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Case Report

Clinical hyperthyroidism in hydatidiform mole: case report

Hipertireoidismo clínico em paciente com mola hidatiforme: relato de caso

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ABSTRACT: *Introduction:* Gestational trophoblastic disease (GTD) is a group of diseases responsible for producing high hCG titers, which may lead to possible complications such as hyperthyroidism and, in more severe situations, the thyrotoxic crisis. Hyperthyroidism is present in only 5% of cases of GTD, and its early diagnosis is important. *Case Report:* A 49-year-old female patient, G6L2A3, presented to the emergency room reporting irregular vaginal bleeding for four months, hyperemesis, irritability, tremors, palpitations, xerostomia, and a history of recurrent miscarriages. Gynecological examination revealed coffee-ground type bleeding through the cervix's external orifice, and at the bimanual touch, there was a pelvic mass above the umbilical scar. TVUS showed a uterine volume of 1302 cc³ and images corresponding to GTD. TSH and FT4 of 0.015 mU/L (RV: 0.4 - 4.5 mU/L) and 2.34 ng/dL (RV: 0.7 - 1.8 ng/dL) respectively, and BhCG plasma dosage > 225,000 mIU/mL. The physical examination showed a slightly enlarged thyroid of parenchymal consistency and a slightly exalted Achilles reflex. There was no family history of thyroid disease and negative screening for anti-TPO, anti-TG, and TRAb antibodies. The patient underwent Manual Intrauterine Aspiration. Due to the maintenance of high BhCG levels, a new TVUS was requested, which suggested GTD. Due to the high risk of neoplasia, absence of metastatic focus, and constituted offspring, it was decided to perform a total abdominal hysterectomy, with bilateral salpingectomy and preservation of the ovaries bilaterally, as a form of treatment. TSH normalized at 0.5 mU/L after surgery. The histopathology showed an Invasive Mole. *Conclusion:* Diseases with elevated hCG may lead to secondary hyperthyroidism. Although this condition is present in only 5% of cases of GTD, the physician cannot ignore the importance of his or her investigation for an early diagnosis to avoid more severe complications such as the thyrotoxic crisis.

Keywords: Gestational trophoblastic disease; Hydatidiform mole; Hyperthyroidism.

RESUMO: *Introdução:* A doença trofoblástica gestacional (DTG) constitui um grupo de doenças responsável pela produção de elevados títulos de hCG, podendo levar a possíveis complicações como hipertireoidismo e, em situações mais graves, a crise tireotóxica. O hipertireoidismo está presente em apenas 5% dos casos de DTG, sendo importante seu diagnóstico precoce. *Relato de Caso:* Paciente feminina, 49 anos, G6PC2A3, apresentou-se no pronto socorro relatando sangramento vaginal irregular por 4 meses, hiperêmese, irritabilidade, tremores, palpitações, xerostomia e histórico de abortos de repetição. Ao exame ginecológico, notou-se sangramento em borra de café através do orifício externo do colo uterino, e ao toque bimanual, massa pélvica acima da cicatriz umbilical. USG/TV mostrou volume uterino de 1302 cc³ e imagens correspondentes à DTG. TSH e T4L de 0,015 mU/L (VR: 0,4 – 4,5 mU/L) e 2,34 ng/dL (VR: 0,7 – 1,8 ng/dL) respectivamente, e dosagem plasmática do BhCG > 225.000 mUI/mL. Ao exame físico, demonstrou tireoide discretamente aumentada de consistência parenquimatosa e reflexo aquileu pouco exaltado. Ausência de histórico familiar para tireoidopatias e rastreio dos anticorpos anti-TPO, anti-TG e TRAb negativo. A paciente foi submetida a Aspiração Manual Intrauterina (AMIU). Em razão da manutenção dos níveis elevados de BhCG, foi solicitado nova USG/TV cujo resultado sugeriu DTG. Devido ao alto risco de neoplasia, ausência de focos metastáticos e prole constituída, optou-se por realizar histerectomia total abdominal, com salpingectomia bilateral e preservação dos ovários bilateralmente, como forma de tratamento. O TSH normalizou em 0,5 mU/L após procedimento cirúrgico. O histopatológico evidenciou Mola Invasora. *Conclusão:* Doenças que cursam com elevação do hCG podem levar a um quadro de hipertireoidismo secundário. Apesar desta patologia estar presente em apenas 5% dos casos de DTG, o médico não pode ignorar a importância de sua investigação para um diagnóstico precoce, com vistas a evitar complicações mais severas como por exemplo, a crise tireotóxica.

Palavras-chave: Doença trofoblástica gestacional; Mola hidatiforme; Hipertireoidismo.

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INTRODUCTION

Gestational trophoblastic disease (GTD) constitutes a heterogeneous group of diseases associated with alterations in trophoblastic tissue proliferation. That group of disorders is related to the placenta. It can be classified as preinvasive lesions, such as a partial or a complete hydatidiform mole and, invasive lesions, such as choriocarcinoma, an invasive mole, a placental site trophoblastic tumor, and an epithelioid trophoblastic tumor[1-3].

During normal embryogenesis, the zygote utilizes half of the DNA from the ovum and half from the spermatozoid. A hydatidiform mole can form when there is an abnormal genetic contribution of gametes that most of the time is formed by a spermatozoid with duplicated genetic matter fertilizing the empty ovum. The product from this conception is inviable; however, it mimics the phases of a normal gestation[4].

The complete hydatidiform mole (CHM) results in abnormal gametogenesis, and it is characterized by pronounced proliferation of trophoblast and the absence of fetal elements[5,6]. The trophoblast tissue is responsible for producing high titers of human chorionic gonadotropin (hCG). Its course includes clinical manifestations as genital hemorrhage, increased uterine volume, hyperemesis, and rarely clinical hyperthyroidism[7].

Hyperthyroidism is a thyroidal disturbance, whereas there are increased levels of Triiodothyronine (T3) and Tetraiodothyronine (T4) with consequential suppression of thyroid-stimulating hormone levels (TSH). The most common causes associated with this pathology are Graves' disease and toxic multinodular Goiter. The hydatidiform mole is a rare cause of hyperthyroidism and palpitations; sweating, weight loss, nervousness, insomnia, heat intolerance, tremors, and weakness are among the most noteworthy clinical manifestations[8-14].

There are homologous molecular structures in HCG and TSH. And due to that, there are high hCG serum levels that can promote thyroidal stimulation with the suppressed release of TSH[3,15,16].

Brancken[17] points out that the hydatidiform mole's prevalence ranges from 0.5 to 2.5 in every 1000 pregnancies worldwide, and hyperthyroidism is manifested in only 5% of hydatidiform mole cases[7,18]. As it is a rare clinical condition, it has become relevant to study this etiology to alert the medical community about possible complications from this preinvasive lesion.

CASE REPORT

The patient is a 49-year-old female, Caucasian, married, self-employed, with a previous history of rheumatic fever, allergy to penicillin, epilepsy, and treatment for depression, without any other comorbidities. She is a social drinker, non-smoker, and has suffered a history of sexual violence.

She presented at the Urgent Care Center at the Santa Casa de Misericórdia de Vitória Hospital (HSCMV) - ES, Brazil, reporting irregular vaginal coffee-ground type bleeding for four months, hyperemesis, irritability, tremors, palpitations, xerostomia, inappetence, and a history of repeated abortions.

The gynecological and obstetric history presents six pregnancies, two Caesarean section births, and three abortions, including reported pre-eclampsia in two pregnancies. The last obstetric event was a Caesarean section birth at forty-two years old. The menarche occurred at fifteen years old, with dysmenorrhea and irregular menstrual cycles. Her sexarc began at twenty-one years old. She has taken oral contraceptives irregularly.

The physical examination confirmed good general health, lucid, oriented in space and time, pallid 2+/4+, hydrated, acyanotic, and afebrile. HBM=100 bpm and AP =110/70 mmHg. AT: 37ºC. Globose abdomen with hydro-aerial sounds present, painless to palpitation, no signs of peritoneal irritation, and palpable mass up to the umbilical scar.

At the gynecological exam, she displayed a normal pilification pattern for her age, with no lesions, dyschromias, or dystopias. There was a trophic vagina in the speculum examination, with elasticity and preserved roughness, without lesions when turning the speculum. Epithelized cervix, cylindrical, external orifice (EO) of the cervix slit, without visible lesions, with coffee-ground like bleeding externalizing from the EO. When performing the vaginal palpation, cervix closed, thick, and posterior, fibroelastic, painless to mobilization, palpable uterus up to the umbilical scar.

The patient was admitted to the HSCMV Gynecological Ward for diagnostic and etiological elucidation. The patient was taking sertraline, alprazolam, clonazepam, and fluoxetine at home. As an initial procedure, a BhCG serum dosage was requested, resulting in over 225,000 IU/ml and a Transvaginal Ultrasound examination. (TV/US) displayed a 1302 cm3 uterine volume, homogeneous myometrium, uterine cavity full with echogenic image, and anechoic areas of varied sizes (Figure 1); the right ovary measures 12.2 cm3, and the left ovary measures 7.5 cm3 (Chart 1).

Based on the (TV/US) result, associated with high levels of BhCG and the clinical condition, the hypothesis of GTD was considered. Based on the main suspected diagnosis, preoperative exams were requested to perform the Manual Intrauterine Aspiration (MIA). The results from the exams are displayed in Chart 1.

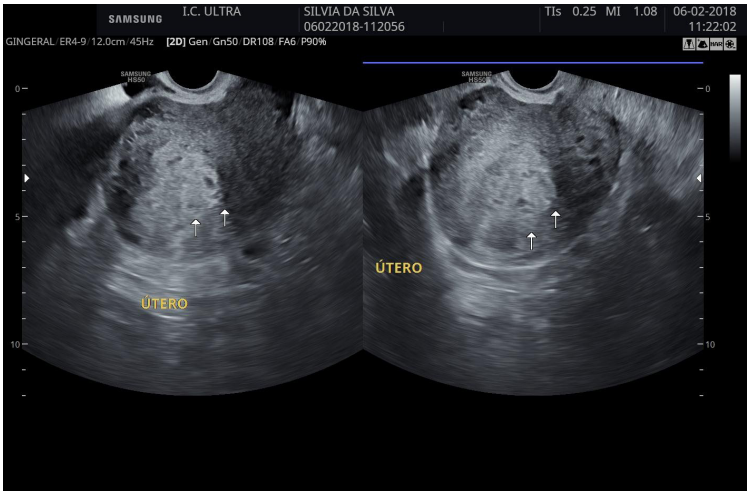


Figure 1: Uterus with echogenic contents and anechoic areas suggestive of gestational trophoblastic disease

Chart 1: Preoperative exams and their respective results

Requested exams	Results
Blood count	Red blood cells 3.9 million/mm3 Hemoglobin 9.9 g/dL Hematocrit 28.5% MCV 92.2 fl MCH pg MCHC 34.7 g/dL RDW 12.6% Leucocytes 12,370 /mm^3 Rods 3% Segmented 72% Platelets 244,000
BhCG	>225,000 IU/mL
TSH	0.015 mU/mL (RV: 0.4 – 4.5 mU/L)
Free T4	2.34 ng/dL (RV: 0.7 – 1.8 ng/dL)
Blood type	A+
HIV and VDRL Serologies	No reagents
Thorax radiography (PA and Profile)	No changes
TVS	Anteflexion of the uterus, 1302 cm^3 volume, homogeneous myometrium, uterine cavity filled with echogenic image and anechoic areas of varying sizes. Right ovary 12.2 cm^3 and left ovary 7.5 cm^3.

Source: Prepared by the authors.

MIA was performed, and there was a large quantity of vesicular material removed suggestive of GTD. The collected material was sent for anatomopathological evaluation that revealed trophoblastic proliferation with atypical and hydropic chorionic villi, with signs of autolysis and degeneration, amid fibrin, necrotic deciduous matter, and blood clots – the morphological condition suggested gestational trophoblastic disease (Hydatidiform mole).

The TSH values were 0.015 mU/mL (RV: 0.4 – 4.5 mU/L) and FT4 2.34 ng/dL (RV: 0.7 – 1.8 ng/dL). There were irritability, palpitations, tremors, and xerostomia added to the clinical symptoms suggesting the need for a joint Endocrinology evaluation. The physical examination showed a slightly enlarged thyroid of parenchymal consistency and a slightly exalted Achilles reflex.

The main antibodies against thyroid antigens were requested for clarification of the diagnosed hyperthyroidism etiology, namely: the thyroid peroxidase antibody (anti-TPO), antithyroglobulin antibody (anti-TG), and TSH anti-receptor antibody (TRAb). There was no family history of thyroid disease and negative screening for thyroid autoimmune diseases.

As the patient was hemodynamically stable, and there was mild symptomatology of hyperthyroidism, it was decided not to start the anti-thyroid medication before the surgery. After molar emptying, the patient continued persistent vaginal bleeding. Thus, a TV/US was performed again, which showed a uterine cavity filled with heterogeneous material suggesting GTD. A second

AMIU was performed, resulting in referral to the GTD Outpatient Facility at HSCMV.

During the outpatient treatment, serial dosages of BhCG were administered, decreased in the first dosages; however, immediately afterward, the values increased (> 225,000 mUI/mL), concurrently the emergence of the complaint of pelvic pain associated with fever. In this case, a computerized tomography (CT) scan was requested of the abdomen and pelvis that revealed an enlarged uterus, with an endometrial cavity extended by heterogeneous contents, without any other noteworthy alterations. The results can be observed in Figure 2.

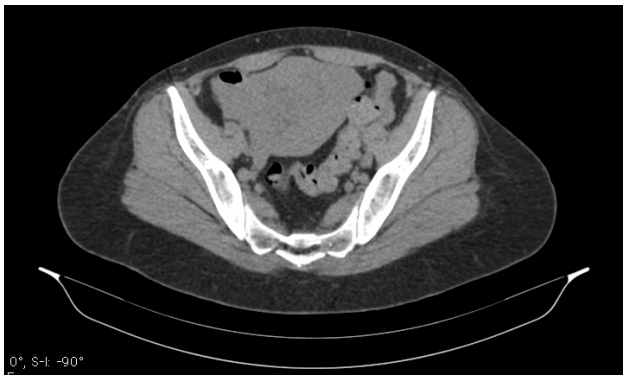


Figure 2: The computerized tomography scan showed a uterine cavity filled with heterogeneous contents suggestive of a hydatidiform mole

The suspected neoplasm corroborated in the CT results and the increased levels of BhCG after the second Manual Intrauterine Aspiration. Furthermore, as the patient is over 40 years old, and her offspring have been fully constituted, a complete abdominal hysterectomy was elected with a bilateral salpingectomy and preservation of the bilateral ovaries as a therapeutic decision. The removed surgical piece (Figure 3) was submitted to an anatomopathological analysis.

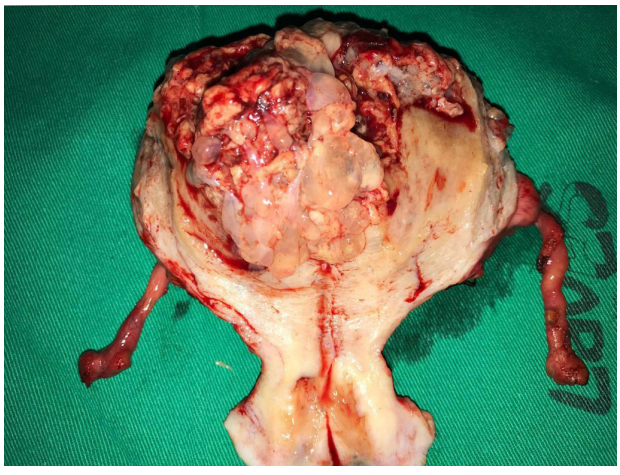
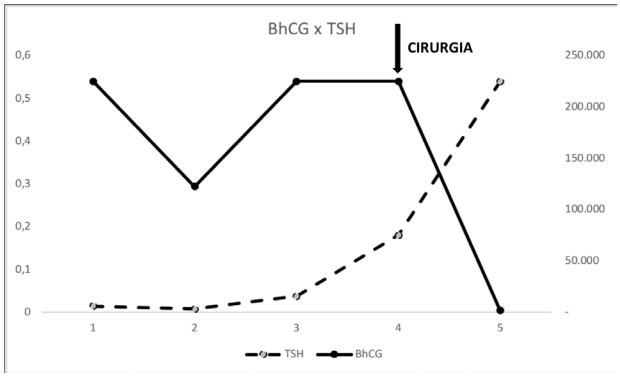


Figure 3: The open uterus, deformed exhibiting a dark vegetative tumor, with vesicles filled with permeated liquid, and firmly adhered to the endometrium

It was possible to view the correlations between the BhCG and TSH values by performing the adopted therapeutic procedures, as shown in Graft 1. The arrow indicates the decreased values of BhCG after the hysterectomy, and the consequently increased TSH values, as expected. The patient continues being monitored at the Outpatient Facility at HSCMV.

Graft 1: Correlation between the BhCG and TSH values



DISCUSSION

The hydatidiform mole is most frequent in patients at the very beginning and end of their reproductive lives (<15 and >45 years old) and having had a previous history of molar pregnancy[19,20]. The Gestational Trophoblastic Neoplasia (GTN) evolution can occur in 50% of cases of a hydatidiform mole, and the other 50% can occur after an abortion, topic, and ectopic pregnancy. It is soon essential to perform adequate therapeutic conduct so that outpatient monitoring is done, measuring the BhCG levels every 1-2 weeks for early diagnosis of a possible neoplasia[20,21].

Metastasis sites are most common in GTN in the lungs, liver, spleen, intestines, and the brain, justifying the need for tracking through Thorax Radiography and Computerized Tomography[21].

We should mention the presence of theca-lutein cysts, early preeclampsia, hyperthyroidism, and more serious clinical conditions such as thyrotoxic crisis and respiratory insufficiency[7].

Hypothyroidism results in the linkage of hCG to TSH receptors in the thyroid, with the consequential suppression of TSH production[16,22]. An increase of 10000U/L of hCG increases by 0.1 ng/dL the free T4 and reduces TSH levels by 0.1 µU/mL. The Lockwood et al.[16] study shows that concentrations above 50000 mU/mL can suppress the TSH to ≤ 0.2 mU/mL values in up to 40% of cases, and concentrations greater than 400000 mU/mL in up to 100% of cases.

Almeida et al.[23] report on the case of an amenorrhea

patient who suffered from abdominal pain and vaginal bleeding, who presented tachypnea, tachycardia (112 bpm), hypertension (165/92 mmHg), paleness, and dehydration. Laboratory exams on admission showed TSH 0.009 mU/mL and values of hCG over 400,000 UI/L. The ultrasound exam showed a uterine volume of 1,780 cm^3, with multiple cystic vesicles compatible with a hydatidiform mole. The patient developed a thyrotoxic crisis after administrating iodine contrast to perform the imaging exam.

The article mentioned above, as well as in this report on mole triggered hyperthyroidism, portrayed one of its possible complications. It also demonstrated that this disease's possible clinical manifestations could occur, ranging from mild to more severe complications, such as the thyrotoxic crisis.

As the patient was hemodynamically stable, and there was mild symptomatology of hyperthyroidism, it was decided not to start anti-thyroid medication. A similar case was described in the report by Virmani et al.[24,] as it was possible to control the symptoms by only using Propranolol.

CONCLUSION

This report's relevance is to make physicians pay attention to understanding the mechanism of the action of the "hCG similar to TSH." The course of diseases that increase hCG can bring about a secondary hyperthyroidism condition. Although this disease is present in only 5% of GTD cases, the physician should not ignore the importance of investigation for early diagnosis, for avoiding more severe complications, such as the thyrotoxic crisis.

Author´s participation: *Elis Camara Francischetto* – Responsible for writing the written text, introduction, case report, discussion, and conclusion. She worked on the pre-submission revision and support in the submission of the article. *Laís Veiga Campanharo* – Writing the written text, introduction, case report, discussion, and conclusion. She adjusted the text for English, pre-submission revision, and support in the submission of the article. *Alice Fernandes de Carvalho* – Writing the written text, introduction, case report, discussion, and conclusion. She adjusted the text for English, pre-submission revision, and support in the submission of the article. *Rubens Bermudes Musiello* – Provided support in the clinical case study and description of the case report. *Rachel Torres Sasso* – Provided support in developing the theoretical portion of this study. *Antônio Chambô Filho* – Provided support in the clinical case study, developing the theoretical portion of this study, and description of the case report. *Carmen Dolores Gonçalves Brandão* – Endocrinologist and Research counselor.

REFERENCES

1. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet. 2010;376(9742):717-29. doi: https://doi.org/10.1016/S0140-6736(10)60280-2.
2. Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, Lurain JR, Massuger L. Update on the diagnosis and management of gestational trophoblastic disease. Int J Gynaecol Obstet. 2018;143(Suppl 2):79-85. doi: https://doi.org/10.1002/ijgo.12615.
3. Seckl MJ, Sebire NJ, Fisher RA, et al. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(Suppl 6):vi39–vi50. doi: https://doi.org/10.1093/annonc/mdt345.
4. National Organization for Rare Disorders (NORD). Gestational trophoblastic disease [cited 2020 March, 13]. Available from: https://rarediseases.org/rare-diseases/gestational-trophoblastic-disease/.
5. Bruce S, Sorosky J. Gestational trophoblastic disease. [Updated 2017 Dec 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470267/.
6. Howat AJ, Beck S, Fox H, Harris SC, Hill AS, Nicholson CM, et al. Can histopathologists reliably diagnose molar pregnancy? J Clin Pathol. 1993;46(7):599-602. doi: https://doi.org/10.1136/jcp.46.7.599.
7. Moraes VP, Marcolino LA, Sá RAM, et al. Complicações clínicas da gravidez molar. Femina. 2014;42:229-34. Available from: http://files.bvs.br/upload/S/0100-7254/2014/v42n5/a4647.pdf.
8. Gadelha PS, Montenegro RM. Interpretação dos testes de função tireoideana. In: Vilar L. Endocrinologia clínica. 6ª ed. Rio de Janeiro: Guanabara Koogan; 2017. p.233-40.
9. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, Laurberg P, McDougall IR, Montori VM, Rivkees SA, Ross DS, Sosa JA, Stan MN; American Thyroid Association; American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011;21(6):593-646. doi: https://doi.org/10.1089/thy.2010.0417.
10. Nayak B, Hodak SP. Hyperthyroidism. Endocrinol Metab Clin North Am. 2007;36(3):617-56. doi: https://doi.org/10.1016/j.ecl.2007.06.002.
11. Freitas MC, Mota VC, Sousa TBB, Cardoso IRA, Vilar L. Diagnóstico e tratamento da doença de Graves. In: Vilar L. Endocrinologia clínica. 6a ed. Rio de Janeiro: Guanabara Koogan; 2017. p.300-18.
12. Brent GA. Clinical practice. Graves' disease. N Engl J Med. 2008; 358:2594-605. doi: https://doi.org/10.1056/NEJMcp0801880.
13. Weetman AP. Medical progress: Graves' disease. N Engl J Med. 2000;343:1236-48. doi: https://doi.org/10.1056/NEJM200010263431707.
14. Burch HB. Overview of the clinical manifestations of thyrotoxicosis. In: Braverman LE, editor. Werner & Ingbar's the thyroid. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2013. p.434-40.

15. Yoshimura M, Hershman JM. Thyrotropic action of human chorionic gonadotropin. Thyroid. 1995;5(5):425-34. doi: https://doi.org/10.1089/thy.1995.5.425.

16. Lockwood CM, Grenache DG, Gronowski AM. Serum human chorionic gonadotropin concentrations greater than 400,000 IU/L are invariably associated with suppressed serum thyrotropin concentrations. Thyroid. 2009;19(8):863-8. doi: https://doi.org/10.1089/thy.2009.0079.

17. Bracken MB. Incidence and aetiology of hydatidiform mole: an epidemiological review. Br J Obstet Gynaecol. 1987;94(12):1123-35. doi: https://doi.org/10.1111/j.1471-0528.1987.tb02311.

18. Erturk E, Bostan H, Geze S, Saracoglu S, Erciyes N, Eroglu A. Total intravenous anesthesia for evacuation of a hydatidiform mole and termination of pregnancy in a patient with thyrotoxicosis. Inter J Obstet Anest. 2007;16(4):363-6. doi: https://doi.org/10.1016/j.ijoa.2006.12.004.

19. Sebire NJ, Foskett M, Fisher RA, Rees H, Seckl M, Newlands E. Risk of partial and complete relation hydatidiform molar pregnancy in relation to maternal age. BJOG. 2002;109:99-102. doi: https://doi.org/10.1111/j.1471-0528.2002.t01-1-01037.

20. Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, Lurain JR, Massuger L. Update on the diagnosis and management of gestational trophoblastic disease. Int J Gynaecol Obstet. 2018;143(Suppl 2):79-85. doi: https://doi.org/10.1002/ijgo.12615.

21. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol. 2010;203(6):531-9. doi: https://doi.org/10.1016/j.ajog.2010.06.073.

22. Kosugi SW, Mori T. TSH receptor and LH receptor. Endocr J. 1995;42:587-606. doi: https://doi.org/10.1507/endocrj.42.587.

23. Almeida CED de, Curi EF, Almeida CRD, Vieira DF. Crise tireotóxica associada à doença trofoblástica gestacional. Rev Bras Anestesiol. 2011;61:607-9. doi: https://doi.org/10.1590/S0034-70942011000500010.

24. Virmani S, Srinivas SB, Bhat R, Rao R, Kudva R. Transient thyrotoxicosis in molar pregnancy. J Clin Diagn Res. 2017;11(7):QD01–QD02. doi: https://doi.org/10.7860/JCDR/2017/28561.10133.

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