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Getting around the gut: a unique management challenge of thyroid storm precipitated by amphetamine-associated duodenal ischaemia leading to compromised enteric absorption

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SUMMARY
Thyroid storm is a rare, life-threatening endocrine emergency with a high mortality rate of up to 30%. We present a unique management challenge of a critically ill patient who developed thyroid storm in the setting of duodenal perforation from amphetamine-associated non-occlusive mesenteric ischaemia. The diagnosis of ‘thyroid storm’ was made based on clinical criteria and a Burch-Wartofsky score of 100. During emergent exploratory laparotomy, a 1 cm duodenal perforation with surrounding friable tissue was found and repaired. Intraoperatively, a nasogastric tube was guided distal to the area of perforation to allow for enteric administration of medications, which was critical in the setting of thyroid storm. Therapeutic plasma exchange achieved biochemical control of our patient’s thyroid storm but ultimately did not prevent in-hospital mortality.

BACKGROUND
Inadequate early management of thyroid storm has a high associated mortality rate of 30%.1 Acute management of thyroid storm relies on the enteric administration of thionamides and adjuvant iodine to reduce thyroid hormone production. Intravenous formulations of thionamides are not available in the USA and are only offered in some European countries.2 3 Thus, when the precipitating event for thyroid storm compromises the gastrointestinal (GI) tract, enteric administration of thionamides is ineffective and alternative strategies must be considered.

We present a case of a patient who presented to the emergency department (ED) with acute abdominal pain in the setting of active methamphetamine use. The clinical presentation and management were complicated by subclinical duodenal perforation and the development of acute thyroid storm and rapid clinical deterioration. Enteric administration of thionamides was compromised and therapeutic plasma exchange (TPE) was initiated emergently with improved clinical and biochemical response.

CASE PRESENTATION
A 40-year-old woman with Graves’ Disease with recurrent hospitalisations for thyrotoxicosis, atrial fibrillation, medication non-adherence and active methamphetamine use presented to the ED with acute abdominal pain, nausea and watery emesis. She was not taking her methimazole due to her active substance abuse, depression and recent homelessness.

On physical examination, the patient was initially alert and oriented. Vital signs were remarkable for tachycardia (atrial fibrillation with rapid ventricular response) without fever or hypotension. Her thyroid gland was enlarged on palpation, and her abdomen was diffusely tender to palpation, but without evidence of rebound or guarding.

INVESTIGATIONS
Abdominal CT angiography showed patent gut vasculature, mesenteric oedema and free fluid but no extraluminal air or bowel thickening to suggest mesenteric ischaemia or gross perforation (figure 1). Laboratory tests revealed a thyroid-stimulating hormone of <0.02 uIU/mL (reference range: 0.35–3.30 uIU/mL), free T4 5.69 ng/mL (reference range: 0.56–1.64 ng/mL) and urine toxicology positive for amphetamines. The patient was admitted to the general medicine service with a diagnosis of thyrotoxicosis. Her Burch-Wartofsky (see table 1) score was 35. Treatment with oral methimazole and propranolol was initiated.

However, within 2 hours of admission, the patient developed increased work of breathing and was in acute respiratory distress. She then became obtunded with a Glasgow Coma Scale of 3 (no eye opening, verbal or motor response) requiring emergent endotracheal intubation and transfer to the medical intensive care unit (ICU). During the first attempt at endotracheal intubation, the esophagus was briefly intubated; however, successful endotracheal intubation was achieved on the second attempt. Severe abdominal distention was noted immediately following intubation. Chest X-ray showed massive pneumoperitoneum (figure 2), suggesting acute gastric or duodenal perforation not previously detected on her initial abdominal CT scan. We suspected that the brief esophageal intubation unmasked and accentuated her pre-existing gut perforation.

Soon after intubation, the patient was diagnosed with shock requiring multiple vasoactive infusions. Her lactic acid was also elevated to 8.5 mmol/L. On bedside point-of-care echocardiogram, she was found to have a new and reduced left ventricular ejection fraction of 25%. A prior baseline echocardiogram had revealed a normal ejection fraction several years prior to admission. Her recalcualted...
Case report

Figure 1  Abdominal CT angiography showing patent gut vasculature, mesenteric edema and free fluid but no extraluminal air or bowel thickening to suggest mesenteric ischaemia or gross perforation.

Burch-Wartofsky score was 100 supporting a diagnosis of thyroid storm (see table 1).

TREATMENT

Due to concern for unreliable oral absorption of antithyroid therapies and the danger of blindly inserting a nasogastric (NG) tube in setting of a perforated viscus, we opted not to administer oral thionamides and instead began rectal propylthiouracil (PTU) enemas (400 mg dose). Intravenous hydrocortisone and propranolol were also administered to prepare the patient for emergent surgery. Despite optimal medical therapy, the patient continued to require multiple vasopressors and a decision was made to proceed with exploratory laparotomy on hospital day 2.

Exploratory laparotomy revealed a 1 cm duodenal perforation with surrounding friable tissue that was repaired with an omental patch. Intraoperatively, an NG tube was inserted and manually guided distal to the repaired perforation and into the third portion of the duodenum. This was performed to allow for safe enteral administration of medications. Given the patient’s tenuous status in the setting of thyroid storm, she was returned to the ICU with a temporary abdominal closure.

Oral administration of PTU was resumed at a dose of 250 mg using her intraoperatively placed NG tube. After 24 hours of PTU administration, five drops of potassium iodide 250 mg were also administered to block the release of preformed thyroid hormone. Two days after the initial exploratory laparotomy with duodenal repair, the patient underwent intraoperative re-exploration and washout. She was found to have a 25 cm segment of non-viable ileum that was resected. The H&E sections of the ileum were notable for inflammatory infiltrate, epithelial sloughing, increased density of blood vessels, serositis and perivascular lymphocytic cuffing suggestive of acute ischaemic changes (figure 3). No thrombi or emboli were observed within the vessels, supporting a diagnosis of non-occlusive mesenteric ischaemia.

Despite these measures, her Burch-Wartofsky score increased to 120 and she subsequently developed shock liver and disseminated intravascular coagulation (DIC). Due to her overall deteriorating clinical status, we decided to initiate TPE on hospital day 3. The patient received plasmapheresis treatments on hospital days 3 and 5 each replaced with plasma and 5% human albumin.

OUTCOME AND FOLLOW-UP

After having completed two sessions of TPE, the patient’s shock resolved and she was weaned off all vasoactive infusions. Free T4 dropped to 1.75 ng/mL (reference range: 0.56–1.64 ng/mL) and free T3 to 3.9 pg/mL (ref range: 1.7–3.7 pg/mL). Her Burch-Wartofsky score dropped to 85 (figure 4).

Unfortunately, her hospital course was complicated by DIC and recurrent severe GI bleeding refractory to embolisation and repeated surgical exploration. She suffered cardiac arrest, and despite successful resuscitative efforts and return of spontaneous

Table 1—Calculated Burch-Wartofsky scores before (A) and after (B) the precipitating event of thyroid storm from methamphetamine-associated non-occlusive gut ischaemia

<table>
<thead>
<tr>
<th>Temperature (°F)</th>
<th>Cardiovascular dysfunction</th>
<th>Central nervous system effects</th>
<th>Gastrointestinal- hepatic dysfunction</th>
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</thead>
<tbody>
<tr>
<td>99–99.95 (A,B)</td>
<td>Tachycardia (beats/min)</td>
<td>Absent 0 (A)</td>
<td>Absent 0 (A)</td>
</tr>
<tr>
<td>100–100.910</td>
<td>99–109 5</td>
<td>Mild (agitation) 10</td>
<td>Mild (pedal oedema) 10</td>
</tr>
<tr>
<td>101–101.915</td>
<td>110–119 10 (A)</td>
<td>Moderate (delirium, psychosis extreme lethargy 20)</td>
<td>Moderate (bibasilar rales) 10</td>
</tr>
<tr>
<td>102–102.920</td>
<td>120–120 15</td>
<td>Severe (seizure, coma) 30 (B)</td>
<td>Severe (pulmonary oedema) 15 (B)</td>
</tr>
<tr>
<td>≥104 30</td>
<td>≥140 25</td>
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<tr>
<td></td>
<td>Atrial fibrillation</td>
<td>Present 10 (A,B)</td>
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<tr>
<td></td>
<td>Absent 0</td>
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<td></td>
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<tr>
<td></td>
<td>Moderate (diarrhoea, nausea vomiting, abdominal pain) 10 (A,B)</td>
<td>Positive 10 (B)</td>
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<td></td>
<td>Severe (unexplained jaundice) 20</td>
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A: Initial Burch-Wartofsky score 35
B: Two hours after admission Burch-Wartofsky score 100

Figure 2  Chest X-ray showing pneumoperitoneum suggesting acute gastric or duodenal perforation not previously detected on her initial abdominal CT scan.

Case report

circulation, she showed no evidence of neurologic recovery. Following goals-of-care discussion with family, life-sustaining therapies were withdrawn and the patient expired on hospital day 16.

DISCUSSION

Thyroid storm is a life-threatening complication of thyrotoxicosis that requires rapid diagnosis and prompt, aggressive management. Distinguishing severe thyrotoxicosis from thyroid storm is difficult to establish because thyroid hormone levels do not directly correlate with the severity of disease as shown in our patient (figure 4). As a result, Burch and Wartofsky developed a standardised scoring system to assess the likelihood of thyroid storm based on clinical criteria that include hyperthermia, altered mental status as well as cardiovascular, GI and hepatic dysfunction. On initial presentation, our patient had a Burch-Wartofsky score of 35, indicating she was at risk for impending thyroid storm. We began treatment with methimazole and propranolol with the goal of starting iodide therapy at least 1 hour after thionamide administration to prevent the release of preformed thyroid hormone as part of conventional management of severe thyrotoxicosis.

Subsequently, her hospital course was complicated by an acute duodenal perforation, which we suspect was secondary to non-occlusive mesenteric ischaemia in the setting of active methamphetamine use. This presumption is supported by our pathologic findings showing microvascular ischaemic changes without macrovascular mesenteric occlusion seen on imaging (see figures 1 and 3) and a positive urine toxicology for amphetamines on presentation. Methamphetamine use can also induce thyroid storm indirectly by stimulating a rise in intracellular catecholamine concentrations, thereby increasing the amount available for release and directly by stimulating the release and inhibiting the reuptake of catecholamines creating the perfect environment required to potentiate thyroid storm.

We suspect the confluence of her active methamphetamine use, non-adherence to her methimazole, followed by the sudden duodenal perforation precipitated our patient’s thyroid storm. The pathophysiology of thyroid storm is not fully understood; however, it usually accompanies a sudden precipitating event that leads to a surge in free thyroid hormone creating a disproportionate increase in metabolic demand, resulting in multiple organ dyscrasias. Known precipitants of thyroid storm include irregular use or discontinuation of antithyroid drugs, infection, diabetic ketoacidosis, severe emotional stress, trauma, labour and drugs including amiodarone and methamphetamine.

In this case, we were also faced with a unique management challenge of treating thyroid storm when enteric administration of conventional antithyroid therapies was compromised. During operative repair, the surgeons placed a NG tube distal to the perforated segment of duodenum to allow for continued enteric administration of antithyroid medications (which are first-line therapies). Despite this, our patient continued to require multiple postoperative vasopressors, thus worsening her underlying mesenteric ischaemia and potentially limiting enteric absorption of antithyroid agents. As a result, TPE was initiated on hospital day 3 as adjuvant therapy.

TPE works by exchanging the patient’s plasma with new plasma and albumin before reinfusion. As a result, TPE removes thyroid hormones bound to serum proteins (accounting for 99% of serum thyroid hormones), cytokines, catecholamines and autoantibodies in the blood. Additionally, the new plasma and albumin bind the T3 and T4 that acts peripherally in the blood. Our apheresis team gave 2 L of plasma with 5% human albumin with each TPE session. Subsequently, our patient’s thyroid hormone profile improved as did her haemodynamics, which was crucial for better management of acute mesenteric ischaemia.

According to the American Society of Apheresis, TPE is currently a grade IIC, category III indication for thyroid storm due to the lack of prospective data supporting its use. Based on a large retrospective review of the Ichushi database, which evaluated 63 cases of thyroid storm treated with TPE from 1953 to 2015, patients who were treated with TPE, showed...
improvement in clinical symptoms, but still had a high mortality rate of 17.4%. However, there have been subsequent case reports showing the benefit of TPE for patients who may not tolerate or are not responding to conventional medical therapy for thyroid storm. For example, Muller et al reviewed 126 case reports of thyroid storm and found that TPE was successfully administered for indications including thyroid storm complicated by acute liver failure, agranulocytosis associated with antithyroid drugs, failure to improve after 24–48 hours after conventional management, preparation before thyroidectomy or other surgery, severe Graves ophthalmopathy and pregnancy.

Furthermore, the optimal time of initiation and frequency of TPE has not been studied in detail. Both the American Thyroid Association and Japanese Thyroid Association report a ‘weak’ recommendation based on case report data to consider TPE if there is no clinical improvement based on hyperthermia, tachycardia and altered level of consciousness within 24–48 hours of initial treatment. TPE conducted daily as opposed to every other day also showed improved outcomes based on case report data. For our patient, we decided to delay her TPE by 1 day in between the first and second sessions given a rising lactic acidosis in the setting of bowel ischaemia requiring prompt removal of the dying bowel as a first priority. However, based on prior case reports using TPE in preparation for surgery, we could have considered providing TPE as a bridge to her surgeries.

The overall incidence of (mostly reversible) complications from TPE is estimated to be approximately 5%. These include transfusion reactions, vasovagal or hypotensive reactions, respiratory distress and seizures. The associated costs of TPE including equipment, nursing staff, replacement fluids for up to

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**Learning points**

- Early recognition and prompt management of thyroid storm is crucial.
- Many antithyroid therapies rely on absorption from the gastrointestinal (GI) tract. However, when the GI tract is compromised, conventional medical therapies may be ineffective. Multidisciplinary care including surgical consultation and therapeutic plasma exchange (TPE) should be considered in a timely fashion.
- Although TPE may lead to a marked improvement in biochemical and clinical responses with initial administration, therapy may not result in a favourable patient outcome. Overall mortality remains relatively high.

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**Patient’s perspective**

Unfortunately, the patient had expired and was unable to comment on the case. Patient’s durable power of attorney and friend, who was appropriately grieving, was contacted about the case report publication. The durable power of attorney and friend was glad we were working on this case report in order to provide information on ways to provide better care for other patients with similarly complex medical issues.
five procedures have been estimated to be approximately $4,638 US dollars. When conventional management is not successful or not applicable, the decision to use TPE should be selective, based on patient comorbidities, potential complications of treatment and the timing relative to other treatments and procedures.

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Contributors JSGL was the medical intern involved in the patient’s care and was responsible for collecting and analysing the patient data, curating the table and figures, searching relevant existing literature on the management of thyroid storm including guidelines and case reports, and was the first author of the case report primarily responsible for the writing the manuscript of the case report. AAZ was senior attending for the patient’s care and was the senior author for the case report who was the final reviewer of the case report assisting with editing the manuscript and providing relevant recommendations on discussion points within the manuscript. IEB provided information on the patient’s surgical management as the primary surgeon involved in the case and assisted with reviewing and editing the manuscript. AMS was the primary endocrinologist involved in the patient’s care and provided recommendations on relevant guideline-based care of thyroid storm and assisted in reviewing and editing the manuscript as well.

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REFERENCES