Type 2 Diabetes Decompensation as the Clinical Presentation of Thyroid Storm – Cause or Consequence?

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This case study aims to discuss the unusual forms of hyperthyroidism presentation, the nonspecific symptoms and precipitating events. A 70-year-old male was taken to the emergency department for hyperglycaemia, nausea, vomiting and altered mental status with a week of evolution. He had a past medical history of type 2 diabetes, hypertension and dyslipidemia. He had no history of any recent intercurrent illness or infection. At the emergency room, besides hyperglycaemia, ketonemia and slightly elevated C-reactive protein, the basic laboratory panel workup was normal, as was the head computed tomography. He was admitted for metabolic compensation and to study the altered neurological status. During hospitalisation, despite the good glycemic control, he had no improvements in neurological status. At day four of hospitalisation, thyrotoxicosis with thyroid storm criteria was diagnosed. He started on adequate treatment with complete clinical recovery. The associated morbidity and mortality of thyroid storm requires immediate recognition and treatment. Elderly patients are frequently misdiagnosed or diagnosed later due to fewer and less pronounced signs and symptoms.

Keywords

Thyroid storm, thyrotoxicosis, Graves' disease, type 2 diabetes, diabetic ketoacidosis, elderly

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In contrast to the classical symptoms and obvious signs of a hypermetabolic state, elderly patients present with fewer and less pronounced symptoms such as fatigue, weakness, depression or relative apathy. Moreover, the symptoms are often masked by ageing-associated diseases.[1–3] Thyroid storm (TS) is a life-threatening exacerbation of hyperthyroidism that requires emergent treatment. This condition is manifested by the decompensation of multiple organs, which is often triggered by severe stress, such as intercurrent illness or perioperative event.[3] Diagnosis is clinical and is based on the presence of hyperthyroidism in a patient with severe and life-threatening manifestations. To make the diagnosis, Burch and Wartofsky proposed a scoring system modified by Akamizu and colleagues. The treatment goals are reduction of the thyroid hormone synthesis and secretion of thyroid hormones, control of its peripheral effects, resolution of systemic manifestations and treatment of precipitating illness.[1,4,5] We report a rare diagnosis of apathetic thyroid storm masked by hyperglycaemia and altered mental status.

Case presentation

A 70-year-old male was taken to the emergency department for hyperglycaemia, nausea and vomiting with a week of evolution. He also presented asthenia, anorexia, dysphagia, psychomotor retardation and generalised decrease in muscle strength. He had no history of any recent intercurrent illness or infection.

He had type 2 diabetes with a previous glycated hemoglobin of 8.8%. He also had hypertension, dyslipidemia and central retinal thrombosis. He was on detemir and aspartic insulins (100 units/daily), vildagliptin 100 mg, lisinopril 20 mg, chlorthalidone 50 mg, atorvastatin 40 mg, clopidogrel 75 mg and acetylsalicylic acid 100 mg. His wife, who managed his medication, denied omission of insulin administration.

On physical examination, he presented signs of dehydration. He was conscious but with temporal disorientation and slowed speech. He had postural tremor. The assessment of muscular strength and visual fields were normal and plantar reflexes were present. The cardiopulmonary auscultation was normal. Body temperature was 36.9ºC, blood pressure 160/85 mmHg and heart rate 100 beats per minute. Capillary glycaemia (388 mg/dl) and blood ketones (3.8 mmol/L) were high.

On admission, the arterial blood gas revealed a plasma bicarbonate level of 17.7 mEq/L (NR: 21.0–26.0), pH 7.4 (NR: 7.37–7.45) and anion gap of 25.6 mEq/L (NR: 8.0–16.0). The serum plasma glucose level was 408 mg/dl and the calculated plasma osmolarity 342 mOsm/L. The laboratory workup are described in *Table 1*. The electrocardiogram showed sinus tachycardia.

Table 1: Laboratory workup at admission

	Results	Reference range
Glucose (mg/dL)	408	<126
Plasma osmolarity (mOsm/L)	342	275–295
Creatinine (mg/dL)	1.3	0.7–1.2
Urea (mg/dL)	107	15–39
Sodium (mmol/L)	141	136–145
Potassium (mmol/L)	4.7	3.5–5.1
C-reactive protein (mg/L)	25.6	<3.0
Haemoglobin (g/dL)	13.0	13.5–17.0
Leukocytes (uL)	6,400	4,000–10,500
Platelets (uL)	162,000	150,000–400,000
AST (U/L)	31	15–37
ALT (U/L)	76	12–78

ALT = alanine transaminase; AST = aspartate transaminase.

Table 2: Diagnostic criteria of thyroid storm based on Burch and Wartofsky score

Criteria	Points
Temperature	
38.5ºC	15
Central nervous system	
Lethargy	20
Gastrointestinal-hepatic dysfunction	
Nausea	10
Cardiovascular dysfunction	
Tachycardia (105 bpm)	5
Heart failure	
Absent	0
Precipitant history	
Absent	0
Total	50

The head computed tomography scan revealed no acute haemorrhagic or ischaemic lesions. However, discrete signs of ischaemic leukoencephalopathy were described.

He started on intravenous fluids and insulin and after 6 hours of continuous insulin perfusion, he achieved glycaemic control with resolution of ketosis and started on subcutaneous insulin. He was hospitalised for metabolic compensation and to study neurological changes.

During hospitalisation, he achieved good glycemic control without improvements in neurological status. On day four of hospitalisation, he was extremely lethargic, and had a fever (38.5ºC), profuse sweating and nausea. The heart rate was 105 bpm. There was no clinical or analytical evidence of infection and blood cultures were negative. The laboratory workup evaluation revealed thyrotoxicosis, suppressed thyroid-stimulating hormone (TSH) (<0.005 uUI/ml; NR: 0.358–3.74) with elevated free T4 (5.76 ng/dl; NR: 0.76–1.46) and free T3 (6.63 pg/ml; NR: 2.18–3.98). He had elevated anti-thyroid peroxidase antibody (TPOAb) (247 UI/ml; NR <35) and positive TSH receptor antibody (20 U/L; NR <9). Based on the Burch and Wartofsky score, thyroid storm was diagnosed (see *Table 2*).[5]

He immediately started treatment with hydrocortisone (loading dose of 200 mg followed by 100 mg every 8 hours), propranolol (80 mg every 8 hours) and thiamazole (20 mg every 6 hours). Lugol solution (8 drops every 6 hours) was initiated one hour after thiamazole. Intravenous fluids and paracetamol were also administrated.

Hydrocortisone, propranolol, *Lugol* solution and thiamazole were tapered gradually and free T4 and T3 became normal after 12 days of therapy. He maintained treatment with thiamazole, with a discharged dose of 10 mg three-times daily.

The cervical ultrasound showed a normal volume thyroid gland with an accentuated and diffusely heterogeneous parenchyma. There were no cervical adenomegalies. Clinical and analytical improvement were noted after therapy and two weeks later he was completely recovered of his neurologic alterations. The metabolic control of diabetes had improved significantly.

Months after the treatment, the thyroid scintigraphy demonstrated a globose gland with diffusely and heterogeneous increased radiopharmaceutical uptake. The definitive remission of Graves' disease was achieved after treatment with radioactive iodine (15 mCi). He developed hypothyroidism and he is currently on levothyroxine 137 ug/daily.

Discussion

Poudel et al. described a case of an 84-year-old woman with type 2 diabetes who developed apathetic hyperthyroidism due to Graves' disease, although without thyroid storm at presentation.[6] A case of thyroid storm associated with Graves' disease masked by diabetic ketoacidosis in a 59-year-old woman was described by Osada et al. However, in contrast with our case, the patient had no history of diabetes.[7] In fact, in the published literature, this is the first case of an elderly man with type 2 diabetes that developed apathetic hyperthyroidism culminating in thyroid storm as a first presentation of Graves' disease.

Apathetic hyperthyroidism was first described by Lahey in 1931.[8] It is most frequently observed in middle-aged and elderly populations and is estimated to occur in 10–15% of older individuals with hyperthyroidism, although it can be underdiagnosed. The pathogenesis of apathetic hyperthyroidism is unclear. A previous report indicated it may be due to a decrease in adrenergic tone and age-related changes in the autonomic nervous system and resistance of tissues to the effects of thyroid hormone.[9,10] A rapid rate of increase in serum thyroid hormone levels, an increased responsiveness to catecholamines, or an enhanced cellular response to thyroid hormone have been proposed as mechanisms to the development of thyroid storm. However, it remains unclear why certain factors result in the development of thyroid storm. The excess of thyroid hormone is typically not more pronounced than that seen in patients with uncomplicated thyrotoxicosis.[11] Thyroid storm can occur in patients with long-standing untreated hyperthyroidism but it is often precipitated by an acute event such as thyroid or nonthyroidal surgery, trauma, infection, an acute iodine load, labor or irregular use or discontinuation of antithyroid drugs. Other conditions known to be associated include cytotoxic chemotherapy, aspirin overdose, ketoacidosis or organophosphate intoxication.[12] In the present case, hyperglycaemia was the only precipitating factor identified, however, it might be a consequence of thyrotoxicosis. Several mechanisms explains the hyperglycaemia in hyperthyroidism, including a diminished insulin half-life secondary to an increased rate of degradation and a higher release of biologically

inactive insulin precursors. Also, there is an increase in glucose gut absorption mediated by the excess of thyroid hormones and an enhanced endogenous production of glucose.[13] We may conclude that the triggering factor remains unknown.

Thyroid storm can happen in hyperthyroidism of any cause but the most common etiology is an underlying Graves' disease.[14] The referred patient had been evaluated for thyroid dysfunction in the previous months and he had normal thyroid function. After thyrotoxicosis was diagnosis, we had positivity for anti-TSH receptor antibodies, an ultrasound and a scintigraphy compatible with Graves' disease, an uncommon disease in males and in the elderly.[15]

In the reported case, the unusual form of hyperthyroidism presentation, the nonspecific symptoms that were compatible with multiple equally serious pathologies, and the absence of known thyroid disease and previous normal thyroid function constituted a diagnostic challenge. Moreover, the concomitant diabetic decompensation lasting for several weeks delayed the diagnosis. The definitive response to antithyroid drug, iodine and steroid, supported the diagnosis of thyroid storm. ❐

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