emphasized.

A Targeted Fetal Anomaly Scan/congenital anomaly scan (CAS) [Figure 2] revealed an intrauterine twin gestation with molar pregnancy and coexisting live fetus at 20 weeks and 2 days age of gestation, in cephalic presentation, with good cardiac and somatic activities. Placenta was located anterior, high-lying, Grade II with posterior echogenic structure with hypoechoic foci measuring 13.3 cm × 9.9 cm × 1.7 cm covering the internal OS with 3.1 cm overlap considering placenta previa totalis**.** The sonographic estimated fetal weight was 332 g, and the CAS showed no gross structural abnormalities.

Due to financial constraints, she failed to comply with her weekly prenatal check-up; hence, serum β-hCG, complete blood count (CBC), and sonologic surveillance were not done.

On her 29th gestational week, she was admitted due to preterm labor and profuse vaginal bleeding. She was conscious, coherent, and anxious with a blood pressure of 130/80 mmHg. The rest of the vital signs were stable. Fundic height was 25 cm and the fetal heart tone rate was at of 104 beats/min. Due to the ultrasound finding of a mass overlying the cervical OS, an internal examination was not done. The speculum examination showed profuse vaginal bleeding. CBC, blood typing, LDH, ALT, serum creatinine, and urinalysis were requested. The plan was to perform a cesarean section hysterectomy with mole *in situ*.

After induction of anesthesia, a spontaneous delivery of the fetal buttocks was noted; thus, a partial breech extraction was done. She delivered a live baby girl, APGAR score of 4,7; Ballard score of 26 weeks, birth weight of 900 g, appropriate for gestational age [Figure 3]. After spontaneous delivery of a normal-looking placenta, heavy bleeding ensued secondary to uterine atony; hence, total abdominal hysterectomy with bilateral salpingectomy was done. The estimated total blood loss was 2500 cc. She was transfused with 2 units of blood.

The intraoperative finding revealed molar tissue with an aggregate diameter of 10 cm × 10 cm implanted at

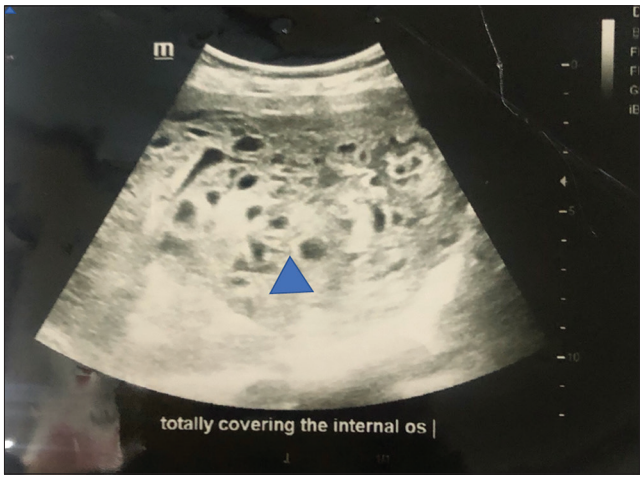

Figure 1: Longitudinal sonographic view scan at 16-week gestation of hydropic villi of partial mole (▲) shows the variable and focal villous edema

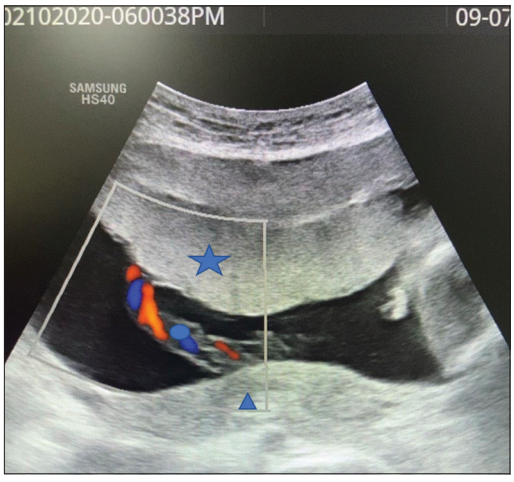

Figure 2: Longitudinal sonographic view scan of the normal placenta (★), normal size umbilical cord (●) and partial molar mass (▲) at 20-week gestation

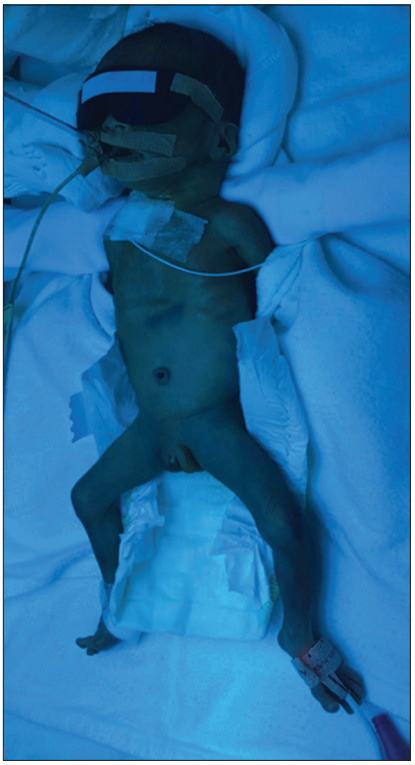

Figure 3: The live birth baby girl, ballard score of 26 weeks and birth weight of 900 g

the anterofundal area with areas of poor demarcation between molar tissue and decidua. Furthermore, at the right anterolateral portion of the uterine cavity, the myometrium was noted to be spongy in consistency [Figure 4]. Both ovaries were grossly normal with theca lutein cysts, measuring 2 cm on the right and 2.5 cm on the left.

The postoperative course was uneventful. The serum β-hCG level markedly declined to 123,008.14 mIU/mL. Anemia was managed with blood transfusion and the patient was discharged well on the 3rd postoperative day.

On her follow-up check-up, the serum β-hCG level further declined to 1490.49 mIU/mL. Methotrexate chemoprophylaxis was deferred due to a surgical site infection.

The uterine mass was examined and reviewed by four pathologists who concurred on a final diagnosis of a partial hydatidiform mole [Figure 5]. The cytotrophoblasts and villous stroma did not exhibit staining with p57, suggestive of a complete mole. The p57 immunohistochemistry study was repeated 3 times revealing the same negative result [Figure 6].

Discussion

A 40-year-old G4P2 (2012) on her 29th week gestational age presented with labor pains and vaginal bleeding.

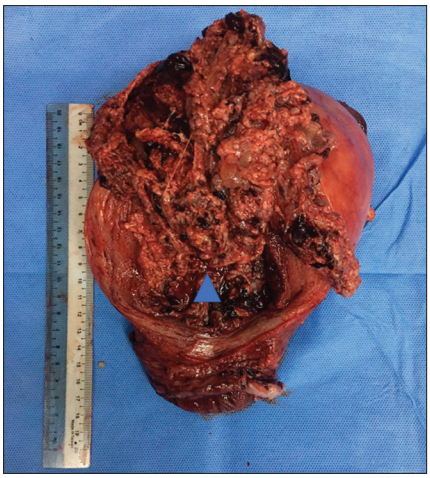

Figure 4: The uterus with the attached molar mass (▲) located on the lower segment of the uterus

A previous ultrasound showed a live fetus with a focal multicystic mass. The serum β-hCG level was 1,500,000 mIU/ml, thus, a twin molar pregnancy was highly considered. The patient delivered through partial breech extraction. Uterine atony was noted after placental delivery and a total hysterectomy with bilateral salpingectomy was performed. Cut section of the specimen showed molar tissue at the anterofundal area. Histopathology confirmed the diagnosis of a partial hydatidiform mole.

The salient features led us to the following differential diagnosis: Placental mesenchymal dysplasia (PMD) and twin Molar Pregnancy.

PMD is a rare placental vascular anomaly with an ultrasound appearance of a large placenta with grape-like vesicles mimicking a molar pregnancy. The serum β-hCG level in PMD is normal or slightly elevated. PMD has a poor prognosis associated with fetal growth restriction, absence of fetal development, fetal, or neonatal death. This is secondary to a fetal vascular obstruction causing prolonged severe fetal hypoxia.[3]

Our patient had a markedly high serum β-hCG level at 1,500,000 mIU/ml. There was no evidence of intrauterine growth restriction on ultrasonography. The baby was carried to 29 weeks gestational age, delivered live, with a size appropriate, or gestational age. The neonatal course was uneventful.

Based on the ultrasound findings and the highly elevated serum β-hCG level, twin molar pregnancy was the primary consideration. The three types of twin molar pregnancy are as follows: (1) Twin gestation of normal fetus and placenta with complete mole; (2) twin gestation of normal fetus and placenta with partial

mole, and (3) normal single fetus with the partial molar placenta (rarest).[4]

Histopathologic findings of a partial mole are focal swelling of chorionic villi and trophoblastic hyperplasia. Moreover, scalloping of chorionic villi and trophoblastic stromal inclusions is present [Figure 7].[2,4]

The use of p57 immunostaining improves diagnostic accuracy for complete hydatidiform moles which are almost always p57-negative. Very rarely do complete moles show abberant expression and this is secondary to the retention of the maternal copy of chromosome 11. Conversely, in rare occasions, p57 immunostaining may show negative staining in partial moles when there is loss of maternal chromosome.[5] In a systematic review and meta-analysis by Madi *et al*., comparing the accuracy of p57 immunostaining for diagnosing complete hydatidiform moles, it was found out that occasional partial hydatidiform moles can demonstrate negative staining secondary to the loss of maternal chromosome.[5]

This case of a twin pregnancy of normal fetus and placenta with partial mole is very rare accounting for 0.005%–0.01% of all pregnancies. It is known as such because it is associated with poor pregnancy outcomes such as abortion, preterm delivery, preeclampsia, fetal death, hemorrhage, and gestational trophoblastic neoplasia (GTN). There are 10 published cases reported cases of partial mole with a coexisting live fetus reaching a viable state. This is the first reported case in the Philippines.

There are three types of twin molar pregnancy. The first type, which is the most frequent of the three, is a twin pregnancy having one normal fetus with a normal placenta and another complete mole. The second type is a twin pregnancy with a normal fetus and placenta and with another partial mole. The third type, being the most uncommon of the three, is a singleton normal fetus with the partial molar placenta.[4] This patient belongs to the rare second type of twin molar pregnancy.

The patient developed severe preeclampsia with HELLP syndrome and hyperthyroidism during the earlier course of pregnancy. Both complications were secondary to the markedly elevated β-hCG levels.[2,6,7] Hyperthyroidism is attributed to the similarity of the chemical structure of the beta subunit of the β-hCG to TSH.[6,7] The patient was made aware that these complications might worsen as the pregnancy progresses and that intensive monitoring will be required. In twin molar pregnancies, counseling the woman about the increased risk of perinatal morbidity and the possible progression to GTN is important.[1,2] Fetal karyotyping is also highly suggested.[2] Other studies suggest amniocentesis as the diagnostic test of choice and termination of pregnancy may be required.[1,2,4]

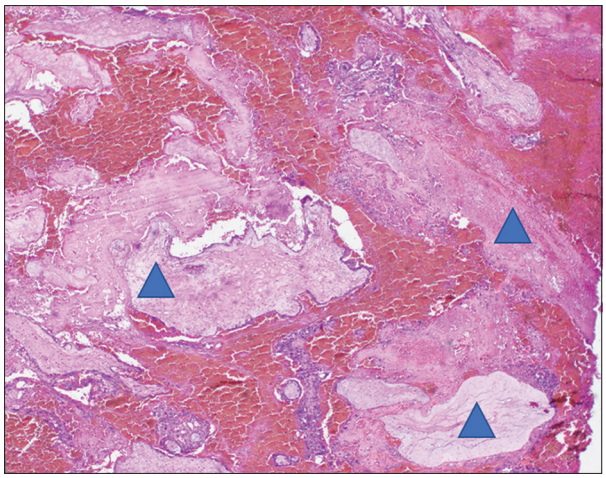

Figure 5: Photomicrograph shows enlarged but predominantly degenerated villi (▲) in a necrotic and hemorrhagic background. (×100 H and E)

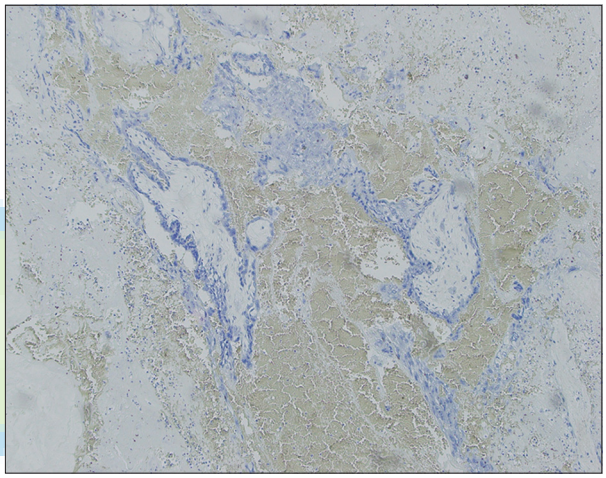

Figure 6: P57 Immunohistochemistry slide (×200 magnification)

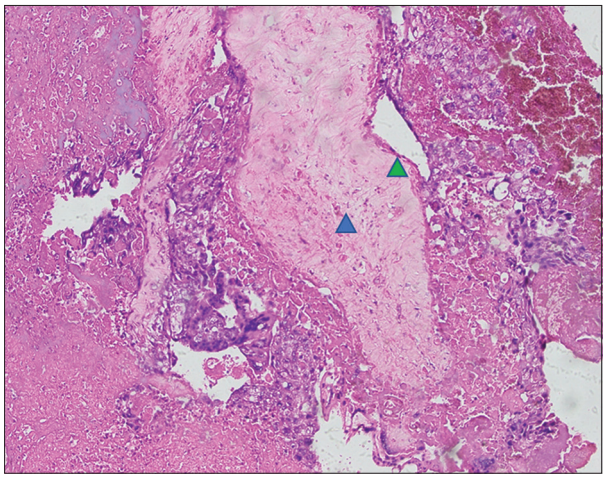

Figure 7: Photomicrograph shows enlarged but degenerated villi (▲) with circumferential trophoblastic (▲) proliferation. (×200 H and E)

The abovementioned complications and highly elevated β-hCG levels at more than 1,500,000 miU/mL are unusual for a partial mole. When a partial mole is accompanied by a normal fetus, the serum HCG and AFP levels can be significantly higher with consequent medical complications.[8]

As exhibited in this case, diagnosing and managing a molar pregnancy with a coexisting live fetus is complex. It can be achieved through ultrasonography and serum β-hCG monitoring.[3] β-hCG is a pregnancy-specific hormone produced by trophoblast cells at the time of implantation.[8] Serum β-hCG levels naturally start to elevate at approximately 100 mIU/mL at the onset of missed menstruation in a natural cycle and further increase to 100,000 mIU/mL by 8–10 weeks. It will then start to decrease after the 10th week. In pregnancies with hydatidiform moles, the β-hCG levels increase to as high as 100,000 mIU/mL to 1,000,000 mIU/mL.[9]

Ultrasonography is considered a reliable and sensitive modality in diagnosing complete hydatidiform mole in the first trimester due to diffuse hydatidiform swelling exhibited by the chorionic villi. A complete mole will demonstrate a characteristic pattern termed as a "swiss cheese appearance." Ultrasonography also supports the diagnosis of partial mole, but the histologic review is more indicative and reliable in diagnosing partial hydatidiform mole.[3]

Important prognostic factors for fetal survival depend on the fetus' standard karyotype, the size of the molar placenta, maternal age, and the coexisting maternal complications.[4]

Karyotyping was not done due to financial constraints.

Ideally, serial β-hCG monitoring is done as scheduled: Immediately after delivery, 24 h postdelivery, weekly for 3 weeks, then every 3 months for 1 year or until the β-hCG level becomes normal. This patient was not able to comply due to financial constraints. Only four β-hCG level determinations were done postpartum. The latest serum β-hCG level done at 10 weeks postpartum was 26.44 mIU/ml [Figure 8].

Chemoprophylaxis is given to patients who are at high risk of developing GTN. Methotrexate chemoprophylaxis was deferred in this case due to a surgical site infection.

Summary

We present a case of a 40-year-old G4P2 (2012) diagnosed with a rare entity of sad fetus syndrome, wherein a live fetus with an normal placenta coexists with a partial hydatidiform mole. The early onset of severe pregnancy complications posed a challenge in the management of this case. Our treatment approach included appropriate diagnostics and monitoring, medical management, counseling, and a good postpartum-postmolar follow-up plan. The risk of developing GTN is significantly higher in twin molar pregnancies. It is crucial to closely monitor these cases to allow prompt intervention when necessary.

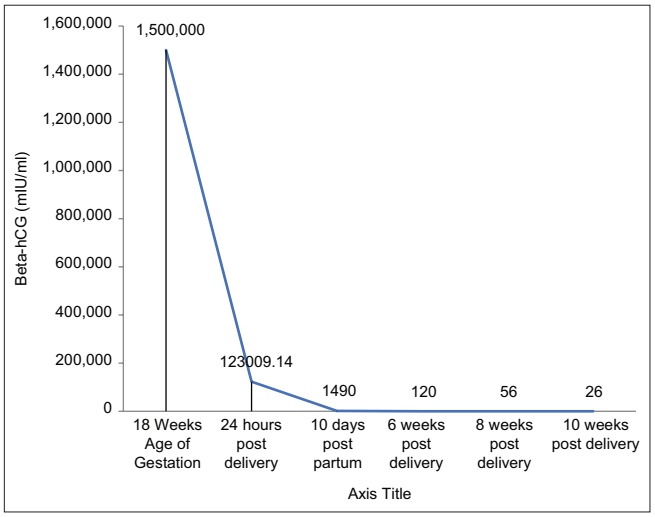

Figure 8: The graph shows the serial beta-hCG monitoring of the patient, beta-hCG: Beta-human chorionic gonadotropin

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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