

## A thyroid-related endocrine emergency in pregnancy

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### Abstract

A 28-year-old woman presented with a thyroid storm while pregnant. Thyroid storm in pregnancy is a rare, life threatening endocrinological emergency. The diagnosis and management can be challenging. Even with early aggressive therapy the maternal mortality is still high and adverse effects on the pregnancy and fetus are common.

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### Case description

A 28-year-old woman, who was 32 weeks pregnant, was following up at her local antenatal care clinic for a seemingly uncomplicated pregnancy. She had her first antenatal visit at 22 weeks. She had a background medical history of hyperthyroidism which had been diagnosed a few years before but she was not on any treatment at presentation. No other significant medical or family history was of note on further enquiry.

At a routine clinic visit she mentioned that she was feeling very anxious and noted a fine tremor. She also complained of significant weight loss, but did not receive any treatment. Two weeks later she went to her local hospital after she became very short of breath and also noted that her heart was racing. There she became disorientated and confused and was transferred to the tertiary hospital two days later.

On arrival the patient was awake but slightly disorientated. Examination revealed that she was hot and sweaty and had a fine tremor. A sinus tachycardia of 134 beats per minute was present, the blood pressure was 140/90 mmHg and the body temperature was 38.9°C. The patient was dyspnoeic (NYHA III) and the respiratory rate was 29 breaths per minute. Cardiac examination revealed the tachycardia, normal first and second heart sounds, and the presence of a third heart sound. No extremity oedema was present and the jugular venous pressure was normal. The respiratory examination showed bilateral coarse crepitations with signs of consolidation in the right lower lobe as well as features of pulmonary oedema which was confirmed with a chest radiograph. On examination of the thyroid it appeared slightly enlarged but with no tenderness and normal consistency. There were no features of Graves' ophthalmopathy present.

Thyroid function tests revealed an elevated level of free thyroxine (42.7 pmol/L) and a decreased level of thyroid stimulating hormone

(0.04 mIU/L). Anti-thyroglobulin, anti-thyroid peroxidase and anti-thyroid receptor antibodies were positive. The NT-proBNP was 1360 ng/L which was significantly elevated and the C-reactive protein was 48.4 mg/L.

On ultrasound the thyroid gland appeared diffusely enlarged with no visible nodes or masses. Cardiac echography was normal and excluded cardiomyopathy and underlying valvulopathy. This was in keeping with high cardiac output failure. Sonography of the fetus showed a viable fetus with a heart rate of 137 beats/minute.

The diagnosis of a thyroid storm was made and the patient was admitted to the medical intensive care unit for management. She was immediately started on carbimazole 60 mg, propranolol 40 mg and Lugol's iodine. Intravenous co-amoxiclavulanic acid was started as treatment for a possible hospital-acquired pneumonia. Intravenous furosemide was given for the pulmonary oedema. The patient unfortunately went into spontaneous labour and a stillborn fetus was delivered. The mother was stabilised and discharged from hospital 12 days later.

### Discussion

Even though thyroid storm is rare, hyperthyroidism in pregnancy is not, with reported prevalence rates ranging from 0.1% to 0.4%.<sup>1,2</sup> Graves' disease is the most common form of hyperthyroidism and accounts for 85% of all cases of hyperthyroidism during pregnancy.<sup>3</sup> Graves' disease usually becomes less active during the late stages of pregnancy. This is possibly due to a change in the activity of TSH receptor antibodies from stimulatory to blocking.<sup>3,4</sup>

Maternal hyperthyroidism is associated with an increased risk of pre-eclampsia, maternal heart failure, spontaneous abortion or fetal loss, preterm delivery, stillbirth and low birth weight.<sup>3,5</sup> The risk of complications for both the mother and the fetus is related to the duration and control of maternal hyperthyroidism. In patients were

the thyrotoxicosis is correctly treated and controlled, the prognosis is usually excellent, but in those patients who remain hyperthyroid, maternal and fetal complications are increased. Thyroid storm is an acute, life-threatening manifestation of thyrotoxicosis. Approximately 1% of pregnant patients with hyperthyroidism will progress to a thyroid storm.<sup>6</sup> This can be fatal if unrecognised or left untreated. Even with aggressive early treatment the mortality of a thyroid storm is 20%.<sup>7</sup>

A thyroid storm is often precipitated by a physiological stressful event such as trauma, infection or surgery.<sup>8</sup> In pregnancy a few cases of a thyroid storm precipitated by pre-eclampsia, labour and Caesarean section have been reported.<sup>1</sup> A thyroid storm has also been reported to be precipitated by discontinuation of antithyroid drugs.<sup>7</sup>

Patients can present with a wide variety of signs and symptoms. The cardiovascular findings on clinical evaluation include the presence of tachycardia, supraventricular arrhythmias or cardiac failure.<sup>6,9</sup> Neuropsychiatric manifestations include irritability, agitation, psychosis, tremor, confusion or alteration in mental status. Gastrointestinal symptoms such as diarrhoea, nausea and vomiting could also be present. The hyper-metabolic state results in increased heat production, with features of hyperpyrexia and increased perspiration.<sup>7</sup>

The diagnosis is usually made on the basis of the clinical features alone since it is difficult to obtain rapid laboratory or nuclear medicine tests confirming hyperthyroidism. Burch and Wartofsky have outlined criteria for the diagnosis of a thyroid storm.<sup>9</sup> The Burch and Wartofsky Score allows for quantifying the probability of and assessing the severity of a thyroid storm (see Table I) Our patient achieved a score which was highly suggestive of a thyroid storm. Laboratory test are also not helpful in making the diagnosis of a thyroid storm, because the serum thyroxine and thyroid stimulating hormone levels are the same as those of uncomplicated hyperthyroidism.

Management of a thyroid storm during pregnancy requires special attention and treatment due to the adverse effects on the pregnancy and fetus.<sup>10</sup> A thyroid storm is a medical emergency and requires early recognition and aggressive treatment. Treatment is aimed at the suppression of synthesis and release of thyroid hormones, symptomatic control of the hypermetabolic state and full supportive management in an intensive care unit.

The antithyroid drugs available are the thionamides propylthiouracil, methimazole and carbimazole (which is metabolised to methimazole). These are all effective and have all been used during pregnancy.<sup>10,11</sup> Thionamides block thyroid hormone synthesis within one to two hours after administration. Propylthiouracil is the drug of choice in pregnancy, based on expert consensus recommendation.<sup>1,3</sup> It has been shown in recent studies that propylthiouracil and methimazole cross the placenta equally and result in an equal chance of inducing fetal or neonatal hypothyroidism.<sup>12</sup> There have, however been reports of teratogenic effects associated with the long term use of methimazole, mostly aplasia cutis and choanal or oesophageal atresia.<sup>1,12</sup> If propylthiouracil is not available (as in South Africa), treatment with carbimazole is acceptable<sup>3</sup> as the potential maternal or fetal risks and the complications due to untreated hyperthyroidism outweighs the risk of congenital abnormalities occurring due to treatment. Carbimazole is given initially as 40 mg three times a day,

Table I: Diagnostic criteria for thyroid storm<sup>9</sup>

Thermoregulatory dysfunction		Cardiovascular dysfunction	
Temperature:	Points:		
< 37.7 ° C	5	Tachycardia:	Points:
37.8–38.3° C	10	99–109	5
38.4–38.8° C	15	110–119	10
38.9–39.4° C	20	120–129	15
39.4–39.9° C	25	130–139	20
> 40 ° C	30	> 140	25
Central nervous system effects		Congestive cardiac failure	
Mild	10	Mild	5
- Agitation		- Pedal oedema	
Moderate	20	Moderate	10
- Delirium		- Bibasilar rales	
- Psychosis		Severe	15
- Extreme lethargy		- Pulmonary oedema	
Severe	30	Atrial fibrillation	10
- Seizures			
- Coma			
Gastrointestinal/hepatic dysfunction		Suggestive/precipitant history	
Moderate	10	Negative	0
- Diarrhoea		Positive	10
- Nausea / vomiting			
- Abdominal pain			
Severe	20		
- Unexplained jaundice			

A score of 45 or more is highly suggestive of a thyroid storm; a score of 25 to 44 supports the diagnosis; a score of less than 25 makes a thyroid storm unlikely.

followed by 40 mg daily. This can be decreased to 20 mg daily or less once the disease is under control.<sup>11</sup> This could be given via a nasogastric tube if the patient is unable to take medicine orally.

High concentrations of iodine are given to inhibit release of stored thyroid hormone from the thyroid gland. It is usually given as potassium iodide, such as Lugol's solution, 10 drops three times daily.<sup>13</sup> This should be given at least one hour after thionamide administration to prevent stimulation of new thyroid hormone synthesis. Beta-blockers are used to inhibit the adrenergic effects of excessive thyroid hormone on the cardiovascular system. Propranolol is used as initial therapy and is given either intravenously 6 mg (1 to 2 mg every 5 minutes) followed by 1 to 10 mg every 4 hours, or orally 20 to 80 mg every 4 to 6 hours.<sup>6,11</sup> It can also be administered via nasogastric tube. The use of glucocorticosteroids in a thyroid storm improves patient outcome. It prevents peripheral conversion of T4 to T3 and may have an effect on the underlying autoimmune disease. Glucocorticosteroids are also effective in preventing the potential development of adrenal insufficiency.<sup>11</sup> Dexamethasone 2 mg 6 hourly or hydrocortisone 100 mg 8 hourly have been used.

If sedation is required, barbiturates are most often used to reduce agitation, because it increases the catabolism of thyroid hormone. In addition, other supportive measures should be undertaken which

include oxygen, intravenous fluids and correction of electrolyte imbalance, and nutritional support.<sup>13</sup> Antipyretics, preferably paracetamol, should be given to control the temperature. Salicylates should be avoided in thyrotoxicosis, because it decreases thyroid hormone protein binding, causing an increase in free thyroid hormone levels.<sup>7,9</sup> Other measures include tepid water sponge bathing and using cooling blankets. Close assessment and continuous maternal cardiac monitoring in an intensive care setting is required.<sup>13</sup>

Fetal well-being should be evaluated sonographically and continuous cardiotocographic monitoring of the fetus is required after 28 weeks of gestation. It is advised to avoid delivery during a thyroid storm, unless the fetal condition demands immediate delivery.<sup>6</sup> After the crisis, patients should be kept in hospital until delivery or until the cardiovascular and metabolic functions have normalised.

Fetal hyperthyroidism occurs in about 1–5% of cases where the mother has hyperthyroidism due to Graves' disease.<sup>14,15</sup> This is due to transplacental crossing of maternal thyroid receptor antibodies with stimulation of the fetal thyroid. This presents with features of fetal hyperthyroidism such as tachycardia, intra uterine growth retardation, small for gestational age babies, advanced bone age and the development of a fetal goitre.<sup>14</sup> Cardiac failure and hydrops foetalis are features of severe disease.<sup>15</sup>

Neonatal hyperthyroidism presents with symptoms of irritability, tachycardia, poor feeding and failure to thrive. In severe neonatal cases respiratory distress, hyperthermia, hypertension, arrhythmias, cardiac failure and death may occur. If the mother has been treated with antithyroid drugs, the symptoms of neonatal thyrotoxicosis are often not evident at birth and clinical signs only occur 5 to 10 days later, when the drug level decreases in the neonate's circulation.<sup>3,15</sup>

## Conclusion

Thyroid storm is a rare and often fatal presentation of hyperthyroidism. It contributes to significant risk in pregnant women with hyperthyroidism. It can be precipitated by trauma, infection, pre-eclampsia, labour, Caesarean section and by discontinuation of antithyroid drugs.

Early recognition and aggressive treatment is fundamental in limiting the maternal, fetal and neonatal morbidity and mortality associated with this condition. Even with aggressive early treatment the mortality of a thyroid storm can be as high as 20%.

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