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CASE REPORT

From Molar Pregnancy, Thyrotoxicosis, to Pulmonary Hypertension: A Case Report

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Abstract

Background: Molar pregnancy is a benign condition with the dominant symptom being dark brown to bright red bleeding from the vagina. This disease can induce hyperthyroidism and result in pulmonary hypertension. This case report describes a patient who had molar pregnancy with thyrotoxicosis and pulmonary hypertension.
Case: A 30-year-old woman presented with complaints of lower abdominal pain for the last month. The patient feels that her stomach has enlarged in the last 3 months. Other complaints include bleeding and observed bubbles from the birth canal, shortness of breath, and chest pain. The serum cobas β-hCG level of 7954.00 mIU/mL. On abdominal ultrasound examination, vesicles formed a honeycomb appearance, measuring 7.4 cm×5.3 cm. Hematologic laboratory tests revealed low TSH levels (<0.01 µIU/mL), T3 levels of 2.35 ng/ml, and FT4 levels of 2.62 ng/dL. The results of the echocardiography examination showed there is a high probability of pulmonary hypertension.
Conclusion: Molar pregnancy can exacerbate thyrotoxicosis through hCG activity. Smoking and breastfeeding also have similar effects. Consequently, increased thyroid hormone levels can worsen or cause pulmonary hypertension.

Keywords: Molar pregnancy, pulmonary hypertension, thyrotoxicosis

INTRODUCTION

A molar pregnancy (sometimes called a hydatidiform mole) is one of the groups of gestational trophoblastic disease (GTD). In a molar pregnancy, it looks like a normal pregnancy at first, but this pregnancy is not accompanied by the development of the baby. A molar pregnancy occurs due to an error in the fertilization of the egg by sperm, which causes abnormal cell growth or the formation of a collection of water-filled sacs in the uterus. There are two types of molar pregnancies, namely complete hydatidiform moles (CHMs) and partial hydatidiform moles (PHMs).(1,2) In CHMs, abnormal cells grow in the uterus after fertilization, and there are no signs of the baby's life.

Hyperthyroidism affects a small percentage of pregnancies, ranging from 0.2% to 0.7%, with the majority of cases (95%) attributed to Graves' disease.(1) Among the various forms of pregnancy-induced hyperthyroidism, hyperthyroidism caused by molar pregnancy is rare but can have severe consequences, such as thyroid storm, a life-threatening complication.(3)

The exact cause of molar pregnancy remains unknown, but age is considered a significant risk factor. Molar pregnancy is more commonly observed in women above the age of 43 or below the age of 15.(4) This condition, known as hydatidiform mole or molar pregnancy, is a genetically abnormal and uncommon occurrence, with partial moles appearing in approximately 1 in 700 pregnancies and complete moles in 1 in 2,000 pregnancies. International estimates indicate that the incidence of molar pregnancy ranges from 0.6 to 8 cases per 1,000 pregnancies.(2)

Molar pregnancies are benign (not cancerous). There is a very small risk that molar cells can become cancerous if they are not completely removed. Symptoms that may appear in patients with a molar pregnancy include dark brown to bright red bleeding from vaginal discharge during the first three months, occasional grape-like cysts oozing from the vagina, pelvic pressure or pain, and severe nausea and vomiting.(4)

Pulmonary hypertension, a serious and potentially life-threatening condition, affects approximately 5-50 out of one million adults. Hyperthyroidism can cause changes in the cardiorespiratory system, resulting in pulmonary hypertension.(5) It is more prevalent in women, being two to four times more common than in men.(6) Among patients with thyrotoxicosis, hyperthyroidism can lead to pulmonary hypertension, increasing the risk of heart failure in 6-16% of cases. Studies have shown that the prevalence of pulmonary hypertension in patients with hyperthyroidism ranges from 41% to 65%.(7) Additionally, pulmonary hypertension is more likely to co-occur with hyperthyroidism rather than with euthyroidism.(5) We describe a patient who had molar pregnancy with thyrotoxicosis and pulmonary hypertension.

CASE REPORT

A 30-year-old woman, gravida 4, para 3, miscarriage 0, presented to the hospital's emergency room with complaints of lower abdominal pain persisting for the last month. The patient also

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noticed an enlargement of her abdomen in the three months prior to admission. Additionally, she experienced bleeding dan observed bubbles from the birth canal, along with shortness of breath and chest pain. The blood discharge is brown and the patient has to change her pads once a day. Furthermore, she feels easily tired, dizzy, has diarrhea, and experiences a feeling of heat. These symptoms are accompanied by redness, pain, and prominent eyes. When coughing, the patient feels a lump in her neck. Pain in the abdomen prevents her from straining during bowel movements. Moreover, she has no appetite and also experiences pain in her right ear accompanied by ringing.

The patient has a normal pregnancy history and uncomplicated spontaneous delivery at full-term gestation. The youngest child is 1 year and 2 months old and still breastfeeding frequently. The child breastfeeds approximately 10 times per day, with each session lasting up to 2 hours. The patient has been smoking for the past 10 years, consuming one pack of cigarettes every two days. The patient's last menstrual period started 5 months before admission to the hospital, with a 7-day cycle.

On examination, the patient was compos mentis ($E_4V_5M_6$). Blood pressure was 168/105 mmHg, pulse rate was 101 bpm, respiratory rate was 26 bpm, body temperature was 36℃, and oxygen saturation was 96%. The patient's weight is 46 kg with a height of 150 cm. Additionally, the uterine fundus is palpable 3 fingers above the umbilicus, and there is edema in both feet. In the birth canal, grape-like appearance tissue was found, indicating a molar pregnancy (Figure 1).

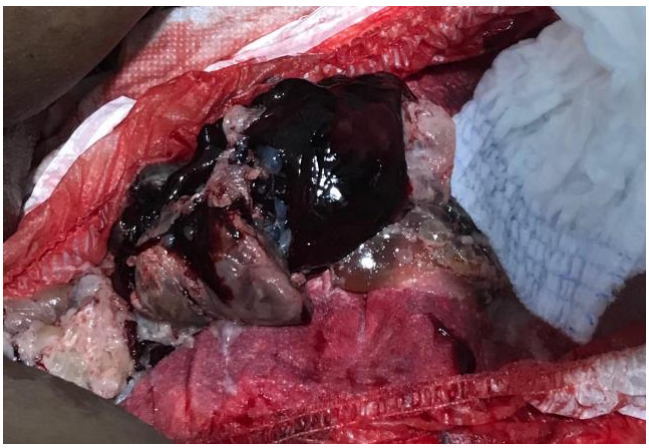

Figure 1. Grape-like appearance tissue in the patient

Hematologic laboratory tests revealed low TSH (Thyroid Stimulating Hormone) levels (<0.01 µIU/mL), T3 levels of 2.35 ng/ml, and FT4 levels of 2.62 ng/dL. Additionally, there was an increase in the number of leukocytes (11.50×103/µL) and a decrease in the number of erythrocytes (3.47×106/µL) and hemoglobin (9.8 g/dL). Neutrophils showed a significant increase (8.1×103/µL). The pregnancy examination yielded a positive result with a serum cobas β-hCG (Beta Human Chorionic Gonadotropin) level of 7954.00 mIU/mL. On abdominal ultrasound examination, vesicles formed a honeycomb appearance, measuring 7.4 cm×5.3 cm. A plain chest x-ray examination of the patient showed enlargement of the right side of

the heart, particularly the right ventricle (Figure 2). The results of the echocardiography examination showed decreased contractility of the right ventricle (TAPSE: 1.5 cm) accompanied by dilation of the right ventricle (RVDB: 3.2 cm) and right atrium (RA major: 5.3 cm, RA minor: 4.2 cm). The IAS and IVS showed no abnormalities. Additionally, the tricuspid valve showed TR severity (TR velocity 3 m/s), and the pulmonary valve had mild PR. Measurements of MPA, LPA, and RPA were 2.8 cm, 0.9 cm, and 1.2 cm, respectively. Based on these findings, there is a high probability of pulmonary hypertension.

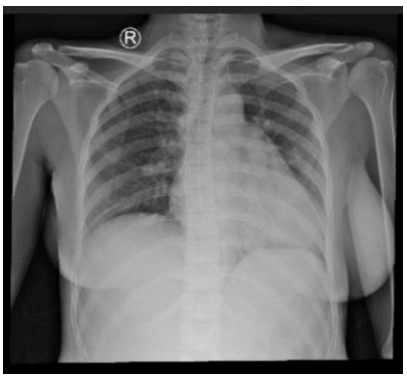

Figure 2. Enlargement of the patient's right-sided heart on a plain chest x-ray

DISCUSSION

Molar pregnancies produce a significant amount of hCG. The hCG molecule is made up of α and β subunits. While the α-hCG subunit is homologous to TSH, the beta subunit provides different specificity for the two.(8,9) As a result, hCG produced from molar pregnancies can directly affect the TSH receptor, leading to an increase in T3 and T4 hormones.(9) Consequently, negative feedback occurs, causing a decrease in TSH levels.(10) Evacuation of the molar pregnancy results in a rapid resolution of hyperthyroidism. The exact cause of thyrotoxicosis resulting from molar pregnancy is not known for certain, but several previous case reports have indicated a range of 1 to 4 months.(3,11)

Smoking is also linked to elevated levels of FT4 and FT3 hormones and reduced TSH levels. However, the exact mechanism by which smoking affects TSH and thyroid hormone levels remains unclear.(12) Additionally, tobacco smoke may contribute to thyroid autoimmunity. Numerous studies have highlighted the significant influence of smoking on Graves' hyperthyroidism, particularly on Graves' orbitopathy.(13) Furthermore, long-term inhalation of nicotine can result in alterations in both systemic and pulmonary blood pressure, along with changes in the structure of the right ventricle. This could potentially lead to the development of progressive and persisting pulmonary hypertension.(14) It is noteworthy that around 20% of patients with pulmonary hypertension also suffer from thyroid disease as a comorbidity, a prevalence higher than that observed in the general population.(15)

Prolactin and oxytocin directly influence breastfeeding. Oxytocin not only serves as a bioactive protein that stimulates prolactin release and lactation but also interferes with the

synthesis and release of thyrotropin-releasing hormone (TRH). Additionally, it inhibits the release of thyroid-stimulating hormone (TSH) induced by TRH, resulting in reduced plasma TSH and thyroid hormone levels due to its impact on the central nervous system.(16) Breastfeeding is associated with higher levels of thyroid-stimulating hormone (TSH).(17) Prolactin exhibits a positive correlation with TSH in cases of both hyperthyroidism and hypothyroidism.(18) Furthermore, oxytocin has the potential to raise pulmonary hypertension by increasing pulmonary vascular resistance.(19)

Thyrotoxicosis can cause World Health Organization (WHO) group 5 pulmonary hypertension, especially in patients who are not regularly taking medication.(6,20) Abnormal thyroid hormone levels can significantly impact the body's hemodynamics, leading to changes in cardiac output, blood pressure, and pulmonary vascular resistance.(15,21) Several case reports published in the past have described patients with hyperthyroidism presenting with right heart failure and tricuspid regurgitation.(6) Hyperthyroidism can manifest with various cardiac features such as cardiomegaly, increased cardiac output, atrial fibrillation (AF), and, in certain cases, congestive heart failure.(22)

The timeframe for the onset of right ventricular hypertrophy in pulmonary hypertension can differ based on the individual and the underlying cause of the condition. It is a gradual progression that happens over time as the right ventricle faces increased stress due to elevated pulmonary artery pressure.(23) The mechanism for the occurrence of pulmonary hypertension due to increased levels of thyroid hormone is still not clearly explained, but several postulates include direct damage to the pulmonary valve, increased workload on the cardiovascular system, endothelial dysfunction, and the presence of an autoimmune process.(24,25) Hyperthyroidism is a reversible cause of pulmonary hypertension, meaning that when the underlying hormonal imbalance is corrected, improved cardiovascular outcomes and reduced symptoms can result.(6)

CONCLUSION

Molar pregnancy can exacerbate thyrotoxicosis through hCG activity. Smoking and breastfeeding also have similar effects. As a result, increased thyroid hormone can worsen or cause pulmonary hypertension.

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The authors declare no competing interest in this study.

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