Partial hydatidiform mole with spontaneous ovarian hyperstimulation syndrome.

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Abstract

The authors present an atypical case of partial hydatidiform mole (PHM). Woman, 36 years old, who went to the emergency room for abdominal pain associated with eleven-week pregnancy. Echography revealed the presence of hyper stimulated ovaries leading to diagnosis of spontaneous Ovarian Hyperstimulation Syndrome (OHSS). Blood sample revealed high levels of hCG (1422000 U/L), which associated with the ultrasound finding of placenta with vesicular areas, led to the suspicion of PHM. With this suspicion and the high value of nuchal translucency, amniocentesis was performed, confirming the diagnosis of PHM – 69, XXX. The pregnant, with history of hypothyroidism, presented analytic hyperthyroidism which is rare in this clinical situation. The medical termination of pregnancy resolved this pathologic situation and also hyperthyroidism condition. Hydatidiform mole, with increased levels of hCG, is one of the three possible mechanisms for spontaneous OHSS.

Keywords: Hydatidiform mole, Partial hydatidiform mole, Ovarian hyperstimulation, Chorionic gonadotropin, Thyrotrophic hormone (TSH).

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Introduction

Hydatidiform Mole (HM) belongs to the group of medical conditions classified as Gestational Trophoblast Disease (GTD). This clinical entity is a proliferative disorder of placenta and it can locally invade the uterus or originate distant metastasis [1].

HM can be classified in two distinct entities – Complete HM (CHM) and Partial HM (PHM). HM always occurs after an aberrant fertilization. PHM is composed by a triploidy (69, XXY; 69, XYY; or 69, XXX) where the extra chromosomes have paternal origin. Molar gestations are originated at villus trophoblast and they are characterized by villous hydrops and trophoblastic hyperplasia due to hyper expression of paternal genes. PHM has lower levels of human chorionic gonadotropin hormone (hCG) than CHM and, for that reason it is less common associated with sequels of stimulation by hCG [2]. The normal or pathologic trophoblast produces hCG [3]. hCG is a glycoprotein composed by 2 subunits, α and β, connected by non-covalent form [4]. Subunit β of GCH and TSH have great homology and, for that reason, hCG can also have thyrotrophic activity. However, this activity is much weaker than TSH activity [5].

Case Report

A 36-year-old woman, Caucasian, G2P1 (eutocic delivery, newborn with 4040 g), went to Emergency room with abdominal pain that started 2 weeks ago. She also complained of abdominal distension and light polypnea. She denied oliguria or dyspnea. At the observation, she had a bulky abdomen, with painful palpation and guarding. Pelvic ultrasound showed an evolutive pregnancy, spontaneous, with 11 weeks and 4 days. Fetus' vital signs and amniotic fluid were normal. Ovaries were visualized and described as bulky (Figures 1 and 2). Patient was admitted with diagnosis of Spontaneous Ovarian Hyperstimulation Syndrome (OHSS). Patient had history of Gestational Hypertension on her first pregnancy and subclinical hypothyroidism controlled with levothyroxine sodium 25 mg id. She was allergic to penicillin and her blood group was 0 Rh+.

On endocrinologic observation, patient was clinically euthyroid, without compressive complains. She denied exophthalmia, diarrhea, sweating, weight loss (weight: 72 kg), tremor or pretibial edema, heart rate of 84 bpm and blood pressure 120/60 mmHg. She mentioned to have taken iodized salt. Physical

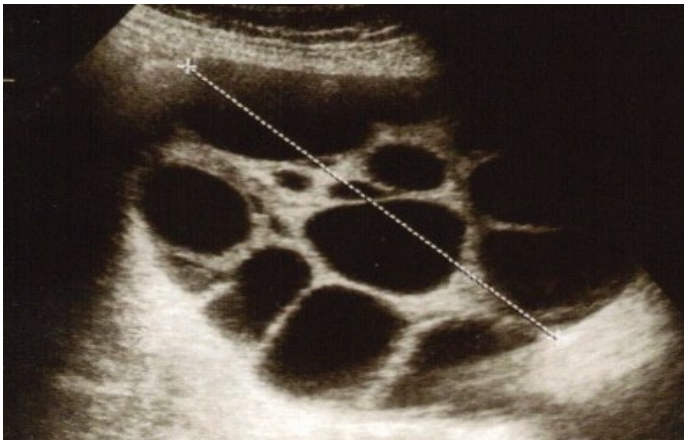

Figure 1. *Right ovary.*

examination showed a palpable thyroid with elastic consistence, painless, mobile and without adenopathies.

Analytic study showed the following values

Hemoglobin 13.3 g/dL; hematocrit 39.6%; Platelets 274000/µL; TSH 0.005 µUI/mL (0.35 – 4.94); free T4 (free Thyroxine) 2.44 ng/dL (0.7-1.48); Anti-Thyroid Antibodies (Anti-TPO) 78.80 UI/mL (0.0 – 60), Thyroglobulin (TG) 71.5 ng/mL (3.5 – 77.0); Anti-Receptors TSH Antibodies (TRABS) 0.82 ng/dL (0.00 – 1.75). Urinary Cortisol (24 Hours Urine) 117.60 µg/24h (4.30-176); hCG 983540 U/L; Estradiol >3000 pg/mL (>11010 pmol/L). Patient stopped Eutirox 25 µg and started propylthiouracil (PTU) 50 mg (Propycil® 1 id). Clinically she had an episode of headache and vomit that resolved with paracetamol.

At third day of admission, we performed another ultrasound that revealed a big placenta with vesicular areas. Fetus was observed with cystic hygroma of 7.9 mm. There was also an image suggestive of holoprosencephaly. Due to these observations, the diagnosis of Partial Hydatidiform Mole was suggested. Thyroid echography was normal.

On 7th day of admission, we performed an amniocentesis to confirm the diagnosis of PHM. Analytic study showed hCG 1492200 U/L and ultrasound showed a viable fetus with cystic hygroma of 6.8 mm (Figures 3 and 4) and bulky placental with "swiss cheese" aspect (Figure 5). Ovaries right and left with 119 mm and 124 mm, respectively, showing theca-lutein cysts with 5 cm of major diameter. No free liquid was observed intra-abdominally or on pelvic floor. Medical Termination of Pregnancy (MTP) was performed, on the same day, followed by uterine curettage with ultrasound control. The procedure occurred without complications and the uterine cavity was apparently empty.

We also performed a thoracic radiography, to exclude pleural effusion, and exam was normal. Patient had medical release on 12th day of admission. Meanwhile, amniocentesis revealed a triploid fetus: 69, XXX.

One month after medical release, patient was clinically euthyroid with normal thyroid function (TSH 0.95 µUI/mL; Free T4 0.83 ng/dL.). Due to that reason, we decided to stop PTU. We performed weekly analytic studies and we observed normal values of hCG by the end of the fifth month (day 141; 136 post MTP).

On tenth month, patient was clinically and analytically euthyroid, and for that reason she was released from consultation. Development of hCG values is shown in Figure 6 (hundreds of thousands of U/L), (Figure 7) (thousands de U/L) and (Figure 8) (hundreds de U/L). This patient is maintained on regular surveillance at Endocrinology and Nutrition consultation.

Discussion

We presented a clinical case of Partial Hydatidiform Mole with an unusual clinical presentation. High levels of hCG are usually associated with Complete Hydatidiform Mole. Pelvic pain was associated with ovarian hyperstimulation that was coincident

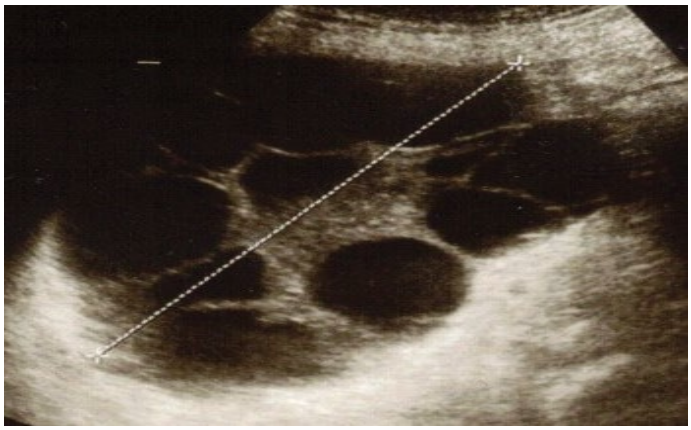

Figure 2. *Left ovary.*

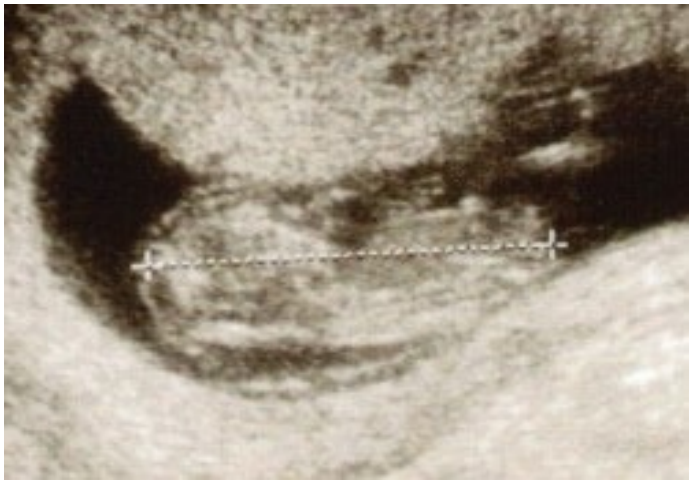

Figure 3*. Fetus with 61 mm of cranio-caudal length.*

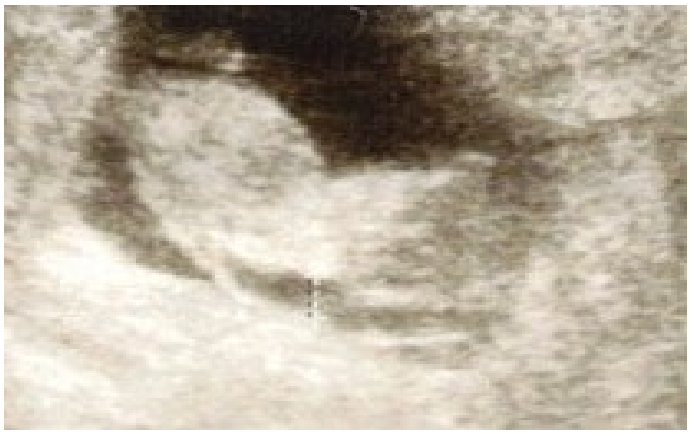

Figure 4. *Increased nucal translucency.*

with a hCG maximum of 1422000 U/L. Ovaries were bigger than 10 cm (with a maximum diameter of 14 cm), with theca-lutein cysts of 5cm.

There are three pathophysiologic mechanisms described that can explain the origin of OHSS

1) In our case, there was a hyperactivation of FSH receptor present in the granular cells of the ovarian by hCG, that lead to ovarian hyperstimulation. CHM and multiple pregnancy might, also, occur with spontaneous OHSS due to this same mechanism.

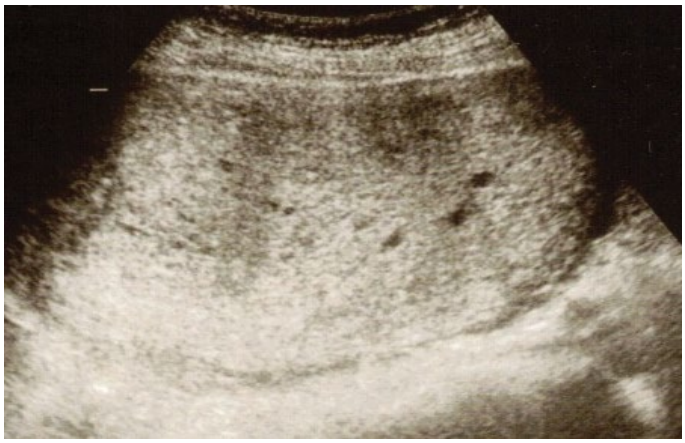

***Figure 5**. Trophoblast.*

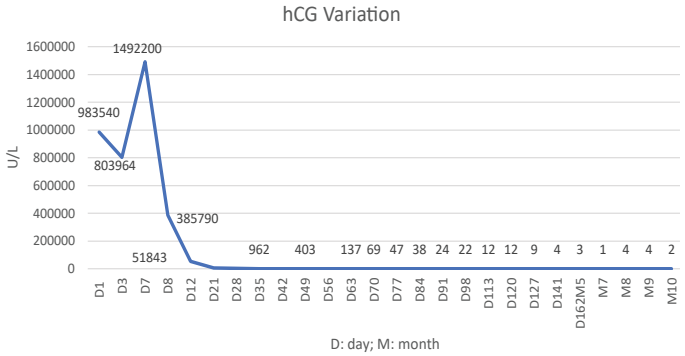

***Figure 6**. Variation of hCG values over time.*

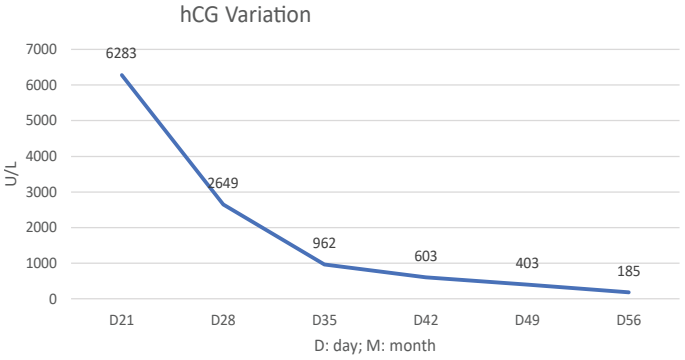

***Figure 7**. hCG values between day 21st and day 56th.*

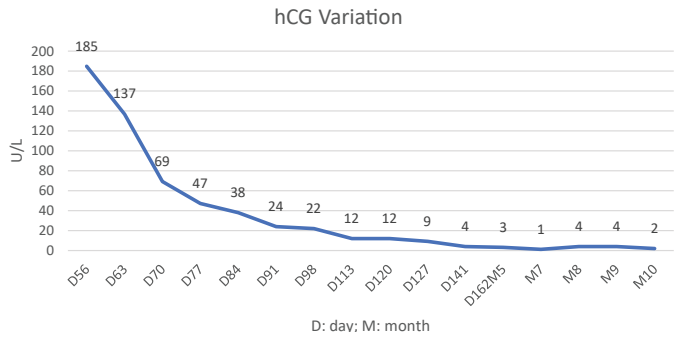

***Figure 8**. hCG values between day 56th and 10th month.*

2) Another mechanism might be the hyperactivation of FSH receptor by TSH hormone, that can appear in cases of elevated TSH, such as in cases of hypothyroidism. This affinity between hCG, TSH and FSH is explained by the structural homology between the three hormones mentioned above [4-6].

3) The third mechanism described is associated with a mutation of FSH receptor that leads to a decrease in its specificity. This can originate an increase of FSH receptor's sensibility to hCG and TSH [7].

The first ultrasound was done at Emergency Room showing an evolutive pregnancy with a viable fetus. At third day, ultrasound revealed nuchal translucency of 7.9 mm and vesicular areas in the placenta.

Serum hCG levels above 200.000 U/L demonstrated to suppress TSH release (less or equal to 0.2 μUI/mL) in 67% of the cases and levels above 400.000 U/L can promote suppression of TSH release in 100% of the cases [8]. In less than 10%, patients can present clinical hyperthyroidism [3]. This patient was clinically asymptomatic, but she had analytical changes on thyroid values.

The supplementation with iodine can precipitate thyrotoxicosis because trophoblastic production of hCG is not blocked by thyroid hormones. In this clinical case, besides ingestion of iodate salt, there was no development of thyrotoxicosis [3].

In a woman with thyroid disease, potassium iodide might be contraindicated, so prescription should be analyzed individually [9]. This patient had hypothyroidism at the beginning of pregnancy, and she took iodized salt during this period. But changed to analytic hyperthyroidism and for that reason we prescribed PTU in a very low dose. This point is still controversial because it was not obligatory to introduce PTU since patient didn't have signs of thyrotoxicosis. PTU was introduced because the high levels of hCG are atypical in a PHM. Hyperthyroidism associated with HM resolved with the treatment of trophoblastic disease. Patients with symptoms of hyperthyroidism might need a β-blocker until normalization of hCG levels [10]. In our case, patient took PTU for 1 month without any complication or lateral effect, and thyroid function normalized after that period.

Increased nuchal translucency, placenta pathological aspect and increased levels of hCG suggest the diagnosis of PHM and for that reason we performed an amniocentesis at 12 weeks of gestation. This exam confirmed the diagnosis of PHM with a 69, XXX karyotype. Surveillance was performed until hCG had negative values. We also performed a thoracic X-ray for exclusion of Gestational Trophoblastic Neoplasia (GTN) with pulmonary metastasis [11-14].

Conclusion

Partial hydatidiform mole diagnosis requires a high grade of suspicion. Quick intervention allows a better clinical resolution and it might avoid the development of GTN. Spontaneous OHSS is a possible complication of PHM. With this in mind, it is fundamental to understand the pathophysiology of spontaneous OHSS to manage this clinical entity.

To our knowledge, after search in PubMed, our case is the 5th of PHM with spontaneous OHSS reported . We had the highest hCG level (1422000 U/L), without severe symptoms. In our opinion that was due to a quick diagnosis and treatment. Curiously, three out of the four case reports had karyotype, and were all 69,

XXX, like our case. To conclude, it is important to remember that in cases of spontaneous OHSS, Hydatidiform Mole should be excluded. Communication between Endocrinology and Obstetrics services is fundamental to achieve control of thyroid function.

Disclosure of Interest

The authors report no conflict of interest.

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