Mola hidatiforme completa invasiva: una causa poco común de hipertiroidismo

Invasive complete hydatidiform mole: a rare cause of hyperthyroidism

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ABSTRACT

Hydatidiform mole (HM) is a form of gestational trophoblastic disease, which can be classified as complete or partial and is characterized by high levels of human chorionic gonadotropin (HCG). Hyperthyroidism results from the effect of β-hCG on TSH receptors.

Clinical case: A 53-year-old multiparous woman, with no relevant history, was admitted to the Gynaecology Emergency Department with a clinic presentation of hypogastralgia and hyperemesis gravidarum with 1 month of evolution and symptoms of hyperthyroidism. The investigation showed a distended uterus with echogenic material with a thickness of 81 mm at filled by uterine cavity. β-hCG> 10000mIU / mL. She was admitted for suction curettage, and the resulting sample was compatible with HM.

The additional analytical study showed primary hyperthyroidism and negative thyroid autoimmunity. Thyroid ultrasound was unaltered. The patient started therapy with metibasol and propanolol, showing clinical and analytical improvement.

She also underwent, total abdominal hysterectomy and bilateral annexectomy with general anaesthesia, without complications. Chest x-ray without changes. Through histological analysis it was determined that the diagnosis was that of an invasive complete HM.

Sixteen weeks after surgery, she presented β-hCG <2mIU / mL and normal thyroid function. The patient is still being monitored in the Gynaecology outpatient consultation.

Thyroid function should be included in the laboratory analysis of HM. Removing the source of β-hCG allows the resolution of hyperthyroidism. However, due to the risk of thyroid storm, it is crucial to control the thyroid function before performing the surgical procedure. Given the possibility of persistence of trophoblastic tissue, it is essential to maintain regular follow-up with β-hCG assays.

INTRODUCTION

Gestational trophoblastic disease (GTD) is a rare entity that encompasses several forms characterized by abnormal proliferation of trophoblastic tissue[1,2], presenting distinct invasion mechanisms.[2]

The hydatidiform mole (HM) is the most frequent form of GTD, and can be classified as complete or partial.[1,2] These entities differ in terms of morphological (macroscopic) aspects, histopathology and karyotype.[1,2]

Given the risk of complete HM evolving into malignant forms (invasive mole or choriocarcinoma) in about 20% of cases [2,3], this is considered a pre-malignant condition, so removal of the products of conception is the standard of care as soon as the diagnosis is established.[2,4] Patients may experience pelvic pain, hyperemesis gravidarum and vaginal bleeding.[2,3]

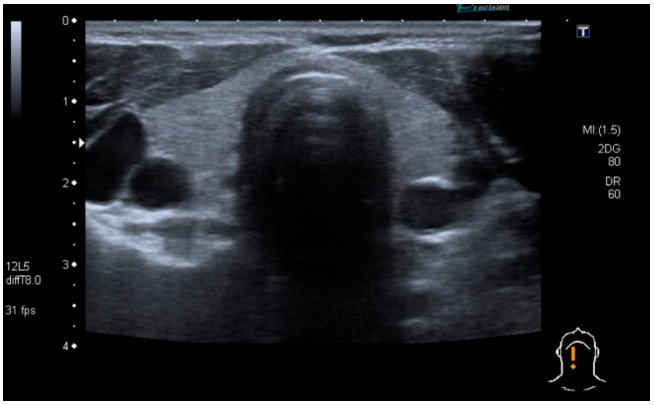
The tumour cells of the hydatidiform mole produce very high concentrations of human chorionic gonadotropin (hCG) which, due to the structural similarity with TSH, lead to thyroid hyperfunction. Although hCG is a weak thyrotropic agonist, in very high concentrations, as well as in the presence of molecular variants in molar pregnancy, it contributes to the increase of its thyrotropic activity.[5]

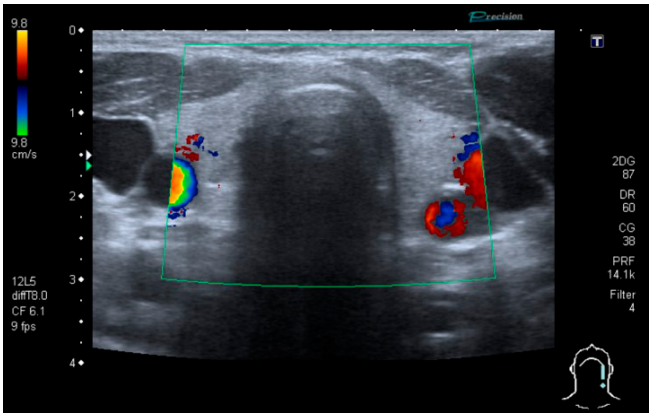
CLINICAL CASE

A 53-year-old caucasian, multiparous (2G2P) woman with a history of breast cysts and depressive disorder, was admitted to the Gynaecology Emergency Department due to complaints of hypogastralgia and hyperemesis gravidarum with 1 month of evolution, aggravated in the previous week. She still had regular menstrual cycles and did not use a contraceptive method. She was on 150 mg / day of venlafaxine.

She also presented fine distal tremor, sinus tachycardia and blood pressure of 130/70 mmHg. She denied recent weight loss. The thyroid was palpable and painless. She did not present exophthalmos.

Figure 1 and 2. Ultrasound and doppler flow of the thyroid.





The gynaecological examination showed hardened hypogastric swelling and blood loss through the external cervical os.

A pelvic ultrasound showed a distended uterus with echogenic material with a thickness of 81 mm that filled the uterine cavity. The

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Table 2. Evolution of the thyroid hormones and B-hCG since the diagnosis of hydatidiform mole and after its removal.

	On diagnosis	Day 6	Day 11	Day 3 after removal	5 weeks later	9 weeks later	11 weeks later	15 weeks later	16 weeks later
TSH (N: 0,27-4,20 µUI/mL)	0,01					2,26			2,17
Free T4 (N: 0,93-1,70 ng/dL)	2,26	1,13	0,86	0,86		0,95			
Free T3 (N: 2,57-4,43 pg/mL)	4,85	2,8	2,19	1,54		3,08			
β-HCG (N:0-2 mUi/mL)	>10000	80998	29290	5023	201,2	59,4	7,8	<2	<2

β-hCG measured was > 10000mIU/mL. A suction curettage was performed, and the resulting sample was compatible with HM.

After the procedure, the thyroid function was measured with the following values: TSH 0.01 µUI / mL, free T4 2.26 ng/dL and free T3 4.85 pg/mL, which confirmed the presence of hyperthyroidism. Hemoglobin 10g/dL. Platelets, ionogram, renal function, transaminases and normal coagulation study. Negative anti-thyroid and anti-TSH receptor antibodies.

The thyroid ultrasound revealed a homogeneous gland, of preserved dimensions, without nodules and normal Doppler flow (Figure 1 and 2).

She started therapy with metibasol 30 mg / day and propranolol 60 mg / day with progressive improvement of the symptoms of hyperthyroidism and normalization of the free T4 and T3 fractions in six days (Table 2), allowing for surgical intervention. The electrocardiogram and chest x-ray showed no changes.

She underwent total abdominal hysterectomy and bilateral adnexectomy under general anaesthesia, which was uneventful.

On the 3rd postoperative day, the β-hCG levels dropped to 5023mIU / mL (Table 2). The doses of propranolol and metibasol were gradually reduced and discontinued when discharged. Through histological analysis it was determined that the diagnosis was invasive complete HM. The ovaries showed no changes.

Sixteen weeks after surgery, she presented β-hCG <2 mUI / mL (Table 2) and normal thyroid function (Table 2). The patient is clinically well, and is also being followed up in the Gynaecology outpatient consultation.

DISCUSSION

The aforementioned patient had a typical clinical presentation of hydatidiform mole, with pelvic pain and hyperemesis gravidarum, simultaneously developing thyroid dysfunction, due to the high level of β-hCG. Tisne et al. reported the first similar case in literature in 1955[6].

Hyperthyroidism is, however, an exception nowadays[6].The widespread use of ultrasound usually allows an earlier diagnosis, which avoids the development of large moles, which are associated with high levels of β-hCG and frequently originate hyperthyroidism[3,6].

In this case, given the hyperthyroidism and the risk of thyrotoxic crisis during the surgical procedure[1,7], the patient started taking metibasol. Synthesis antithyroid drugs - Metibasol and propylthiouracil - are the first-line drugs in the treatment of hyperthyroidism[5,7].In high doses they allow the normalization of the free fractions of thyroid hormones in a short period of time. TSH will remain reduced for a period of time, so it should not be dosed again within 6 to 8 weeks. Beta-blockers also prove to be very useful as an adjunctive therapy in controlling the symptoms of hypermetabolism (palpitations, anxiety), with propranolol, usually being the beta-blocker of choice, because in addition to its beneficial effects on the cardiovascular system, it has the ability to inhibit the peripheral conversion of thyroid hormones[7]. However, the removal of the mole proves to be essential[2,6].

In the case of women who do not wish future pregnancies, like our patient, total hysterectomy and bilateral annexectomy is the most appropriate procedure[2,5]. A histopathological analysis was essential to obtain a diagnosis of the form of GTD, regardless of echographic findings[1,3].

MHC is the result of the fertilization of an egg without an active nucleus with a sperm, which means that every gene is of paternal origin (uniparental disomy). Thus, 90% have a 46, XX karyotype and the remaining 10%, 46, XY[1,3].Histologically, MHC is characterized by the absence of an embryo, pronounced trophoblast proliferation and a higher frequency of atypias[1]. The lymphovascular invasion of the myometrium depicted allows the classification of the invasive form, which is rare when it is the case of a partial mole[8].

In the case we are presenting, pulmonary metastases were excluded with a chest x-ray. After the surgery, circulating levels of β-hCG persistently decreased until they reached normal values, which seems to support the hypothesis that the mole is apparently confined to the uterine cavity. The need to undergo chemotherapy remains controversial in these situations[2,3], and has not been applied in this case. In contrast, in malignant forms, circulating levels of β-hCG tend to rise or stabilize at abnormal values[3].

The risk of recurrence of gestational trophoblastic neoplasia is established in about 3% of the cases in the first year of follow-up[8]. Given the diagnosis of invasive MHC and the possibility of persistence of trophoblastic tissue, it is essential to maintain regular follow-up with measurements of the levels of β- hCG[1].

CONCLUSION

Thyroid function should be included in the laboratory evaluation of HM. Removing the source of β-hCG allows the resolution of hyperthyroidism. However, due to the risk of thyrotoxic crisis, it is crucial to control the thyroid function before performing any surgical procedures. Given the possibility of persistence of trophoblastic tissue, it is essential to maintain regular follow-up with β-hCG assays.

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