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

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ABSTRACT

Background: Preeclampsia is defined as the 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 with less than 20 weeks of gestation.

Case description: 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 ultrasound. Obstetricians who showed images of snowflakes, without fetuses and annexes, with multiple thecal-lutein cysts. Atypical preeclampsia was identified using the severity data for complete hydatidiform mole.

Conclusion. Given the possibility of serious complications that may endanger the life of the maternal–fetal binomial, atypical forms of preeclampsia should be suspected.

Key words: Mola, pregnancy, preeclampsia, arterial hypertension.

BACKGROUND

Traditionally preeclampsia has been defined as blood pressure over 140/90 mmHg after 20 weeks of gestation¹,² 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 ≥ 1+ in a reactive urine strip), thrombocytopenia < 100,000/YL, 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 neurologic 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.2

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, being the last ones the most frequent form of presentation, 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 a complication of preeclampsia.

There are various theories regarding the physiopathology 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 or associated with antiphospholipid syndrome8. Early recognition is very important, even in the first trimester, when making 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 familiar 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 found to be conscious, with hyperreflexia and anasarca, cardiac sounds augmented in frequency, low-intensity respiratory sounds in the basal areas, 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, posterior cervix, large, semi-soft, closed, without any secretion or bleeding, limbs with 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, also annexes were found with increased volume, with images suggestive of theca-lutein cysts, the right ovary with a cyst >3 cm.

Pregnancy was terminated by manual intrauterine aspiration. Substantial trophoblastic tissue was extracted from grape bunches (Fig 1). Subsequently, the patient started experiencing pain and abdominal distention, and a second abdominal ultrasound was performed. Approximately 2 L of free-liquid in the paracolic sulc and right subphrenic space was found, with a right annexal image (probably a plastron) and endometrial echography in the medium line of 5 mm (fig 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 with a larger theca lutein cyst reported in USG, but without any alteration in any of the ovaries.

Pulmonary USG was also performed, which revealed bilateral pleural infusion (Fig 3). Follow-up 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; this was performed in order to find a specific etiology and in this case due to the suspicion of atypical preeclampsia\textsuperscript{16, 17}.

Blood pressure control was achieved with nifedipine, hydralazine, and alfa-metildopa, which decreased gradually until the withdrawal of the last two. Finally, the patient was discharged to receive follow-up in outpatient care of gynecology every 2 weeks to monitor levels of B-hCG to document hormonal clearance and dismiss any malignant cause that remained elevated (fig 5).

DISCUSSION

The 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\textsuperscript{1}. The ultrasonographic exam of the uterus in the 1st trimester and in particular the colour Doppler vaginal echography has made it possible to detect anomalies in the early pregnancy like the hydatidiform mole, that even when the diagnosis is made mostly by this technique, the histologic exam of the evacuated material (fig. 4) is vital to confirm the diagnosis\textsuperscript{11}. This disease has to be considered as pre-malignant, because it has been described that 15-20% of complete mole 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 the 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\textsuperscript{12}. In 10-20% of patients in whom the B-hCG levels remain high, various courses of chemotherapy may be required, depending on the FIGO and WHO stratification for gestational trophoblastic neoplasia\textsuperscript{13}. In general, patients are no longer required to receive prophylactic chemotherapy in the diagnosis of mole; this produces an unnecessary exposure in 80% of the cases and should only be offered in patients who would not receive the appropriate follow-up\textsuperscript{12}. The complications of molar pregnancy are another topic that should be considered in addition to the risk of neoplasia evolution. First, one of the most relevant is hyperthyroidism (because of the similarities between the $\alpha$ subunits of HCG and TSH), in which a beta-adrenergic blockade could be required to prevent and revert metabolic and cardiovascular complications of a thyroid storm\textsuperscript{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 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\textsuperscript{13}. All the afore mentioned 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\textsuperscript{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. Other clinical entity, although not very frequent that clinicians should also considered is the ghost hCG where the patients contain heterophilic antibodies that react with antibodies of certain analysis kits which generates a false positive result of hCG\textsuperscript{15}. In general, the patients with history of molar pregnancy either partial or complete can have other reproductive successful attempts, they only posses a higher risk of recurrence between 1-1.9% and after 2 or more molar pregnancies it increases to 15-17.5%\textsuperscript{16}. Lastly, it can result fatal not to maintain a suspicious of preeclampsia in an 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 this patients that coursed with severity criteria preeclampsia.

CONCLUSION

When treating a pregnant woman, we need to always consider, independently of the gestational stage, the possibility of severe complications that can threatened the life of the binomial. It is vital to know the updated definitions according to the latest guidelines of any disease that we are treating, although we also need to take in count atypical cases that could not match entirely with the definitions and that make us think in
differential diagnosis or look at atypical forms of presentation of a disease, like it was the case of this patient.

DECLARATIONS

Ethics approval and consent to participate

Consent for publication

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

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests

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REFERENCES


Figure 1. Abundant trophoblastic tissue in the form of grape racemes.

Figure 2. Pelvic ultrasound post-uterine aspiration where the uterus was observed practically floating in “free liquid,” which allowed the observation of its ligaments.
Figure 3. Pulmonary ultrasound that allow to observe the pleural infusion.

Figure 4. Histologic view where degradation of the trophoblastic tissue is observed, dilatated cisterns, trophoblastic inclusions, corial villi and decidual reaction, with absence of embryonic tissue, typical of the
Figure 5 Timeline

Complete moles.