Case report: a patient with thyroid storm, refractory cardiogenic shock, and cardiac arrest treated with Lugol’s iodine solution and veno-arterial extra corporal membrane oxygenation support

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Background
Thyroid storm is a life-threatening condition. Refractory cardiogenic shock and cardiac arrest are rare complications of thyroid storm and the treatment options are limited.

Case summary
A 35-year-old woman treated for Grave’s disease was admitted with thyrotoxicosis complicated by infection and neutropenia caused by thionamide treatment. After treatment including beta-blockers, steroids, and Lugol’s iodine solution, she went into cardiac arrest. Echocardiography after resuscitation demonstrated severe biventricular heart failure. The patient was in refractory cardiogenic shock with recurrent cardiac arrest and mechanical circulatory support with a veno-arterial extra corporal membrane oxygenation (V-A ECMO) circuit was established. After 2 days on V-A ECMO and supportive treatment with iodine solution, glucocorticosteroids, and levosimendan, her myocardial function recovered and thyroid hormone levels were normalized. Veno-arterial extra corporal membrane oxygenation was discontinued, and the patient was treated with early total thyroidectomy. The patient made a full recovery with no neurological/cognitive impairment, as assessed after 4 weeks.

Discussion
Adverse reactions to standard treatment of hyperthyroidism contributed to this patient’s development of thyroid storm and the following refractory cardiogenic shock. When she was critically unstable, levosimendan improved myocardial function while inotropic support with dobutamine was ineffective, likely due to prolonged beta-antagonist administration. Temporary support with V-A ECMO, until effective lowering of thyroid hormone levels and improvement in myocardial function were obtained, was life-saving in this young patient and may be considered in refractory cardiogenic shock caused by thyroid storm.

Keywords
Case report • Thyrotoxicosis • Cardiogenic shock • Cardiac arrest • Veno-arterial extracorporeal membrane oxygenation • Levosimendan
Primary specialties involved other than cardiology
Anesthesiology, Intensive care medicine, Endocrine surgery.

Introduction
Hyperthyroidism affects the heart and the peripheral vasculature by increasing blood volume, heart rate, contractility, cardiac output, and decreasing systemic vascular resistance. Pulmonary hypertension may also be associated with hyperthyroidism and is a contributing cause of right-sided heart failure in these patients. Thyroid storm is an extreme form of hyperthyroidism with heart failure as the leading cause of mortality and a mortality rate as high as 30% in patients developing cardiogenic shock.

Timeline

| Day    | Event Description |
|--------|-------------------|
| Two years before admission | Diagnosed with autoimmune hyperthyroidism. Received treatment with stand-alone thionamide (carbimazole) for two months before it was discontinued due to neutropenia. |
| Four weeks before admission | Signs and symptoms of hyperthyroidism (free thyroxine (T4): 79 pmol/L, free triiodothyronine T3: 47 pmol/L), prescription of thionamide and a non-selective beta-blocker. |
| Two days before admission | Thionamide was discontinued again due to neutropenia. |
| Day 0 | Admitted to her local hospital with fever, tachycardia, neutropenia, tonsillitis, suspected sepsis and a diagnosis of thyroid storm. |
| Day 1-3 | Treatment with beta-blocker, antibiotics, glucocorticoids and (commencing on day 3) iodine solution. |
| Day 4 | Sudden circulatory collapse with pulseless electrical activity (PEA). Cardiopulmonary resuscitation (CPR) was started and return of spontaneous circulation (ROSC) was obtained after 4 minutes. Transferred to tertiary care university hospital. Echocardiography demonstrated severe biventricular cardiac failure (severely hypokinetic left ventricle with ejection fraction <20%). Inotropic support with dobutamine was ineffective. Recurrent cardiac arrests, with PEA. Established on V-A ECMO support. Iodine solution dosages were increased and levosimendan infusion was started. |
| Day 7 | Complete recovery of myocardial function. V-A ECMO circuit was discontinued and she was extubated the next day. |
| Day 12 | Surgery with total thyroidectomy. |
| Day 28 | Discharged without cognitive sequelae and with normalized cardiac function. Close follow-up by endocrinologist. |

Case presentation
The patient, a 35-year-old woman without prior heart disease or other comorbidities, was diagnosed with autoimmune hyperthyroidism (Grave’s disease) 2 years before the current event. She received standard treatment with thionamides (carbimazole) for 2 months after being diagnosed with Grave’s. Carbimazole was the discontinued due to development of neutropenia. The patient had untreated Grave’s disease for 2 years. Increased thyrotoxic symptoms forced her to see a doctor. Grave’s disease was again diagnosed (Free T4: 79 pmol/L, free T3: 47 pmol/L, and TRAB-thyroid receptor antibody were high). Treatment was started with carbimazole 10 mg twice daily and a non-selective beta-blocker (propranolol 20 mg 1–2 tablets daily).

One month later, 2 days after discontinuation of carbimazole due to recurring severe neutropenia, she was admitted to her local hospital. At the time of admission, she had high fever, sinus tachycardia (heart rate 110 beats per minute), and general fatigue. Physical examination revealed normal auscultation of the heart and lungs. A diagnosis was made of thyroid storm and a suspected neutropenic sepsis (leucocytes 0.8 × 10⁹/L (ref. 3.5–10.0 × 10⁹/L) and neutrophils 0.0 × 10⁹/L (ref. 1.5–7.3 × 10⁹/L)) related to clinical signs of tonsillitis. Treatment with broad-spectrum antibiotics (penicillin 3 g four times daily and gentamicin 240 mg once daily, both intravenous), high dosage of glucocorticosteroids (hydrocortisone 100 mg four times daily intravenously), and increased dosage of the non-selective beta-blocker propranolol (20 mg four times daily) was initiated. Lugol’s iodine solution (4.5 mg three times daily) was added to the treatment on Day 3. High fever and tachycardia were still present. On the fourth day after admission, acute dyspnoea developed together with circulatory collapse and subsequent cardiac arrest with pulseless electrical activity (PEA). Cardiopulmonary resuscitation (CPR) was started, and a return of spontaneous circulation (ROSC) was obtained after 4 min. After ROSC, she remained severely hypotensive (blood pressure 60/40 mmHg) with sinus tachycardia. She was transferred to the university hospital in a critical unstable state.

Learning points
• Refractory cardiogenic shock with cardiac arrest is a rare complication of thyroid storm
• Extracorporeal life support in combination with iodine treatment may be a treatment option in severe cases
On arrival at the university hospital’s emergency department the initial clinical examination revealed a conscious, but cognitively impaired patient, respiratory rate of 30–50 per minute, blood pressure 60/40 mmHg, heart rate 120 beats per minute, temperature 37.8°C, normal respiratory sounds, Graves’ ophthalmopathy, and arterial blood gas showed severe lactic acidosis (lactate 17 mmol/L (ref. 0.4–0.8 mmol/L), pH 7.2 (ref. 7.35–7.45) pCO2 2.9 kPa (ref. 4.7–6.0 kPa), and pO2 19 kPa (ref 10.0–14. kPa).

Acute pulmonary embolism was suspected as the cause of the cardiac arrest. Bedside echocardiography demonstrated severe biventricular cardiac failure (left ventricular ejection fraction <20%) with the paradoxical movement of the septum (Figure 1A and B) and tricuspid regurgitation. Pulmonary embolism could not be excluded based on these findings and computed tomography (CT) pulmonary angiography was indicated but was not performed immediately due to the prohibitive requirement for iodine-containing contrast agents in this setting. Due to the patient’s clinical instability, thrombolysis was given to cover for the possibility of pulmonary embolism. Eventually, a CT scan was performed in the emergency department and pulmonary embolism was excluded.

The patient was transferred to the intensive care unit (ICU) in cardiogenic shock with ongoing circulatory support with high doses of norepinephrine, dobutamine, and phenylephrine. Immediately after arriving to the ICU, the patient experienced recurrent episodes of cardiac arrest with PEA with the only temporary effect of CPR.

As the patient was severely haemodynamically unstable due to refractory cardiogenic shock and recurrent cardiac arrest caused by the thyroid storm, the decision was made for a mechanical circulatory support by a veno-arterial extra corporal membrane oxygenation (V-A ECMO) circuit. Support on V-A ECMO was established without complications. Coronary angiography demonstrated normal coronary arteries and an intra-aortic balloon pump (IABP) was inserted. The thyroid storm was treated pharmacologically with escalating doses of iodine solution (Lugol’s iodine solution 22 mg three times daily) and glucocorticoids (hydrocortisone 100 mg four times daily intravenously). Rapid normalization of thyroid hormone levels was obtained (Figures 2A and 3B). Beta-blockers were discontinued and levosimendan was commenced on the theoretical consideration of an enhanced inotropic effect compared to conventional β-adrenergic agonists. Myocardial function recovered rapidly (Figure 3A and B). After 3 days, V-A ECMO was discontinued, and the patient was extubated the next day. Uneventful total thyroidectomy was performed 5 days later. The patient was discharged after 4 weeks of hospitalization without cognitive sequelae, without any symptoms of heart failure, with normalized myocardial function as judged by echocardiography, and with scheduled close follow-up by endocrinologist.

Discussion

We herein report on a patient in cardiogenic shock with cardiac arrest due to thyroid storm who was successfully treated with temporary support on V-A ECMO, Lugol’s iodine solution, and surgical thyroidectomy. Cardiogenic shock and cardiac arrest are extremely rare complications of thyrotoxicosis and associated with high mortality, but as demonstrated here, with a potential for complete recovery of myocardial function with excellent prognosis if the patient survives the critical phase. Standard treatment of thyrotoxicosis with non-selective beta-blockers may be detrimental in patients developing heart failure with severely reduced stroke volume due to their negative inotropic and chronotropic effect in a situation where heart rate is critical to maintain cardiac output.

Beyond beta-blockers, standard treatment for autoimmune hyperthyroidism includes thionamides. Our patient developed agranulocytosis, a rare (0.2–0.5%) adverse effect. Occurrence of agranulocytosis mandates immediate discontinuation of the drug and administration of broad-spectrum antibiotics. The patient was in need of rapid reduction of the markedly elevated thyroid hormones. Glucocorticoids inhibit the conversion of T4 to T3 and are indicated...
Lugol’s iodine solution rapidly decreases thyroid hormone levels and reduces glandular blood flow. The role of iodine here is worthy of further comment: when our patient acutely deteriorated a CT scan was warranted to exclude pulmonary embolism. Administration of iodine-containing contrast is usually contraindicated in thyrotoxicosis due to the risk of worsening hyperthyroidism. Iodine administration to patients with latent or manifest thyroid disease may have a two-fold effect: early on and within hours, high-dose iodine administration blocks the release of thyroid hormones and inhibits the iodination of thyroglobulin. Since this rapid effect of iodine on lowering thyroid levels usually is transient, only short-term use is recommended. As iodine also is a substrate for new thyroid hormone formation, iodine given over time may lead to hypersecretion of thyroid hormones, usually developing over 2–12 weeks. Since Lugol’s solution also reduces blood flow within the gland, it is used preoperatively before thyroidectomy. When our patient became critically unstable with cardiogenic shock, she was non-responsive to inotropic support with dobutamine. Dobutamine is an inotropic with an affinity for β1-adrenergic receptors and was probably ineffective due to concomitant use of high dosages of propranolol. The α1-adrenergic receptor agonists norepinephrine and phenylephrine had minimal effects on blood pressure in this case. The binding affinities of individual catecholamine’s may be diminished under extreme situations with hypoxia.
and/or acidosis and our patient had severe lactic acidosis [lactate 17 mmol/L (ref. 0.4–0.8 mmol/L)]. Hyperthyroidism may directly reduce systemic vascular resistance through arterial smooth muscle relaxation. In addition, preclinical data suggest that thyroxine may attenuate the \(\alpha_1\)-receptor-mediated vasoconstrictory effect of adrenaline on the vasculature.

The mechanisms underlying the rapid development of severe myocardial dysfunction and cardiogenic shock in our patient are complex and not fully understood. A combination of myocardial dysfunction and reduced diastolic filling time secondary to sustained tachycardia resulting in a hyperdynamic cardiocirculatory state, a negative inotropic effect of beta-blocker administration in a setting with severely reduced stroke volume, and finally, a direct vasoplegic effect of thyroxine resulting in low systemic resistance may have contributed to the clinical scenario.

Here, treatment with Lugol’s iodine solution resulted in rapid decrease in free T3 levels. While hemodynamic support was maintained by V-A ECMO and IABP, stroke volume improved gradually (Figure 3A and B). Levosimendan infusion was added in an attempt to further augment contractility. Levosimendan is believed to mediate an inotropic effect through calcium sensitization in addition to phosphodiesterase-3 inhibition, is not affected by beta-blockade and may facilitate weaning from V-A ECMO. Fortunately, our patient responded rapidly to the above treatment, and was only supported by V-A ECMO for 3 days. The definitive treatment of her hyperthyroidism was a total thyroidectomy which was performed without complications. Levothyroxine substitution was started, cardiac function recovered completely, and the patient was discharged without cognitive sequelae or symptoms of heart failure. The potential for complete normalization of myocardial function is a crucial factor in determining whether one should initiate V-A ECMO treatment as a bridge to recovery in similar severe cases of thyroid storm and cardiogenic shock.

Lead author biography

Marianne Voll, MD, graduated from Semmelweis University, Budapest, in 2012. Since then she has worked in her home country Norway as a resident in internal medicine and cardiology at Notodden Hospital, then as a resident in internal medicine at Bærum Hospital and now she is a resident in cardiology at Oslo University Hospital, Ullevål. Her field of interest is acute cardiovascular care, including cardiogenic shock, cardiac arrest, and acute heart failure.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

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