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Case study: Thyrotoxicosis on women with complete hydatidiform molar pregnancy

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Case Report

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ABSTRACT

Thyrotoxicosis defined as a clinical manifestation of excess circulating thyroid hormone. Epidemiologic investigation reports 0.2% of thyrotoxicosis is caused by hydatidiform mole. The New England Trophoblastic Disease Centre (NETDC) mentioned that 20% of hydatidiform mole cases have thyrotoxicosis as one of its complications. The basic pathogenesis of thyrotoxicosis is the similarity of the HCG subunit to TSH which results in excessive stimulation of thyroid hormone. We present thethyrotoxicosis case in a 15-weeks pregnant woman with complete hydatidiform mole. The patient admitted to the hospital with blackish-red coloured bleeding and several hyperthyroidism complaints, laboratory test showed elevated levels of HCG and thyroid hormone and decreased TSH. Imaging studies done with ultrasound showed with snowflake pattern. The patient then treated with thyroid hormone suppressant therapy before the hydatidiform mole evacuation. Normalization of thyroid hormone levels should be made immediately before the mole evacuation to avoid life-threatening thyroid storm complications.

Tirotoksikosis merupakan manifestasi klinis akibat kelebihan hormon tiroid yang beredar dalam darah. Hasil epidemiologi mencatat sekitar 0,2% kasus tirotoksikosis dapat disebabkan oleh mola hidatidosa. The New England Thropoblastic Disease Centre (NETDC) menyebutkan 20% kasus mola hidatidosa di benua Asia memiliki komplikasi tirotoksikosis. Patofisiologi dasar tirotoksikosis adalah kemiripan subunit HCG dengan TSH yang mengakibatkan stimulasi produksi hormon tiroid yang berlebihan. Pada kesempatan ini dilaporkan sebuah kasus tirotoksikosis pada seorang wanita hamil usia 15 minggu dengan mola hidatidosa komplit. Pasien mengeluh perdarahan banyak berwarna merah kehitaman, disertai beberapa keluhan hipertiroidisme, hasil laboratorium menunjukkan peningkatan kadar HCG dan hormon tiroid, penurunan TSH disertai gambaran snowflake pattern pada hasil USG. Pasien kemudian diberikan terapi penekan hormon tiroid sebelum dilakukan evakuasi mola. Penekanan kadar hormon tiroid harus dilakukan segera sebelum tindakan evakuasi mola agar komplikasi badai tiroid yang dapat mengancam keadaan pasien dapat dicegah.

INTRODUCTION

Thyrotoxicosis defined as a clinical manifestation of excess circulating thyroid hormones. Thyrotoxicosis has many etiologies, the most frequent causes are hyperthyroidism in graves disease which accounted for approximately 76% cases, and about 0.2% of are caused by hydatidiform mole.[1,2] The new

England trophoblastic disease center (NETDC) estimates that 20% of hydatidiform mole cases in Asia have thyrotoxicosis complications, but only 5% of all cases have clear clinical signs.[3]

Some research was trying to reveal the magnitude of the cases in Indonesia. One research in determining the prevalence of thyrotoxicosis cases in hydatidiform mole has been done in Prof. dr. R. D. Kandou Manado central goverment hospital from 1 January to 31 December 2014. In the study, 35 cases of hydatidiform mole were found and within one year 54.5% cases complicate with thyrotoxicosis.[4] Based on primary source in 2015, our hospital had about 50 hydatidiform mole patients but only several patients including this patient that have equivocal presumptive of thyrotoxicosis and have a risk to become thyroid storm. Therefore we discuss about peri-operative treatment to avoid thyroid storm during and after evacuation procedure. The high incidence rate of thyrotoxicosis caused by hydatidiform mole requires more attention because sometimes it shows some inconclusive symptoms.[4]

CASE REPORT

A 29-year-old woman who was 15^{+4} weeks pregnant (Gravid 2, Parity 1) admitted to the obstetric clinic at Margono Soekarjo Hospital with red-blackish coloured bleeding. The patient also complained trouble sleeping, sweating easily, heat intolerance, palpitations, nauseous, and increased appetite. The patient had no prior these complaints history, heart diseases, and metabolic endocrine diseases. The patient had a regular antenatal examination at the local midwife clinic. Patient was a housewife and has little activity outside the house. The patient lives in a densely populated environment in the Gandatapa area.

On physical examination, blood pressure was 130/70 mmHg, pulse rate 92 bpm, respiratory rate 22 bpm, and the body temperature was 36.7^{0} C. The patient fundal height is palpable at the level of one finger under umbilicus which was consistent with 20 weeks gestational age. Visual examination of cervix revealed the opening of the cervix and presence of red-blackish coloured discharge.

Laboratory hematologic examination was entirely within normal limits except for haemoglobin 8.9 g/dl. The level of HCG detected at > 10,000 mIU/ml. FT3 and FT4 increased significantly (10.3 pg/dL and 4.46 pg/dL), with very low TSH levels at <0.005 μIU / ml. The ultrasound examination of the uterus revealed a snowflake pattern.

Patients were diagnosed with a complete hydatidiform mole with thyrotoxicosis complications. Management taken for the patient was hospitalization and thyroid suppressant therapy. Drugs include thiamazole 10 mg and propanolol 10 mg each given every twelve hours. After seven days of treatment, the thyroid hormone level was successfully suppressed to normal and subsequently, the patient undergoes the mole evacuation. Two days after the mole evacuation, thiamazole and propranolol were titrated gradually. Communications, information and education were provided to patients and families about the risk factor and the potential complications. The prognosis of this patient is *dubia ad malam.*

DISCUSSION

The diagnosis of hydatidiform mole can be established at gestational age less than 20 weeks through a series of history taking and physical examination. Based on the degree of proliferation and changes in tissue, the hydatidiform mole can be divided into the complete hydatidiform mole and partial hydatidiform mole. Patients with hydatidiform mole will usually complain of experiencing discharge of reddish-black coloured blood or having uterine enlargement beyond the gestational age. Uterus ultrasound can be performed to establish the diagnosis based on appearance of "a snowflake pattern" for a complete mole or "multicyst pattern" for partial mole followed by a significant increase in HCG levels, but the gold standard is based on gross morphology of the specimen, histopathologic feature and Karyotype as the complimentary.[5,6] In this patient, we found red-blackish coloured

bleeding from our history taking, snowflake pattern on ultrasound examination (Figure 1) and following with HCG detected at > 10,000 mIU/ml, so the patient was appropriate with a complete mole.

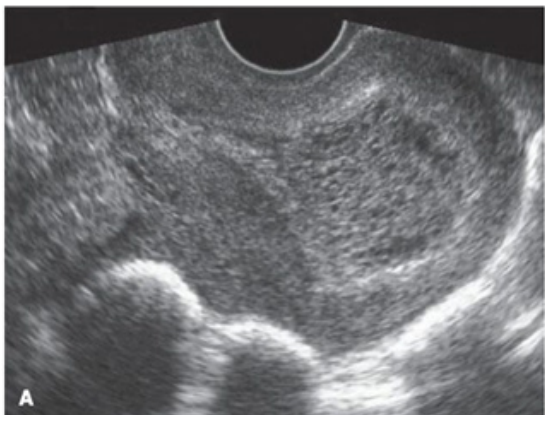

Figure 1. Ultrasound of Snow flake pattern.[5]

One of the complications of hydatidiform mole pregnancy is thyrotoxicosis, although not all molar patients can have such complication. The diagnosis of thyrotoxicosis in molar pregnancy is no different from other causes of secondary thyrotoxicosis. Calculation of hypermetabolism state by Wayne index can be performed in conjunction with laboratory hematologic results. Patients with Wayne index score above 20 is said to have symptoms of thyrotoxicosis. But a patient with true laboratory thyrotoxicosis may result under 20 points in Wayne score because in some cases, thyrotoxicosis causes subjective unclear symptoms. Relying on laboratory result of increase thyroid hormone and decrease thyroid-stimulating hormone is best establishing the diagnosis.[7] In this patient, we found a score of 16 (equivocal) according to the Wayne index (Table 1), but we had laboratory finding FT3 and FT4 increased significantly with very low TSH levels at <0.005 μIU/ml so the presumptive of thyrotoxicosis cannot be ignored.

Table 1. Wayne's index of sign and symptoms scoring.[9]

Symtomps of recent onset and/or increased severity	Scores	Signs	Only if present	Only if absent
Dyspnoea on effort	(+)1	Palpable thyroid	(+)3	(-)3
Palpitation	(+)2	Bruit over tllyroid	(+)2	(-)2
Tiredness	(+)2	Exophthalmos	(+)2	
Preference for heat	(-)5	Lid retraction	(+)2	-
Preference for cold	(+)5	Lid lag	(+)1	-
Excessive sweating	(+)3	Hyperkinesis	(+)4	(-)2
Nervousness	(+)2	Hands: hot	(+)2	(-)2
Appetite: increased	(+)3	moist	(+)1	(-) 1
decreased	(-)3	Casual pulse rate:		
Weight: increased	(-)3	> 80/min	-	(-)3
decreased	(+)3	> 90/min	(+)3	-
		Atrial fibrillation	(+)4	-

Total score interpretation:
> 19 = toxic
11-19 =equivocal
< 11 =eutnyrotd/not toxic

The equivocal score could be happening because the presence of elevated FT3 and FT4 concentrations could be partly due to the brief duration of increased hormonal levels in patients. A previous case report in India explained that despite the patient had normal thyroid hormone level and equivocal of Wayne's index, the patient developed a thyroid storm after evacuation procedure without suppressing thyroid hormones level. Altered tolerance of the nervous system to thyronines or an alteration in catecholamine/thyroxine relationship maybe is the possible reason thyroid storm has occurred.[8]

In a molar pregnancy, the hormone that plays the main role causing thyrotoxicosis is HCG (human chorionic gonadotrophin). HCG is a glycoprotein compound produced by syncytiotrophoblasts cells which have 2 HCG sub-units, including alpha-HCG and beta-HCG, both of those subunit has a chemical structure similar to TSH (thyroid-stimulating hormone). Although structurally similar, the potential for HCG to stimulate the TSH receptor in releasing thyroid hormone is lower than actual TSH. In a normal pregnancy HCG levels will increase in the first trimester and will peak between 8 to 10 weeks followed by a gradual decline. High levels of HCG stimulate thyroid hormone through TSH receptors to produce T3 and T4 by about 40%. This is necessary as a physiological adaptation for fetal growth and development in the first trimester.[5]

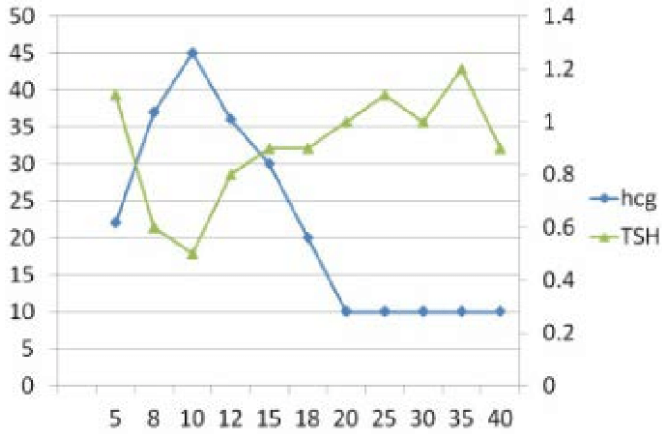

Figure 2. Normal HCG level in Pregnant Women.[3]

In a molar pregnancy, elevated HCG levels occur not only in the early trimester, but also continue to rise to the level above 100.000 mIU/ml. The HCG increase then will stimulate the thyroid gland through the TSH receptor to produce and release T3 and T4 excessively. When the thyroid hormone is released in the bloodstream, these hormones still harm thyroid releasing hormone (TRH) and TSH, this explains why thyrotoxicosis patients in hydatidiform mole will show very low TSH levels.[3,10]

Delaying evacuation of hydatidiform mole because of controlling thyrotoxicosis could increase the perioperative morbidity and complication, but ignoring to control thyrotoxicosis before evacuation procedure can develop a thyroid storm too. So we have to do aggressive medical management to control thyroid levels first, following with removal of molar tissue for the successful outcome in the patient and prevent morbidity.[8]

The definitive therapy of hydatidiform mole is the evacuation of the molar tissue. Evacuation and curettage, ideally went under ultrasound guidance, is the chosen method of evacuation of a molar pregnancy independent of uterine size if maintenance of fertility is needed so it is recommended that a 12–14 mm suction cannula is used.[11] Evacuation should be done once patients hemodynamically are stable. Evacuation of the

mole with thyrotoxicosis without suppressing thyroid hormone levels will trigger thyroid storm. Thyroid storm is the most severe and life-threatening condition in thyrotoxicosis.[1,12] There is a case of thyroid storm that occurred after mild hydatidiform mole evacuation. This is due to inflammation in the evacuation process will cause increased metabolism thus triggering the production of more thyroid hormone. Excess hormone in circulation will stimulate increased activity from receptor organs, thus causing more organ dysfunction.[3]

Propylthiouracil (PTU), carbimazole, and methimazole or thiamazole are the drug of choice for inhibiting the function of thyroid peroxidase (TPO), as well as decreasing oxidation and iodide influx so that the production of thyroid hormone can be inhibited. Methimazole or thiamazole have to administer 20-40 mg/day and may be used as a single daily dose if the patient has reached or approached euthyroid state.[1,13] Besides, beta-blockers such as propranolol or atenolol may be used to control adrenergic symptoms, especially in the early stages while waiting for antithyroid drugs to show the desired effect.[14] The use of steroids was believed to inhibit the conversion of T4 to T3,but the effectiveness of the steroid is still in doubt.[15]

CONCLUSION

A hydatidiform molar pregnancy can cause thyrotoxicosis because the HCG hormone has similar structure with TSH. HCG binds to TSH receptors causing excessive release of thyroid hormone. Thyrotoxicosis in molar pregnancy sometimes shows unclear symptoms because of the brief duration of increased hormonal levels. This requires more attention to the patient's thyroid hormone status before mole evacuation. The normal level of thyroid hormone should be reached immediately before the evacuation of the mole to prevent the effects of thyroid storms which is a life-threatening condition.

CONFLICT OF INTEREST

No conflict of interest.

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