


CASE REPORT

A case report of atypical preeclampsia with severity criteria for hydatidiform complete mole

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Key Clinical Message

Preeclampsia is defined as elevation of blood pressure and any of the following severity criteria: proteinuria, thrombocytopenia, elevation of creatinine in the absence of another renal pathology, elevation of transaminases, pulmonary edema, or neurological symptoms. However, after 20 weeks of gestation in a previously normotensive patient, cases of preeclampsia associated with molar pregnancy have been described in patients at less than 20 weeks of gestation. A 26-year-old woman, at 14.1 weeks of gestation was admitted to the lower extremities with facial edema, holocranial headache, nausea, epigastralgia, phosphenes, and photophobia, with a double-length uterine fundus for gestational age and ultrasonography. Obstetricians who showed images of snowflakes without fetuses and annexes had multiple thecal-lutein cysts. Atypical preeclampsia was identified using the severity data for complete hydatidiform moles. Given the possibility of serious complications that may endanger the life of the maternal-fetal binomial, atypical forms of preeclampsia should be suspected.

KEYWORDS

arterial hypertension, Mola, preeclampsia, pregnancy

1 | BACKGROUND

Traditionally preeclampsia has been defined as blood pressure over 140/90 mmHg after 20 weeks of gestation^{1,2} in a previously normotensive patient and any of the following characteristics: proteinuria (more than 300 mg in a 24 h urine collection or a protein/creatinine index ≥ 0.3 mg/

mg in a random sample or $\geq 1+$ in a reactive urine strip), thrombocytopenia $< 100,000/\mu\text{L}$, creatinine elevation > 1.1 mg/dL or double over the basal measure in absence of any other renal pathology.

There are other severity criteria, even in the absence of proteinuria: transaminase elevation at least doubles the superior normal limit, pulmonary edema, and

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neurological symptoms, such as headache, phosphenes, or blurred vision. However, it has been described as atypical preeclampsia at <20 weeks of gestation, associated with molar pregnancy.³

On the other hand, trophoblastic gestational disease encompasses a wide spectrum of pathologies originating in the placenta, such as trophoblastic tumors of the placental vessels, epithelioid trophoblastic tumor, choriocarcinoma, invasive mole (chorioadenoma destruens), and hydatidiform mole, partial or complete, with the latter being the most frequent form of presentation, accounting for almost 80% of gestational trophoblastic disease.⁴ These pathologies, although caused by separate conglomerates of different epidemiology, for example, in a systematic review, 4.6% of global pregnancies⁵ had preeclampsia as a complication.

Various theories have been proposed regarding the pathophysiology of preeclampsia. The one that is more accepted refers to an incorrect implantation of the placenta, which causes the spiral arteries to lose their property of high blood flow, producing placental ischemia, which also produces inflammatory factors that ultimately produce a systemic response because of peripheral vascular resistance, pro-thrombotic status, and endothelial dysfunction.⁶

There are uncommon cases of preeclampsia before 20 weeks of pregnancy, but it has been reported in molar pregnancies⁷ and associated with antiphospholipid syndrome.⁸ Early recognition is important, even in the first trimester, when making a differential diagnosis with lookalike pathologies, such as lupus nephritis, thrombocytopenic purpura, and hemolytic uremic syndrome.^{9,10}

A 26-year-old woman, at 14.1 weeks of gestation, had a family history of hypertension in her mother and two sisters with repetitive abortions, without any other relevant personal risk factors.

She was admitted at 14.1 weeks of gestation by the last date of menstruation, with 5-day evolution symptoms of inferior limbs and facial edema, headache, intense nausea, vomiting on various occasions, epigastralgia, phosphenes, and photophobia, without any transvaginal secretions.

Her blood pressure at admission was 175/108 mmHg, heart rate was 131 bpm, respiratory rate was 24 breaths per minute, temperature was 36.3°C, oxygen saturation was 94%, 1.55 cm of height, and 54.5 kg of weight.

On physical examination, the patient was conscious, with hyperreflexia and anasarca, cardiac sounds augmented in frequency, low-intensity respiratory sounds in the basal areas, and increased abdominal perimeter due to gestational uterus with a fundus at 22 cm (double of the expected according to the gestational age table by Fescina et al.), and no fetal heart rate. Vaginal exploration revealed mild edema of the genitalia, euthermic cavity, and posterior cervix, large, semi-soft, closed, without any secretion or bleeding, limbs with the correct anatomy, and edema reaching the knee.

Pelvic ultrasound was performed and a uterus of 24×18 cm with a “snowflake” image was found in the interior, as well as multiple hypoechoic images, without a fetus, and annexes were found with increased volume, with images suggestive of theca-lutein cysts, and the right ovary with a cyst >3 cm.

Pregnancy was terminated using manual intrauterine aspiration. Substantial trophoblastic tissue was extracted from grape bunches (Figure 1). Subsequently, the patient experienced pain and abdominal distention, and a second abdominal ultrasound was performed. Approximately 2 L of free liquid was found in the paracolic sulc and right subphrenic space, with a right annexal image (probably a plas-tron) and endometrial echography in the medium line of 5 mm (Figure 2). This led us to think that in a broken ectopic pregnancy, exploratory laparotomy was performed in which only abundant serous liquid in the right annex was found, which corresponds to a larger theca lutein cyst reported in USG, but without any alteration in any of the ovaries.

A pulmonary USG was also performed, which revealed bilateral pleural infusions (Figure 3). Follow-up was continued in the intensive care unit, with hemodynamic monitoring and assessment. Routine rheumatology was performed, which included complement levels, anti-DNA antibodies, antinuclear antibodies, lupus anticoagulant, and thyroid hormones, which were normal, in order to determine a specific etiology and in this case, due to the suspicion of atypical preeclampsia.

Blood pressure control was achieved with nifedipine, hydralazine, and alfa-metildopa, which decreased gradually until withdrawal of the last two. Finally, the patient was discharged to receive follow-up in outpatient care of gynecology every 2 weeks to monitor the levels of B-hCG



FIGURE 1 Abundant trophoblastic tissues in grape racemes.



FIGURE 2 Pelvic ultrasound post-uterine aspiration where the uterus was observed floating in “free liquid,” which allowed the observation of its ligaments.



FIGURE 3 Pulmonary ultrasound allow to observe the pleural effusion.

to document hormonal clearance and dismiss any malignant cause that remained elevated (Figure 4).

2 | DISCUSSION

Complications in the third trimester of pregnancy, although well described, can be fatal, and any abnormality requires an integral assessment, especially with the first appearance of hypertension, associated or not with proteinuria.¹ The ultrasonographic exam of the uterus in the 1st trimester and in particular the color Doppler vaginal echography has made it possible to detect anomalies in early pregnancy, such as the hydatidiform mole, that even when the diagnosis is made mostly by this technique, the histologic examination of the evacuated material (Figure 5) is vital to confirm the

diagnosis.¹¹ This disease has to be considered pre-malignant because it has been described that 15%–20% of complete moles and 1% of incomplete moles can generate malignant degradation of the invasive mole type, choriocarcinoma, and in rare cases, trophoblastic tumors of the placental vessels. After the evacuation of the mole, the patients should be closely monitored with quantification of B-hCG at least every 2 weeks until non-detectable measures are obtained. Subsequently, normal values should persist and be evaluated monthly for a minimum of 6 months.¹² In 10%–20% of patients in whom B-hCG levels remain high, various courses of chemotherapy may be required, depending on the FIGO and WHO stratification for gestational trophoblastic neoplasia.¹³ In general, patients are no longer required to receive prophylactic chemotherapy in the diagnosis of mole; this produces unnecessary exposure in 80% of the cases and should only be offered to patients who would not receive the appropriate follow-up.¹² In addition to the risk of evolution of neoplasia, complications of molar pregnancy are another topic that should be considered. First, one of the most relevant is hyperthyroidism (because of the similarities between the α subunits of HCG and TSH), in which a beta-adrenergic blockade could be required to prevent and reverse the metabolic and cardiovascular complications of the thyroid storm.¹⁴ Second, the thecal-lutein ovarian cysts, secondary to the ovarian hyperstimulation, could be twisted or spontaneously broken (this might have been the cause of the abdominal syndrome that the patient presented with posterior to the evacuation of the mole; however, this was not evidenced in the moment of rupture with laparotomy). Finally, cardiopulmonary symptoms are associated with trophoblastic emboly.¹³ All the aforementioned studies showed a general trend of resolution according to the decrease in B-hCG levels. Patients with hyperemesis related to pregnancy in 8%–28% generally in earlier stages of gestation and with more severity because of the high levels of these hormones related to different isoforms or mutations in the receptors of this hormone.⁷ The total level of hCG is crucial for the follow-up of patients with gestational trophoblastic disorders. The chemical exams should measure all the portions of the molecule in particular the free-beta subunit, the hCG hyperglycosylated, hCG “nicked” and the hCG without the terminal carboxyl segment, because these segments in particular are higher in neoplasia than the total hCG.¹⁵ In general, the patients with history of molar pregnancy either partial or complete can have other reproductive successful attempts, they only possess a higher risk of recurrence between 1% and 1.9% and after 2 or more molar pregnancies it increases to 15%–17.5%.¹⁶ Lastly, it can result fatal not to maintain a suspicion of preeclampsia in early pregnancy before 20 weeks in a clinical context that results relevant, although the prevalence is low like it could have been in the case of these patients that coursed with severity criteria preeclampsia.

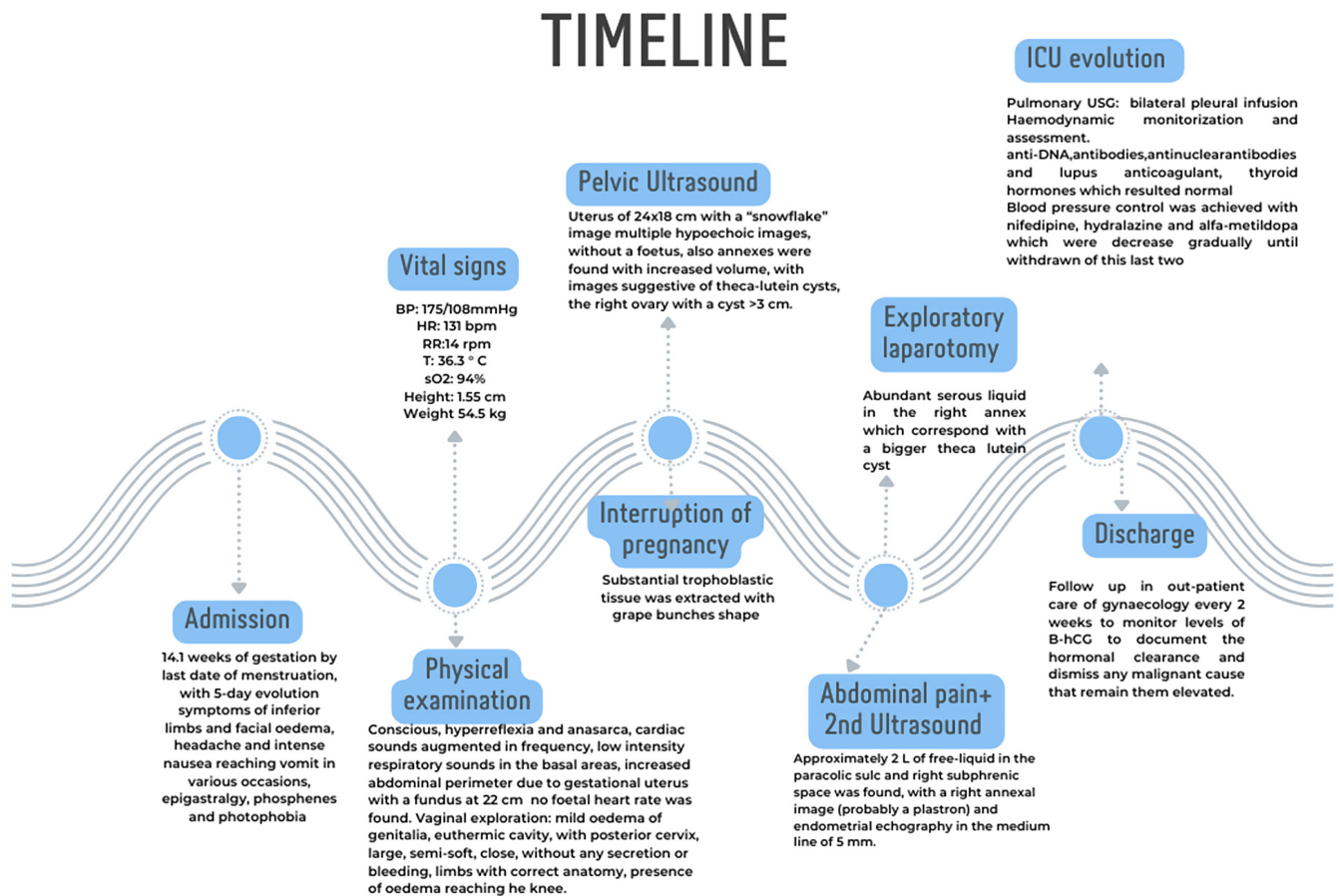


FIGURE 4 Timeline.

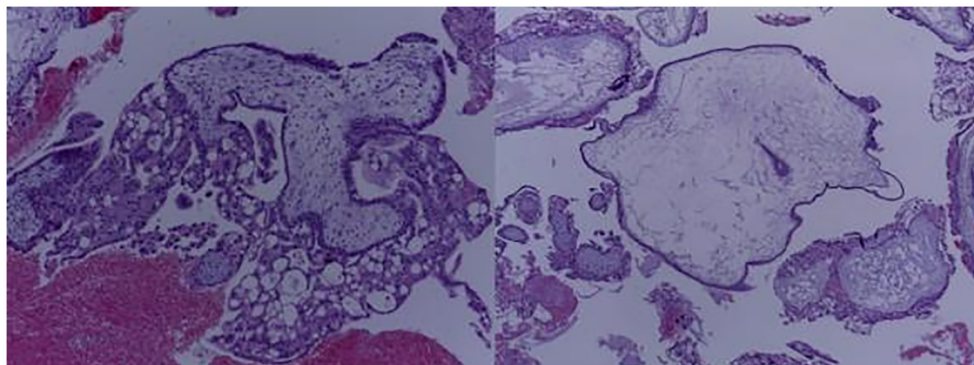


FIGURE 5 Histologic view showing degradation of the trophoblastic tissue, dilatated cisterns, trophoblastic inclusions, corial villi, and decidual reaction, with the absence of embryonic tissue, typical of the complete moles.

3 | CONCLUSION

In summary, it is imperative to prioritize the consideration of severe complications that pose a threat to the lives of pregnant women, regardless of the stage of pregnancy. Staying abreast of the latest guidelines and updated

definitions pertaining to the diseases under treatment is vital. However, it is equally crucial to acknowledge the existence of atypical cases that may not perfectly align with established definitions, necessitating the exploration of differential diagnoses and vigilance toward unusual disease presentations. This patient's case serves as a

reminder of the importance of such vigilance and adaptability in clinical practice.

AUTHOR CONTRIBUTIONS

Orlando Rubén Pérez-Nieto: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing – original draft. **Christian Alberto Herrera-Venegas:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing – original draft. **Karen Pamela Pozos-Cortés:** Conceptualization; data curation; investigation; project administration; supervision; validation; writing – original draft. **Raymundo Flores-Ramírez:** Conceptualization; data curation; investigation; methodology; project administration; supervision; validation; writing – original draft. **Jesus Salvador Ugalde-Real:** Formal analysis; investigation; methodology; project administration; writing – original draft. **Jardiel Argüello-Bolaños:** Conceptualization; formal analysis; investigation; methodology; project administration; visualization; writing – original draft. **Marian Elizabeth Phinder Puente:** Formal analysis; project administration; validation; visualization; writing – review and editing. **Éder Iván Zamarrón-López:** Investigation; methodology; project administration; supervision; validation; writing – original draft. **Ernesto Deloya-Tomas:** Formal analysis; methodology; project administration; supervision; validation; visualization; writing – original draft.

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Not applicable.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

CONSENT

The authors certify that they obtained all appropriate patient consent forms. The patient provided written consent for the publication of his images and other clinical information in the journal. 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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