

PERI-OPERATIVE CONCERNS IN A PATIENT WITH THYROID STORM SECONDARY TO MOLAR PREGNANCY

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INTRODUCTION

Hydatidiform mole results from abnormal trophoblastic proliferation. Incidence in India is 1:400.^[1] The New England Trophoblastic Disease Centre has not reported even one case of trophoblastic hyperthyroidism from 1988 to 1993. Biochemical hyperthyroidism has been reported by Walkington *et al.* in 7% of patients treated with chemotherapy for gestational trophoblastic neoplasia between January 2005 and January 2010 in United Kingdom.^[2] However in a developing country like India, we still encounter such cases due to ethnic differences and delayed presentation at the ante natal clinics which leads to detection at a later stage when levels of β human chorionic gonadotropin (HCG)

are high. Thus, it is of utmost importance to be aware of this endocrine emergency. Clinical presentation of hyperthyroidism namely, tachycardia and heat intolerance can be attributed to hypermetabolism of pregnancy and thus missed out.

Our hospital is a Tertiary Care Referral Centre for obstetrics and gynaecology. We have anaesthetised 50 patients for the evacuation of molar pregnancy from 2008 to 2013. Until date, only one patient has presented with clinical features suggestive of a thyroid storm and we discuss the peri-operative challenges encountered in anaesthetising this patient.

CASE REPORT

A 25-year-old lady (gravida 2, para 1), 50 kg, 160 cm (body mass index 19.5 kg/m²) presented to the obstetric emergency with 20 weeks amenorrhea, pain abdomen, vomiting and bleeding per vaginum. She also gave history of cough and breathlessness (New York Heart Association-III). On examination, she was febrile (102°F) and haemodynamically stable (blood pressure - 108/64 mm Hg) with a pulse rate (PR) of 122 beats/min and respiratory rate

(RR) of 30/min. Jugular venous pressure was not raised and pedal oedema was absent but a mid systolic murmur was heard in the aortic area. On per abdominal examination, a cystic, mobile, non-tender uterine mass (approximate size of 24 weeks) was felt. Ultrasound reported a uterine size of 25 cm × 15 cm × 12 cm with innumerable vesicles which was suggestive of a molar pregnancy and bilateral theca lutein cysts.

Confirmation of a molar pregnancy raised suspicion of hyperthyroidism which was subsequently proved by her laboratory reports. The presence of thyroid storm was confirmed by Burch and Wart of sky score of 55.^[3] Patient was shifted to the Intensive Care Unit (ICU) for observation and further treatment. Results of biochemical investigations reported derangement of thyroid function tests (hyperthyroidism), anaemia (haemoglobin of 5 g/dl) and high levels of β hCG [Table 1]. Propylthiouracil 50 mg TDS, propranolol 40 mg BD, Lugol's iodine 10 drops 6 hourly and injection dexamethasone 2 mg 6 hourly were administered to control the thyroid storm. She also received 3 units of packed red blood cells. However, she continued to have bleeding per vaginum and thus after 48 h she was shifted to the operation theatre for suction and evacuation. Her Hb before emergency surgery was 8 gm/dl. Saddle spinal block was targeted with 1.5 ml of 0.5% bupivacaine (heavy). Intraoperative period was uneventful except for an estimated blood loss of 600 ml. Post-operatively, she was shifted to the ICU.

An hour after evacuation, the patient was conscious and oriented but complained of breathlessness and anxiety. Her PR was 140 beats/min, blood pressure was 156/100 mmHg, RR was 35 breaths/min, pulse oximetry was 88% and temperature was 101°F. Bilateral basilar rales were auscultated on chest examination and fine tremors were noted in the hands. Burch and Wart of sky score was now 75.^[2] Chest X-ray (CXR) was suggestive of pulmonary oedema but echocardiography was normal. Oxygenation was maintained with ventimask (FiO₂ of 0.4) and her oxygen saturation varied between 90% and 94%. Esmolol was administered in a loading dose of 0.5 mg/kg over a period of 1 min followed by an infusion of 50 μ g/kg/min which was later increased to 100 μ g/kg/min after a period of 10 min. Intravenous injections of frusemide (20 mg TDS) and morphine (3 mg stat and 8 hourly) were also administered. Dose of all the antithyroid drugs was increased; tablet propranolol 40 mg TDS, tablet propylthiouracil 100 mg TDS, Lugol's iodine 15 drops 6 hourly and injection dexamethasone 2 mg 6 hourly. Rate of infusion of esmolol was gradually tapered and stopped in next 8 h. She was stabilised in 24 h, kept in ICU for 48 h and discharged home after 6

days. She was asked to continue tablet propranolol 40 mg BD and tablet propylthiouracil 50 mg BD. Her β HCG levels normalised by the end of the month and all her medicines were stopped after 2 months.

DISCUSSION

Evacuation of the molar pregnancy is the definitive management of the thyroid function abnormality in patients with trophoblastic hyperthyroidism. Optimum time needed for stabilization of the hypermetabolic state in this subset of patients is not known. However combined use of propylthiouracil, iodide and dexamethasone has been shown to restore serum T_3 concentration to within normal range within 24-48 h.^[1] Thus, theoretically it is safe to perform evacuation after this time interval. Hyperthyroidism secondary to choriocarcinoma may take an even longer time to resolve and thus it is advisable to be extra cautious when administering anaesthesia to this subgroup.

In our case, we had taken up the patient for evacuation after 48 h of initiation of anti-thyroid medications. Despite this, the patient developed a thyroid storm; it is not uncommon to find reports of thyroid storm in a patient with normal thyroid hormone levels.^[4] Altered tolerance of the nervous system to thyronines or an alteration in the catecholamine/thyroxine relationship is the probable explanation for the occurrence of thyroid storm in such cases.

Delaying evacuation of molar pregnancy for controlling hyperthyroidism is known to increase the peri-operative morbidity and complication rate and is thus of no advantage in patients with molar hyperthyroidism where removal of the molar tissue is the only definitive management.^[5]

Only 2-4% of pregnant patients with inadequately treated hyperthyroidism develop a thyroid storm.^[6] The reported mortality rates are high and vary from 30% to 60%. Combination of drugs is thus used to control this endocrine emergency; drugs are used to block the peripheral effects of thyroid hormones, to inhibit hormone synthesis and release and to prevent the peripheral conversion of T_4 to T_3 . Aggressive medical management in the ICU and timely removal of the molar pregnancy was responsible for the successful outcome in our patient.

Biological half-life of beta blockers is shortened by the excess of thyronines and we thus recommend the use of increased doses of beta blockers in patients with trophoblastic hyperthyroidism. We administered esmolol infusions at the rate of 100 μ g/kg/min and

continued it until an adequate response was achieved that is, heart rate <100 beats/min. Esmolol infusions are preferred for acute management of thyroid storm as the β -1 selectivity increases the safety of the drug and shorter half-life ($t_{1/2}$ α and β for esmolol are 2 and 9 min, respectively) enables rapid titratability.^[7] Diagnosis of thyrotoxic cardiomyopathy is an absolute indication for the use of esmolol and absolute contraindication for the use of propranolol. Dose of 200 $\mu\text{g}/\text{kg}/\text{min}$ of esmolol has been safely used by Duggal *et al.*^[8] to control thyroid storm in an asthmatic patient with past medical history of Graves disease.

HCG secreted by the placenta and molar thyrotropin have intrinsic thyroid-stimulating activity and hyperthyroidism is clinically evident when HCG levels exceed 300 IU/ml.^[9] Very high levels of HCG are needed to produce symptoms because it is a weak thyrotropin. Trophoblastic hyperthyroidism is characterised by lower serum T_3/T_4 ratio in contrast to patients with Graves disease and toxic nodular goitre in which the ratio is >20 and this biochemical difference can be used to differentiate between the two.^[6]

Clinical presentation and natural history of women with thyroid function abnormalities secondary to molar pregnancies is highly variable. Biochemical hyperthyroidism is common in a large majority of patients.^{[4],[5]} Absence of clinical features of hyperthyroidism in the presence of elevated T_3 and T_4 concentrations could be partly due to the brief duration of increased hormonal levels in patients with molar pregnancies. Symptomatic patients, however, mainly report of fatigue, weight loss, muscle weakness, sweating, nervousness, heat intolerance, tachycardia and minimal enlargement of the thyroid gland. Ophthalmopathy is characteristically absent in these patients.

Saddle spinal block was used as it is known to be associated with minimum haemodynamic perturbations. Clinical signs of hyperthyroidism are promptly recognised in an awake patient and hence regional anaesthesia is preferred. However, haemodynamic instability due to acute blood loss is a definitive indication for administration of general anaesthesia.^[10] The pressor response to laryngoscopy and tracheal intubation is exaggerated in hyperthyroidism and needs to be adequately managed when administering general anaesthesia.

Reported incidence of acute cardiopulmonary distress in perioperative period is 27% in patients with molar pregnancy and a uterine size of greater than 16 weeks. It is attributed to: Trophoblastic embolisation (>50%), hyperthyroidism (inotropic, chronotropic and lusiotropic effects of thyroid hormone), anaemia (congestive heart failure), pulmonary hypertension,

acute respiratory distress syndrome, pulmonary oedema and transfusion related acute lung injury.^[11] Constant monitoring is thus needed in either an ICU or a high dependency unit.

CONCLUSION

All patients with the gestational trophoblastic disease need to be screened for thyroid function abnormalities. Comprehensive pre-operative workup, laboratory investigations and optimization with antithyroid drugs is imperative in symptomatic patients but does not ensure absolute protection from thyroid storm. The choice of general or regional anaesthesia is dictated by the patients' clinical profile and the surgical procedure planned. The hyperthyroid state rapidly resolves after surgical evacuation of hydatidiform mole.

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Conflicts of interest

There are no conflicts of interest.

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