A CASE OF HYPOTHERMIA SECONDARY TO UNDIAGNOSED HYPOTHYROIDISM IN A RURAL SETTING

By: Kayla Neumann (Med 2)

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Supervisors: Dr. Melissa Caswill, Dr. Margie Hesom & Dr. Heather Lehmann

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Abstract

While accidental hypothermia from exposure is a more common presentation, hypothermia induced by another medical condition is less widely witnessed[1]. Here we report a case of a patient presenting with odd behaviour and shivering in the ED. The patient was found to have a core body temperature of 34 °C, as well as serum TSH and T4 levels of 22 mU/L and 3.1 pmol/L respectively. This patient's treatment, while successful, was more complex due to her atypical presentation of hypothermia as part of a myxedema coma, due to underlying severe, primary hypothyroidism.

Introduction

Hypothermia is termed as an involuntary drop in core body temperature below 35 °C[2]. Hypothermia is typically staged by core body temperature with the three stages being: mild (32 - 35 °C), moderate (28 – 32 °C) and severe (< 32 °C)[1]. Hypothermia can be categorized into one of two types of pathophysiology: primary exposure to cold, or secondary impairment of thermoregulation due to underlying disease. The mortality of patients admitted to hospital with moderate to severe accidental hypothermia is close to 40%, making this a very serious medical condition that requires immediate treatment[2]. This makes it even more important to recognize the signs and symptoms of hypothermic patients, including more atypical presentations consistent with underlying, secondary causes. A MedlinePlus search to answer the question "what can cause confusion and shivering in a patient presenting to the emergency department?" yielded several articles about alcohol use, depression and anesthetics. While there was an article referring to hypothermia, it discussed cold exposure-induced hypothermia in relation to cardiovascular disease[3]. Since most instances of patients presenting with hypothermia occur during the winter months in areas of the world with extreme cold seasons, it may be underrecognized during warmer months or more temperate climates, especially when due to secondary causes.

Case Report

Our patient is a 37-year old female who was brought in to the emergency department by her husband, presenting with slurred speech, lethargy and "odd behaviour". Her symptoms started while sitting outside on the front porch of their house, around 8:00 pm on a warm, humid summer evening. Temperatures were in the range of 24-26 °C at this time. It was

about 30 minutes after her symptoms began when the patient and her husband arrived at the hospital.

At triage, the patient appeared confused and was noted to be shivering intensely. On primary survey, the patient's respiratory rate was 8 breaths/min, the airway was patent, breath sounds were auscultated bilaterally, and no adventitial breath sounds were appreciated. The patient's heart rate was measured as 48 bpm, blood pressure was 92/64 and distal pulses were palpable, but weak. The patient appeared very lethargic and scored 8 on the Glasgow Coma scale. On secondary survey, the patient displayed slow speech, sluggish movements, and was cold to the touch. A tympanic temperature of 34 °C was obtained. The patient appeared to have swelling of her face, with periorbital edema, and a distended abdomen. There was no recent trauma, and the rest of the physical exam was unremarkable.

Due to her low body temperature, the patient then underwent passive external rewarming, which involved wrapping her in warm blankets. The room temperature was increased to 28 °C over the course of approximately 30 minutes. Blankets were changed and replaced with warmer ones over time to continue the rewarming process, with the intent to rewarm the patient at a rate of 1°C/hour until a goal core body temperature of 37 °C was reached. Warm IV fluids were kept close by in case the need arose.

Significant initial laboratory results were as follows[4]:

- Serum potassium = 5.6 mmol/L (high)
- Serum sodium = 121 mmol/L (low)
- pH = 7.30 (low)
- Lactate = 3.1 mmol/L (high)
- Glucose = 2.4 mmol/L (low)
- SaO_2 = 88% (low)
- $PaCO_2$ = 57 mmHg (high)

Upon these results, a further history was taken; most of the information was provided by her husband, as follows. The patient had no prior environmental exposure to cold nor recent trauma. The patient did not have any alcohol and was not known to use illicit drugs. The patient reported feeling very tired, which was confirmed by her husband with a history of approximately 5 months in duration. The patient was described as "always cold" and "wrapped up in blankets or sweaters most of the time" as per her husband. The patient was on 150mg sertraline daily, used over the counter stool softener as needed, and supplemental iron pills daily. Her medical history was significant for anemia, constipation and depression. Family history was significant for a sister diagnosed with depression, mom with a "thyroid issue," and dad diagnosed with diabetes mellitus.

Additional laboratory testing for T4, TSH, and cortisol was conducted. The following results were obtained: T4 = 4.7 mmol/L, TSH = 8.3 mmol/L, cortisol = 124 mmol/L.

Finally, a chest radiograph was obtained to check for potential pericardial effusion and enlarged cardiac silhouette[5]. An ECG was also performed. The chest radiograph was unremarkable, and ECG did not show anything additional to bradycardia.

The patient was admitted to ICU soon after and diagnosed with severe hypothyroidism: currently presenting with a myxedema coma[5]. An IV was inserted, and the patient was given a small bolus containing 300 mg of levothyroxine (T4), 10 mcg of liothyronine (T3) and 100 mg of hydrocortisone, intravenously. The patient was placed on mechanical ventilation, and given IV fluids containing a dose of norepinephrine at a rate of 8 mcg/min until her blood pressure and hemodynamic state were sufficiently corrected. In addition, the patient was given a dose of 10g of dextrose, IV to correct her hypoglycemia, and was kept on ECG to monitor for potential arrythmias. The patient appeared to be more comfortable at this point and had a esophageal temperature of 35.5 °C. The final temperature obtained that night was 37 °C.

8 hours after her initial hormone dosing, the patient was given 5 mcg of T3 and another 100 mg hydrocortisone, IV. The next morning, the patient was given 75 mcg T4, and a short low-dose ACTH stimulation test was performed, in order to rule out adrenal insufficiency[5]. Serum cortisol was measured immediately before the patient was given 1 mcg of cosyntropin IV, and again 30 minutes after the administration, as per the test protocol[6]. The serum cortisol was observed to increase significantly upon the second measurement, and as a result the patient's exogenous hydrocortisone administration was discontinued. The patient was taken off mechanical ventilation later that day. The patient was kept in hospital for two additional days on the same dosing schedule for T3 & T4, and then was discharged with a follow up appointment to her family doctor in one week's time, and a referral to endocrinology.

Discussion

Preliminary recognition of hypothermia in presenting patients is vital to their treatment and prognosis. Diagnosis and classification are dependent upon core body temperature, most accurately measured by an esophageal probe[1]. However, this method can only be used in moderate to severe cases with patients requiring intubation. For other cases where patients are conscious, low-temperature-reading rectal, or tympanic thermometers may be used. Bladder temperature is also commonly measured. It is important to note that rectal and bladder temperatures may inaccurately reflect true core body temperature, by lagging

behind any changes in temperature, especially when internal rewarming methods are used[1].

Classification of hypothermia depends on measured core body temperature, and also the apparent signs and symptoms of the patient in question[2]. One typical classification method uses three stages of core body temperature: mild (32 - 35 °C), moderate (28 – 32 °C) and severe (< 32 °C)[1]. The clinical manifestations characteristic of each stage are described in Figure 1.

Clinical manifestations of accidental hypothermia

	Mild	Moderate	Severe
Neurologic	Confusion, slurred speech, impaired judgment, amnesia	Lethargy, hallucinations, loss of pupillary reflexes, EEG abnormalities	Loss of cerebrovascular regulation, decline in EEG activity, coma, loss of ocular reflexes
Cardiovascular	Tachycardia, increased cardiac output and systemic vascular resistance	Progressive bradycardia (unresponsive to atropine); decreased cardiac output and BP; atrial and ventricular arrhythmias, J (Osborn) wave on ECG	Decline in BP and cardiac output, ventricular fibrillation (<28°C; 82.4°F) and asystole (<20°C; 68°F)
Respiratory	Tachypnea, bronchorrhea	Hypoventilation, decreased oxygen consumption and CO2 production, loss of cough reflex	Pulmonary edema, apnea
Renal	Bladder atony, cold diuresis	Cold diuresis	Decreased renal perfusion, oliguria
Musculoskeletal	Increased shivering	Decreased shivering (<32°C; 89.6°F) muscle rigidity	Patient may appear dead ("pseudo-rigor mortis")
Metabolic	Increased metabolic rate, hyperglycemia		Decreased metabolic rate, hyper- or hypoglycemia
Hematologic	Increase in hematocrit, decreased platelet count and white blood cell count, bleeding diathesis, DIC		
Gastrointestinal	Ileus, pancreatitis, gastric stress ulcers, hepatic dysfunction		

BP: blood pressure; CO2: carbon dioxide; DIC: disseminated intravascular coagulation; ECG: electrocardiogram; EEG: electroencephalogram.

Figure 1: Clinical Manifestations of accidental hypothermia[1]. *[Image courtesy of UpToDate: Accidental Hypothermia, Table 3]*

A second, commonly referred to classification method is the Swiss Staging or ICAR-MEDCOM system, as seen in Table 1.

Stage	Core Temperature	Clinical Presentation
HT I	32-35 °C	Clearly conscious, shivering
HT II	28-32 °C	Impaired consciousness, not shivering
HT III	24-28 °C	Unconscious, no shivering, vital signs may be present or absent
HT IV	13.7-24 °C	Unconscious, no vital signs, apparent death
HT V	< 13.7 °C	Death due to irreversible hypothermia

Table 1: Swiss Staging System of Hypothermia[1].

'ABC's should be conducted to assess airway, breathing and circulation of the patient. Additionally, 'D': disability (a neurologic evaluation) and 'E': exposure/environment control should be included in these cases[2]. In this discussion, E will be referred to as the methods of rewarming the hypothermic patient. CPR should be initiated in patients with hypothermia also presenting with cardiac arrest. It is important to note that hypothermic patients should be treated with caution during their hospital course, as they are at a greater risk of developing cardiac arrythmias upon movement with physical exam or transport[1].

Before moving on to orders of laboratory requests or scans, the patient should be examined for signs of cold injury or trauma. Frostbite often occurs with hypothermia in the setting of exposure to cold environments for prolonged periods of time.

Once a diagnosis of hypothermia is made, it is protocol to order the following tests[1]:

- Blood sample: CBC, serum electrolytes, BUN, urea, lactate, fibrinogen, creatinine kinase, glucose
- INR & PT
- Arterial blood gas
- Chest radiograph
- ECG

The findings of these tests help us to determine if there are any complications or emerging comorbidities, and can help give an estimate of the prognosis of the patient. Markers of poor prognosis, as indicated in Figure 2, can help guide treatment in more severe cases, and help develop procedures as to when to continue resuscitation efforts and when to stop CPR, etc.

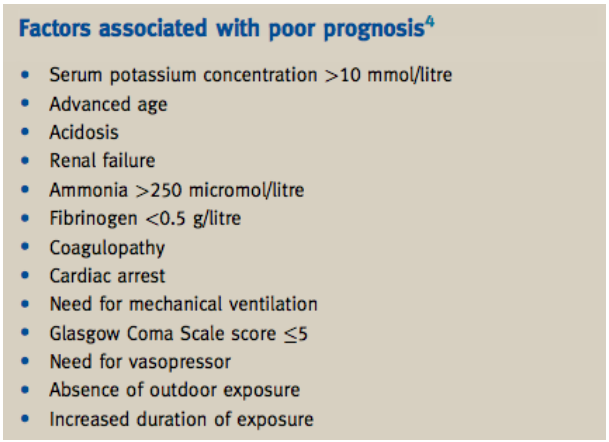

Figure 2: Markers associated with poor prognosis in hypothermic patients[2].

The chosen course of treatment is dependent on the severity of the hypothermia. In general, treatment of hypothermia can be grouped into different levels of rewarming: passive external rewarming, active external rewarming, active internal (core) rewarming, and extracorporeal blood rewarming[1]. Passive external rewarming consists of the removal of wet clothing of a patient, before wrapping them in blankets or other insulators[1]. Active external rewarming uses things such as warm blankets, immersion in a warm bath or forced warm air to increase the patient's core body temperature[1]. Active internal, or core, warming involves the administration of warmed (38-42 °C) IV fluids in boluses, and peritoneal or pleural lavage[1]. While previously used, irrigation of the bladder is no longer practiced as the affected surface area is too small to cause any real benefit[1]. Finally, extracorporeal blood rewarming can consist of the patient being placed on hemodialysis, a cardiopulmonary bypass being performed, or the use of ECMO (extracorporeal membrane oxygenation)[1]. With more mild cases, healthcare providers would begin with passive external rewarming, and progress to more aggressive, active rewarming methods in moderate or severe cases, or in mild cases not responding to initial rewarming attempts.

According to both the Swiss Staging System and the 3-stage classification methods, our patient had mild, Stage 1 (HT I) hypothermia. What made it difficult for us to diagnose her was that she did not have any prior trauma or exposure to cold: the two most common causes of accidental hypothermia. When patients present with a core body temperature of < 35 °C and display some of the symptoms of hypothermia, but do not have a history of exposure or trauma, secondary causes must immediately be searched for. When discussed later with a group of residents, the answers that came up the most as underlying causes of hypothermia were drug and/or alcohol intoxication, sepsis, and malnutrition/anorexia nervosa. However, the list of differential diagnoses is long for secondary hypothermia, as can be seen in Figure 3. It therefore becomes even more important to obtain a thorough history from the patient if possible, and/or any friends or family members present, in order to not miss any of the less discussed secondary causes.

In our case, our patient and her husband were able to provide a substantial history. Information that caught our eye and ultimately led to the diagnosis of severe hypothyroidism included: her medical history of depression, anemia and constipation, as well as a 5 month history of excessive fatigue, and a longstanding history of cold intolerance. In addition, the patient reported her mom had a 'thyroid issue;' while vague this piece of information also fit with the final diagnosis. In addition to her history and findings on physical exam, the lab tests were the final piece of the puzzle. To confirm a diagnosis of hypothyroidism, TSH and T4 levels must be measured. Significantly elevated TSH and very low T4 blood levels indicate primary hypothyroidism, while in secondary or tertiary hypothyroidism, the TSH levels may be low, normal or only slightly elevated, with

significantly depressed T4 levels[7]. In severe cases of hypothyroidism, a medical emergency called myxedema coma can arise; characterized by decreased mental status and hypothermia, as well as bradycardia, hyponatremia, hypoglycemia and decreased blood pressure[6].

Causes of hypothermia

Mechanism	Clinical disorder
Increased heat loss	Environmental exposure
	Induced vasodilation
	Drugs
	Alcohol
	Toxins
	Skin disorders
	Burns
	Psoriasis
	Exfoliative dermatitis
	Iatrogenic
	Cold infusion
	Emergent deliveries
	Cardiopulmonary bypass
	Continuous renal replacement therapy
Decreased heat production	Endocrinologic disease
	Hypopituitarism
	Hypoadrenalism
	Hypothyroidism
	Insufficient fuel
	Hypoglycemia
	Malnutrition
	Neuromuscular inefficiency
	Extremes of age
	Impaired shivering
	Inactivity

Mechanism	Clinical disorder
Impaired regulation	Peripheral
	Spinal-cord transection
	Neuropathies
	Diabetes mellitus
	Central
	Cerebrovascular accident
	Subarachnoid hemorrhage
	Parkinsonism
	Hypothalamic dysfunction
	Multiple sclerosis
	Anorexia nervosa
	Drugs: Intoxicants, anxiolytics, antidepressants, antimanic agents, antipsychotics, opioids, oral antihyperglycemics, beta blockers
Other	Sepsis
	Pancreatitis
	Carcinomatosis
	Uremia
	Vascular insufficiency
	Trauma

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Figure 3: Underlying conditions/diseases that can cause hypothermia, secondary to themselves. *[Image courtesy of UpToDate: Accidental Hypothermia, Table 5]*

As hypothyroidism is a fairly prevalent condition, it should immediately be considered in patients presenting with secondary, underlying causes of hypothermia; especially if those patients display any of the symptoms consistent with hypothyroidism (listed below).

Signs & Symptoms of Hypothyroidism[8]	
Signs:	*Symptoms:*
Slow movements	Fatigue
Slow speech	Cold intolerance
Bradycardia	Puffiness of face
Pallor	Coarse hair & skin
Non-pitting edema (myxedema)	Skin cool to touch
Periorbital edema	Decreased sweating
Anemia	Skin discolouration
Decreased CO	Hair loss
Pericardial effusion	Enlarged tongue
Decreased resp rate	Vocal hoarseness
Hypoventilation	Decreased exercise capacity
Respiratory muscle weakness	SOB on exertion
Weight gain	Rhinitis
Ascites	Constipation

In this case in particular, it is an atypical mild hypothermia presentation from what one would expect with simply accidental hypothermia due to exposure. According to figure 1, we would expect a patient with mild hypothermia to be tachycardic, with increased blood pressure as both cardiac output and systemic vascular resistance increase as compensatory mechanisms[1]. We would also expect to see tachypnea and hyperglycemia – all of which the patient displayed the complete opposite pattern with bradycardia, hypotension, bradypnea and hypoglycemia.

Because of this atypical presentation with core body temperature < 35 °C, secondary causes should have immediately been considered – myxedema coma being at the top of the differential diagnosis list. This would have led to a reduction in time to treatment of the medical emergency resulting from the patient's underlying condition of severe hypothyroidism.

Education about secondary, underlying causes of hypothermia is essential in catching atypical cases with patients presenting with no previous environmental exposure. Because of the emergent nature of myxedema coma, the sooner it is identified, the better the survival rate for the patient[6]. It may therefore be helpful to include inquiries for serum T4 and TSH levels, along with initial laboratory tests because of the severity of this condition. In broader terms, it may be beneficial for both patients and healthcare providers to order other tests looking for markers of other secondary causes of hypothermia sooner upon presentation as well. For example, blood EtOH levels could be measured, and tests looking for a variety of drugs in the blood could be conducted simultaneously. Vitamin and nutrient levels in the blood could also be considered to be measured earlier on.

Conclusion

Exposure is the most widely recognized cause of accidental hypothermia[1]. Occurrences of underlying conditions leading to secondary hypothermia are less familiar and are examined to a lesser degree in literature surrounding hypothermia[3]. This can make it difficult to identify and treat hypothermic patients appropriately. Education surrounding additional causes of hypothermia, how to test for them and how to treat the underlying condition alongside rewarming, is essential to improve awareness. Earlier testing for markers of these secondary causes may be beneficial for patients, and help decrease mortality rates, especially in emergency situations such as myxedema coma.

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