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REPORTE DE CASO

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PARTIAL MOLAR PREGNANCY WITH LIVE FETUS COMPLICATED BY INTRAUTERINE GROWTH RESTRICTION AND SEVERE PREECLAMPSIA. CASE REPORT AND REVIEW OF THE LITERATURE

Mola parcial con feto vivo, complicado con restricción de crecimiento intrauterino y preeclampsia severa. Reporte de caso y revisión de la literatura

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ABSTRACT

Objective: To report the case of a partial molar pregnancy with live fetus and conduct a review of the literature regarding maternal and fetal complications associated to this condition.

Materials and methods: Case report of a partial mole with a 33 weeks live fetus complicated by intrauterine growth restriction, oligohydramnios and severe preeclampsia. We report satisfactory maternal and neonatal outcomes and 1-year follow-up. A search was conducted in the Medline via Pubmed, LILACS, Ovid, Uptodate and Google Scholar databases using the following MESH terms: hydatidiform mole, partial mole, live fetus, coexisting live fetus. Case series and case reports of pregnant women with coexisting partial mole and live fetus at the time of diagnosis were selected and information regarding maternal and fetal prognosis was extracted.

Results: Initially, 129 related titles were identified. Of these, 29 met the inclusion criteria, and 4 articles were excluded due to failed access to the full text. Overall, 31 reported cases were included; 9 ended in miscarriage, 8 in fetal demise or perinatal death, and 14 (45 %) resulted in a live neonate. The most frequent maternal complication was preeclampsia in 6 (19.35 %) cases.

Conclusion: The coexistence of a partial mole with a live fetus poses a high risk of adverse perinatal outcomes and preeclampsia. The volume of information regarding this rare condition must be increased in order to better determine potential interventions in cases of euploid fetuses and to provide adequate counseling in clinical practice. Therefore, reporting these cases is important to

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build sufficient evidence about the natural course of this condition.

RESUMEN

Objetivo: reportar un caso de mola parcial con feto vivo y realizar una revisión de la literatura sobre las complicaciones maternas y fetales asociadas a esta condición.

Materiales y métodos: se presenta el reporte de un caso de mola parcial y feto vivo de 33 semanas, complicado por restricción de crecimiento intrauterino, oligoamnios y preeclampsia severa. Después de seguimiento del recién nacido a un año reportamos un resultado satisfactorio materno-fetal. Se realiza una búsqueda de la literatura en Medline vía PubMed, LILACS, OVID, Uptodate y Google Scholar, con los siguientes términos MESH: "hydatidiform mole", "partial mole", "live fetus", "coexisting live fetus". Se seleccionaron estudios de series de caso y reportes de caso de gestantes con coexistencia de mola parcial y feto vivo al momento del diagnóstico, y se extrajo información sobre el pronóstico materno-fetal.

Resultados: se identificaron inicialmente 129 títulos relacionados, de los cuales 29 cumplieron los criterios de inclusión, 4 artículos fueron excluidos por no obtener acceso al texto completo. Se analizaron 31 casos reportados, 9 casos terminaron en aborto, 8 terminaron en óbito o muerte perinatal y 14 (45 %) casos terminaron con un recién nacido vivo. La complicación materna más frecuente fue preeclampsia, en 6 (19,35 %) casos.

Conclusión: la coexistencia de mola parcial con feto vivo presenta un riesgo alto de resultado perinatal adverso y preeclampsia. Se requiere más información sobre esta rara condición para determinar de mejor manera posibles intervenciones en los casos de fetos euploides y dar una adecuada asesoría en la práctica clínica, por lo que es importante el reporte de estos casos para tener suficiente evidencia sobre el comportamiento natural de la enfermedad.

Palabras clave: mola parcial; feto vivo; preeclampsia; restricción de crecimiento intrauterino.

Key words: Partial mole; live fetus; preeclampsia; intrauterine growth restriction.

INTRODUCTION

Together with choriocarcinoma and placental site trophoblastic tumor, hydatidiform mole is one form of presentation of gestational trophoblastic disease (1). The hydatidiform mole is a placental abnormality characterized by hyperproliferation of placental villi and hydropic degeneration (2). The mole is classified as either complete or partial (3).

A complete molar pregnancy is characterized by a placental abnormality consisting of a diploid set of chromosomes of paternal origin, with absent fetal tissue (4). From the cytogenetic stand point, it develops after an oocyte with lost or damaged genetic material is fertilized by one or two spermatozoa, resulting in a diploid zygote of androgenetic origin (3). The karyotype is 46 XX in 90% of cases and 46 XY in 10% (1). A partial molar pregnancy is characterized by placental abnormality plus the presence of fetal tissue (5). Candelier states that, according to Golubovsky's theory, it results from the fertilization of a normal oocyte by two spermatozoa, giving rise to triploidy in most cases and a fetus with multiple malformations that ends in miscarriage (2). However, there are reported cases of euploid fetuses that may result in viable pregnancies (6).

The incidence of complete moles varies by regions, the highest being found in Southeast Asia at 13 for every 1000 pregnancies, and the lowest of 0.3 for every 1000 being found in South America (3). The incidence of partial moles is 3 in 1000 (1) and the incidence of coexistence of a live fetus with a partial mole ranges between 1 in 22,000 and 1 in 100,000 (6,7).

A molar pregnancy coexisting with a live fetus may be due to the presence of a multiple pregnancy, where one is normal, with normal fetus and placenta and the other is a mole, either complete or

partial. The other less frequent possibility, as already mentioned, is a partial molar pregnancy with a live euploid fetus, of which there are very few cases reported in the literature (6,8).

Three important reviews of the coexistence of molar pregnancy with live fetus are available: the first by Vejerslev in 1991 analyzes the literature between 1903 and 1989 and reports 113 cases of complete molar pregnancy coexisting with a live fetus, with 3 cases corresponding to a partial mole with live fetus (6). The second review by Wee and Jauniaux in 2005 reports 174 cases of complete molar pregnancy and live fetus (9). The third review by Lin reports a series of 72 cases of multiple pregnancies with complete mole and live fetus, together with a review of 9 articles adding up to an additional 173 cases (10).

Prenatal diagnosis of molar pregnancy and live fetus is based on elevated beta hCG levels and ultrasound findings (9). Sensitivity and specificity of first-trimester ultrasound have been reported at 44% and 74%, respectively, and differential diagnosis includes incomplete miscarriage and unembryonated egg (11).

In terms of management of molar pregnancy with live fetus, some authors recommend the use of amniocentesis for determining fetal karyotype (6,9). In early pregnancy, Bruchim recommends termination when diagnosis is made during the first half of gestation; however, this author advises watch-and-wait management if no malformations are detected and karyotype is normal (12). There is little information on the management of live fetuses after 22 weeks until delivery. Lin reports the need for termination of pregnancy in 40% of cases due to medical complications (10). Persistent trophoblastic disease may occur after delivery, more frequently in cases of complete mole and live fetus (21%) (13), although it has also been described in 1% of cases of partial molar pregnancies (2). For this reason, weekly follow-up of beta fraction chorionic gonadotrophin (B-HCG) is performed after the end of gestation until it becomes negative (14).

It has been described that the presence of a twin pregnancy with a mole and a live fetus is associated with increased maternal complications such as pre-eclampsia in 20 to 30% of cases (6, 9), vaginal bleeding in 46%, and hyperemesis gravidarum 17% (6); and wide variability is reported regarding neonatal survival, ranging from 25% (9) to close to 60% (6, 10). Significant association with intra-uterine growth restriction and preterm delivery is reported in these fetuses (6).

As observed, several publications report complete mole and live fetus, but there is a paucity of information specifically regarding treatment in accordance with gestational age at diagnosis and fetal and maternal prognosis in partial molar pregnancies with live fetuses. Consequently, our objective is to report a case and conduct a review of the literature, focusing on maternal and fetal outcomes in this condition.

CASE REPORT

We present the case of a 19-year-old primigravida with 33 weeks of gestation, living in the rural area of the eastern plains in the Department of Meta in Colombia, who presented after one week of generalized edema and blood pressure of 154/94, and was referred to the city of Bogota with a diagnosis of preeclampsia. She had no prior history of a medical condition or surgery, but a family history of a hypertensive mother.

On the first prenatal visit at 16 weeks, maternal weight and height were 53 kg and 160 cm, respectively. Mandatory prenatal laboratory test results were normal and thyroid stimulating hormone (TSH) was within normal ranges. The patient had three prior ultrasound scans. The 16-week ultrasound showed normal fetal anatomy, normal fluid and placenta. The 22-week scan showed fetus with liver cyst, normal amniotic fluid, and placental abnormality suggestive of placenta accreta. The 32-week scan showed intra-uterine growth restriction with biometrics for 28 weeks, oligohydramnios Amniotic Fluid Index (AFI) of 4 cm, and suspected placenta accreta.

In March 2018, the patient was admitted to the maternal-fetal section of La Victoria hospital, a Level III institution in Bogota that serves patients covered by the state-subsidized Social Security System in Colombia. The patient was conscious, hydrated, weight 61 kg, blood pressure at 150/100, uterine height 28 cm, grade II edema of the lower limbs, with all other physical findings being normal. Laboratory tests and detailed ultrasound were requested.

The detailed anatomical obstetric scan showed estimated fetal weight of 830 g and growth under the 3rd percentile for gestational age. Placental assessment revealed an image of 90 x 167 mm, with multiple honeycomb hypoechoic patterns suggestive of gestational trophoblastic disease (Figures 1 and 2). Amniotic fluid assessment confirmed oligohydramnios (AFI = 3 cm). Placenta accreta was ruled out on Doppler examination. Fetal hemodynamic Doppler showed increased umbilical artery resistance, normal middle cerebral and ductus venosus resistance. Fetal assessment revealed a female fetus with a 25 x 26 mm focal lesion in the right lobe of the liver of irregular hypoechoic appearance with small septations suggestive of hepatic mesenchymal hamartoma (Figure 3); the rest of the fetal anatomy was normal. Diagnostic impression of a 33-week gestation, preeclampsia with no severity criteria, trophoblastic disease with live fetus coexistence, intrauterine growth restriction, oligohydramnios, and fetal hepatic cyst: suspected hepatic hamartoma. As for laboratory results, complete blood count showed hemoglobin, 14g/dl; hematocrit, 41%; leukocytes, 12,300/mm^3; platelets, 166,000/mm^3; creatinine, 0.6 mg/dl; transaminases: AST, 32 IU, ALT, 34 IU; 24-hour proteinuria, 400 mg. Gonadotropin was not measured due to advanced gestational age.

The patient went into spontaneous labor 6 hours after admission, at 33 weeks of gestation, with no complications. Following 6 hours of labor, a female baby was born by vaginal delivery, with a birthweight of 900 g, and APGAR of 8, 9 and

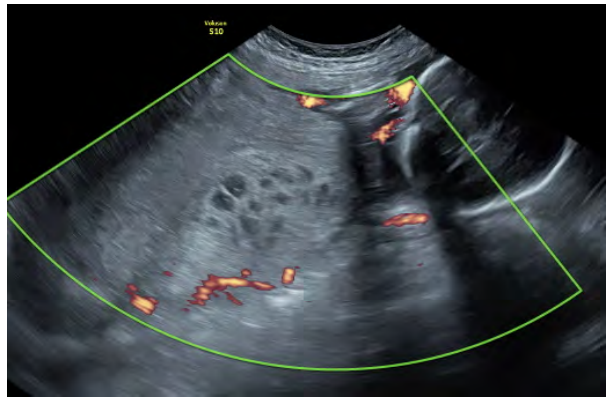

Figure 1. Ultrasound image with normal and abnormal placental zones, showing hydropic degeneration. Patient with live fetus and partial molar pregnancy, Bogotá (Colombia), 2018

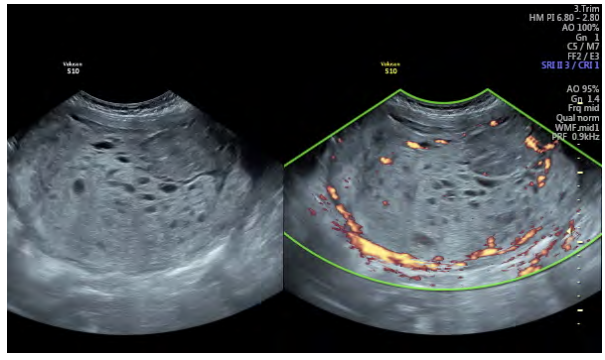

Figure 2. Close-up of the placenta showing the classical honeycomb pattern suggestive of gestational trophoblastic disease. Patient with live fetus and partial molar pregnancy, Bogotá (Colombia), 2018

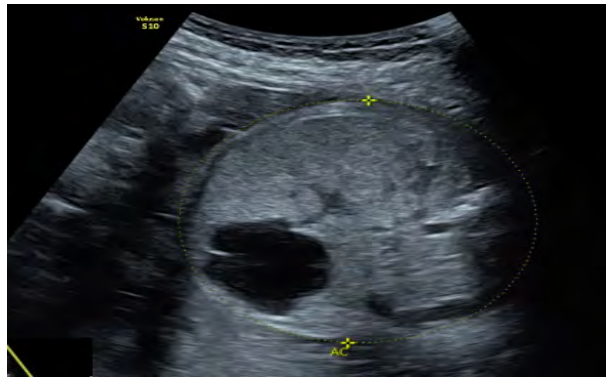

Figure 3. Fetal intra-hepatic cystic suggestive of hamartoma. Patient with live fetus and partial molar pregnancy, Bogotá (Colombia), 2018

10 at 1, 5 and 10 minutes. Complete Shultze-type placenta. After delivery, in the immediate postpartum period, the patient developed hemorrhage secondary to uterine atony, with a heart rate of 114 beat/minute and blood pressure of 148/95 mmHg. The postpartum bleeding protocol, called red code in Colombia, was activated (15); bleeding was controlled with oxytocin-based pharmacological management. Uterine exploration was performed under anesthesia and the patient received transfusion of 2 U of red blood cells. Laboratory results during red code implementation were hemoglobin, 11 g/dl; hematocrit, 34%; platelets, 183,000/mm^3; fibrinogen, 775 mg/dl; D dimer, 30 ng/ml.

During the early postpartum period, the patient had blood pressure values consistent with severe preeclampsia (184/111 mm/Hg) that could not be reverted with the administration of nifedipine and clonidine and required transfer to the intensive care unit for management with a continuous infusion of labetalol at a rate of 1 mg/min. The patient reported transient loss of sight that prompted computed tomography imaging (CT) of the brain, which was reported as normal. Increased proteinuria (6.3 g) was identified in 24-hour urine, and other tests to determine the severity of preeclampsia were normal. After 72 hours, the patient was discharged from the intensive care unit, and discharged from the hospital 15 days later on a prescription of losartan 150 mg/day, nifedipine 90 mg/day and clonidine 900 mcg/day. The final placental pathology result was of a monochorionic monoamniotic placenta weighing 550 g with chorionic villi with hydropic degeneration, reported as gestational trophoblastic disease of the partial mole type.

The neonate received two doses of surfactant and required ventilation support for 5 days. She developed neonatal sepsis due to ESBL *Kluyvera ascorbata*, which evolved favorably after management with ertapenem. The following tests were carried out during hospitalization: total abdominal ultrasound showing a cystic image consistent with hamartoma, normal transfontanelle ultrasound, normal echocardiogram, normal renal ultrasound and normal 46XX karyotype. The neonate was assessed by the pediatric surgeon who considered outpatient follow-up. The baby remained in the hospital for 62 days and was discharged on supplemental oxygen due to moderate lung dysplasia. At 1-year follow-up of the mother and the baby there is no evidence of persistent trophoblastic disease, with negative b-HCG and no need for antihypertensive medication. The baby evolved satisfactorily.

Ethical considerations. The patient was informed of the diagnosis, signed informed consents for each of the procedures, and signed a specific informed consent for the publication of this case. All steps were taken to ensure confidentiality of the information and patient anonymity; photographs were taken by the authors.

MATERIALS AND METHODS

To answer the question about maternal and fetal complications associated with cases of live fetus and partial molar pregnancy, a literature search was conduced in the Medline via PubMed, Google Scholar and Lilacs databases, using the following MESH terms: "hydatidiform mole," "partial mole," "live fetus," "coexisting live fetus," in English and Spanish, with no time restriction. Inclusion criteria for the studies: case reports or case series; population type: pregnant women with a diagnosis of incomplete mole and live fetus. The snowball method was used and a search was conducted based on the references cited in each article. Data selection and extraction were carried out by one of the authors and verified by the other. Information on the following variables was collected: country where the case occurred, maternal age, gestational age, diagnosis, diagnostic method, type of diagnosis, type of management (expectant, termination of pregnancy), delivery type (cesarean or vaginal delivery), fetal outcome (fetal demise, live neonate, intrauterine growth

restriction, congenital malformations), maternal complications (antepartum, intrapartum or postpartum), neonatal complications. Results are presented in narrative form.

RESULTS

Initially, 128 titles and abstracts were identified; of these, a total of 29 studies met the inclusion criteria and access to the full text was possible in 25, while 4 in which only access to the abstract was obtained were discarded from the review (16-19). The 25 included studies were case reports.

In total, 31 cases of incomplete mole coexisting with a live fetus were found.

Country of the study: 5 studies were conducted in the United States (13,20-23), 3 in India (24-26), 2 in Mexico (27,28), 2 in China (29,30) 2 in Turkey (34, 41), while the remaining reports came from Australia (31), The Netherlands (32), England (33), Pakistan (35), Nepal (36), Poland (42), Bangladesh (37), Chile (38), Malaysia (39), Italy (43), and Canada (40).

Maternal age was found to be in the range of 17 to 29 years in 25 cases (13,22-29,32-37,39-42), 30 to 39 years in 6 cases (20,21,23,30,31,43) and 40 or older in no case. Gestational age at the time of diagnosis was less than 22 weeks in 17 cases (20-23,25,28,30,33- 35,40), between 23 and 27 weeks in 4 cases (29,32,38,41), 28 to 37 weeks in 6 cases (24,27,36,37,39), and 37 weeks or more in 4 cases (13,26,31). The method of diagnosis was prenatal ultrasound in 21 cases (20,21,23-25,27,28,30,32-35,37,40,42-43), and at birth or with pathology testing in 10 cases (13,26,29,31,36,38,39,41,43). Termination of pregnancy was offered in 4 cases (20,23).

Gestational age at the time of termination of pregnancy ranged between 15 and 40 weeks, with 9 cases at 22 weeks or less (20,22,23,28,40); 4 cases between 23 to 27 weeks (29,32,34,38); 13 cases between 28 and 37 (21,24- 25- 26-28,30,33,36,39,41,42- 43) and 5 cases between 38 and 42 semanas (13,26,31,35,37). As for the type of delivery, there were 12 cases of cesarean delivery (8, 21,26,27,30-34,39,42,43) and 10 cases of vaginal delivery (13,25,28, 29,35-37,41,42).

Fetal outcome: 9 cases ended in miscarriage (20,22,23,28,40); there were 8 cases of fetal demise or early neonatal death (24,28,29,32,34,38,39,41); 6 cases of intrauterine growth restriction (24,25,27,37,39,43); 2 cases with fetal malformations; 1 case with Dandy-Walker malformation (26), and 1 case of myeolomeningocele (38). A live viable fetus was born in 14 cases (13,21,25,26,27,30,31,33,35-37,42,43). Reported maternal complications were preeclampsia in 6 cases (6,23,28,31,34,40), one case of postpartum bleeding requiring hysterectomy (27), persistent trophoblastic disease in 3 cases (4,23), one case of hyperthyroid crisis (41); and no cases of sepsis or maternal mortality.

The details of the case reports are shown in Table 1.

CONCLUSION

Coexisting partial mole and live fetus poses a high risk of adverse perinatal outcome and preeclampsia. More information is required about this rare condition in order to determine potential interventions in cases of euploid fetuses and to provide adequate counseling in clinical practice, hence the importance of case reporting to build sufficient evidence regarding the natural course of this condition.

AUTHORS' CONTRIBUTIONS

The two authors had an equal participation in the preparation of this paper, from its inception, design, data collection, review of the intellectual content, through to the approval of the final version submitted to the editorial process.

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Table 1.
Case report studies included in the review of the literature on partial molar pregnancy and live fetus

Author	Country	Maternal age (years)	GA (weeks)	Neonatal weight (g)	Neonatal sex	Fetal complications	Maternal complications
Jones *et al.*, 1975 (13)	USA	17	40	2900	F	None	None
Hartfiel *et al.*, 1983 (20)	Australia	36	39	2700	M	None	Preeclampsia
Crooij *et al.*, 1985 (21)	The Netherlands	23	27	980	F	Early neonatal death	None
Deaton *et al.*, 1989 (22)	USA	33	15	ND	F	Miscarriage	None
Thomas *et al.*, 1987 (23)	England	23	29	1150	F	None	None
Cheung *et al.*, 1992 (24)	China	24	27	970	F	Neonatal death	Persistent trophoblastic disease
Hsieh *et al.*, 1999 (25)	USA	30	32	1551	F	Anemia	None
Lembert *et al.*, 2000 (26)	Turkey	28	23	560	M	Fetal demise malformation	Preeclampsia
Parveen *et al.*, 2004 (27)	Pakistan	23	39	2700	F	None	None
Guven *et al.*, 2007 (28)	Turkey	21	28	800	F	Demise	Hyperthyroid crisis
Tamrakar *et al.*, 2011 (29)	Nepal	26	32	1100	M	None	None
Shobhau *et al.*, 2011 (30)	India	21	37	1500	M	Demise IUGR	None
Sak *et al.*, 2012 (31)	Poland	28	37	2800	F	None	None.
Rathod *et al.*, 2014 (32)	India	23	34	1400	F	IUGR	None
Ara *et al.*, 2016 (33)	Bangladesh	26	40	1500	M	IUGR	None

Continued Table 1

Author	Country	Maternal age (years)	GA (weeks)	Neonatal weight (g)	Neonatal sex	Fetal complications	Maternal complications
Florez 2016 (34)	Chile	21	25	610	M	Fetal demise Multiple malformations	No
García *et al.*, 2017 (35)	Mexico	27	33	1417	F	IUGR	Bleeding
Atuck *et al.*, 2018 (36)	Malasia	21	28	990	F	IUGR. Early neonatal death	Preeclampsia
Zeng *et al.*, 2019 (37)	China	32	29	1050	F	None	None
De Francicis 2019 *et al.*, (38)	Italia	37	31	880	M	IUGR	None
Hassan *et al.*, 2018 (39)	USA	25	20	200	M	Miscarriage	None
Saurbrei *et al.*, 1980 (40)	Canadá	27	21	225	F	Miscarriage	Preeclampsia
		22	20	450	M	Miscarriage	Preeclampsia
Teng *et al.*, 1984 (41)	USA	30	15	400	F	Miscarriage	Persistent trophoblastic disease
		22	15	300	M	Miscarriage	Persistent trophoblastic disease
		24	20	300	Fem	Miscarriage	Preeclampsia
Juárez et al., 2009 (42)	México	24	20	300	F	Miscarriage	Preeclampsia
		21	31	1050	F	Perinatal death	None
		22	19	480	M	Miscarriage	None
Dhingra *et al.*, 2009 (43)	India	28	38	2300	F	None	None
		22	34	1400	F	None	None

GA: Gestational age
IUGR: Intrauterine growth restriction

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