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■ Case Report

A Case of Acute Neurologic Deficit and Hypoglycemia in the Setting of Thyroid Storm and Diabetic Ketoacidosis: A New Clinical Scenario

Alena Aleksashina[1], Svetlana Rachina[2,*], Gayrat Kiyakbaev[2], Girindu Hewathanthirige[3], Yulia Cherdantseva[2]

[1]City Clinical Hospital Named after S.S. Yudin, Moscow, Russian Federation
[2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation
[3]Peoples' Friendship University of Russia, Moscow, Russian Federation

The simultaneous development of diabetic ketoacidosis (DKA) and thyroid storm (TS) is a rare but potentially life-threatening condition that requires immediate and targeted treatment. However, their combined diagnosis poses a serious challenge because of the similarities between their clinical manifestations. To date, only a few dozen cases have been described; most of which have been linked to the progression of thyrotoxicosis or uncontrolled hyperglycemia as contributing factors. We present the case of a 37-year-old woman with type 1 diabetes mellitus and Graves' disease who presented with both TS and DKA. She was initially admitted to the emergency department as a suspected case of stroke. Severe hypoglycemia significantly lowered her alertness to TS and probably provoked a sharp hyperthyroid decompensation, thereby leading to subsequent DKA development.

Keywords: Thyroid Storm; Diabetic Ketoacidosis; Hypoglycemia; Graves' Disease; Type 1 Diabetes Mellitus; Burch-Wartofsky Point Scale; Case Report

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*Corresponding Author: **Svetlana Rachina** https://orcid.org/0000-0002-3329-7846
Tel: +7-9107158955, Fax: +7-495-212-8506, E-mail: rachina_s_a@staff.sechenov.ru

INTRODUCTION

Autoimmune thyroid diseases and type 1 diabetes mellitus (T1DM) are the most common autoimmune endocrinopathies collectively contributing to the development of autoimmune polyglandular syndrome type 3A.[1)]

Acute complications of these diseases, such as thyroid storm (TS) and diabetic ketoacidosis (DKA), are life-threatening conditions and therefore require rapid verification and treatment.[2,3)] Untimely diagnosis and treatment can result in mortality rates as high as 10% in patients with TS.[3)]

The simultaneous development of TS and DKA presents a mortality risk of 15%, thus requiring special attention. A combined diagnosis is often challenging because of the similarities between their clinical manifestations, various predisposing factors, and clinical masks at the outset.[4)] In contrast to DKA, the diagnosis of TS remains complicated; it is not based on laboratory parameters but on clinical symptom scoring, which may be obscured when both conditions co-exist. In most instances, hyperglycemia is considered as an initiating mechanism having less frequent associations with thyrotoxicosis exacerbations.[4,5)] There is a pathophysiologic substantiation between the mutually potentiating effects of thyrotoxicosis and hyperglycemia or DKA.[6)] However, isolated cases with an unusual combination of hypoglycemia and thyrotoxicosis or TS have been reported.[7,8)]

In this article, we present a case of simultaneous TS and DKA development in a patient with both T1DM and Graves' disease, with an initial presentation of hypoglycemia and neurologic deficits.

CASE REPORT

Patient K is a 37-year-old female without a history of alcohol consumption, smoking, or drug use. She was admitted to a city hospital's emergency department as a suspected case of acute cerebrovascular accident (ACV). Upon hospitalization, the patient exhibited the following symptoms: dizziness, unsteady gait, bilateral upper and lower extremity numbness, generalized weakness, cognitive deficits, and an episode of confusion.

The patient has been suffering from T1DM for 5 years and has been receiving insulin therapy (insulin glargine 300 units/mL [18 units] and insulin aspart [1.0–1.7 units per meal]). Six months before admission, the patient had maintained a hemoglobin A1c level of 6.3%. Occasional mild episodes of hypoglycemia (54–70 mg/dL) occurred approximately once a month, thus leading to palpitations and vestibular issues; these episodes were resolved by consuming easily digestible carbohydrates. The patient had not been previously diagnosed with DKA.

Upon hospitalization, the patient had a body temperature of 37.2°C, a body mass index of 19.6 kg/m^2, a blood pressure of 137/85 mm Hg, and a heart rate of 120 beats/min. The patient's skin was clean and dry. Neurologic status showed an episode of confusion and quadriparesis, with a strength of up to 4 points in the arms and up to 3 points in the legs. Babinski's signs were positive on both sides. Coordination tests revealed severe ataxia in both sides. The thyroid gland was not enlarged; no eye symptoms or exophthalmos were observed. Other organ systems remained intact.

Laboratory investigations (Table 1) revealed hypoglycemia (45–47.61 mg/dL) and mild acidemia. Prior electrocardiogram revealed sinus tachycardia with a heart rate of 118 beats/min.

Following a comprehensive evaluation including cerebrospinal fluid analysis, there was no evidence of stroke or infection. Changes in the central nervous system (CNS) were attributed to encephalopathy of dysmetabolic genesis.

The patient's condition improved after receiving the following: a bolus injection of 100 mL of 50% dextrose with subsequent infusion, neuroprotective therapy, and metoprolol 50 mg (Betaloc ZOK; AstraZeneca AB, Södertälje, Sweden). Consciousness and lower-extremity movements were restored; although, the patient continued to experience generalized weakness, occipital pain, and dizziness. Glycemic levels were controlled by administering a short-acting insulin. The patient was then transferred to the therapeutic department on the second day of hospitalization.

Six years prior to admission, the patient had been diagnosed with Graves' disease. She received thiamazole (Thyrozol; Merck KGaA, Darmstadt, Germany) for 12 months (at an initial dose of 30 mg with a gradual dose reduction to 5 mg), but was discontinued upon achieving clinical and laboratory remissions. Subsequently, the symptoms of thyrotoxicosis recurred, primarily in the form of hand tremors. The patient intermittently resumed thiamazole treatment without laboratory control until her symptoms subsided.

Approximately 1 month prior to the current hospitalization, the patient noticed a decrease in her appetite, which she attributed to emo-

Table 1. Laboratory investigation

Variable	Day of hospitalization				
	1	5	7	10	Reference
pH	7.333	7.130	7.315	7.434	7.350–7.450
Glucose (mg/dL)	45/47	277.4	225.2	113.5	70–108
cHCO$_3$ (mmol/L)	22	6.3	13.9	27.9	26.0–32.0
Anion gap (mmol/L)	15	36.3	43.9	11.1	10–12
Hemoglobin (g/L)	123	119	104	95	120–140
Leukocyte count (10^9/L)	8.6	19.8	11.7	5.9	4.0–9.0
Neutrophil, absolute (10^9/L)	7.4	11.9	9.9	5.4	1.8–6.6

tional stress due to her child's serious illness. Moreover, clinical symptoms, including shortness of breath, tremors, and palpitations, appeared 2 days before hospitalization. The patient assumed that these symptoms were manifestations of hyperthyroid relapse; thus, she resumed thiamazole treatment at 10 mg per dose.

On the 3rd day of hospitalization, the endocrinologist decided to continue thiamazole treatment at a dose of 10 mg/d while awaiting hormonal profile test results, considering the clinical data showing the probability of thyrotoxicosis recurrence. Ultrasonography revealed diffuse heterogeneity in the thyroid gland parenchyma and an enhanced vascular pattern in its tissues. The patient was also prescribed an intermediate-acting insulin (8 units, 2 times/d) and insulin aspart (1.0–1.7 units) to control hyperglycemia.

On the 4th day of treatment, the patient experienced a single episode of vomiting, along with hyperglycemia (up to 315 mg/dL) and ketonuria (45.3 mg/dL). Despite adjusting the insulin dose, the patient's condition rapidly deteriorated the following day. This deterioration was marked by recurrent vomiting, vestibulo-ataxic symptoms, fever of up to 38.2°C, a decreased level of consciousness, tachycardia with a heart rate of up to 150–160 beats/min, and a respiratory rate of up to 20 cycles per minute. Subsequently, the patient was transferred to the intensive care unit.

Laboratory investigations conducted on the 5th day revealed the following (Table 1): leukocytosis (19.8 thousand), increased C-reactive protein levels (23.4 g/L), increased blood glucose levels (277.4 mg/dL), severe ketonuria (greater than 45.3 mg/dL), and glycosuria (504.4 mg/dL). The results of the acid-base status test indicated the development of DKA, as characterized by severe anion gap as well as fluid and electrolyte imbalances (Na+ 131, K+ 3.5, and Cl- 101 mmol/L). Liver parameters and procalcitonin levels remained within normal ranges throughout hospitalization.

Considering the manifestation of fever and signs of inflammatory syndrome, which are not typical of DKA, additional investigations were conducted; these included serological and microbiological diagnostics, a chest computed tomography scan, and ultrasound examinations of the abdominal cavity and small pelvis. However, the tests did not reveal any underlying pathologic findings. Therefore, the observed changes in the CNS were attributed to metabolic disorders caused by acutely decompensating carbohydrate metabolism. Therefore, intensive DKA therapy as well as correction of fluid and electrolyte imbalances were initiated, thereby involving insulin infusions as well as sodium chloride and electrolyte solutions.

Despite the partial resolution of metabolic derangements, the patient continued to experience obtundation, fever, tachycardia, and vomiting on the 7th day following hospitalization. These symptoms prompted an assessment for TS development. According to the Burch-Wartofsky Point Scale (BWPS), the patient scored 65 points as follows: body temperature of 38.2°C (10 points), a heart rate of 150–160 beats/min (25 points), nausea and vomiting (10 points), and moderate severity of neurological manifestations (20 points) (Table 2).[9] These scores indicated the presence of TS. Furthermore, when considering a history of hypoglycemia as a precipitating factor, the likelihood of TS increased to 75 points. Using the Japanese scale, the patient was categorized under the TS 2 (alternative combination) criteria for a diagnosis of TS.[3]

Table 2. The Burch-Wartofsky Point Scale for diagnosis of thyroid storm[9]

Criteria	Points
Temperature (°F [°C])	
99–99.9 (37.2–37.7)	5
100–100.9 (37.8–38.2)	10
101–101.9 (38.3–38.8)	15
102–102.9 (38.9–39.2)	20
103–103.9 (39.3–39.9)	25
≥104.0 (≥40.0)	30
Heart rate (beats/min)	
100–109	5
110–110	10
120–129	15
130–139	20
≥140	25
Atrial fibrillation	
Absent	0
Present	10
Congestive heart failure	
Absent	0
Mild (pedal edema)	5
Moderate (bibasilar rales)	10
Severe (pulmonary edema)	15
Gastrointestinal-hepatic dysfunction	
Absent	0
Moderate (diarrhea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20
Central nervous system effects	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy)	20
Severe (seizures, coma)	30
Precipitating event	
Absent	0
Present	10
Total score	
>45	Thyroid storm
25–45	Impending storm
<25	Storm unlikely

The dose of thiamazole was increased to 20 mg every 6 hours; that of metoprolol was adjusted to 25 mg every 6 hours. In addition, Prednisolone was administered at 30 mg every 6 hours. The patient continued to receive insulin infusions as well as rehydration and electrolyte imbalance correction, accompanied with urine volume and central venous pressure monitoring on a per-hour basis. Due to hypoalbuminemia (26 g/L), supplementary parenteral nutrition was administered. After 3 days of treatment, which was on the 10th day of hospitalization, the patient experienced a cessation of vomiting, normalization of body temperature, a reduction in heart rate to 78 beats/min, increased motor activity, the return of appetite, and resolution of DKA. Laboratory tests confirmed the presence of thyrotoxicosis as follows:

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thyroid-stimulating hormone <0.01 (0.35–5.5 μIU/mL), free thyroxine 3.31 (0.89–1.76 ng/dL), free triiodothyronine 7.07 (2.3–4.2 pg/mL), thyroid-stimulating hormone receptor antibodies 3.16 (0–0.75 IU/L). Owing to positive clinical dynamics, the thiamazole and metoprolol dosages were adjusted to 40 mg/d and 50 mg/d, respectively; Prednisolone was continued at 30 mg/d orally, with a recommendation to gradually reduce its dose by 5 mg every 5 days until discontinuation.

On the 14th day of treatment, the patient was transferred to the therapeutic department. Based on sustained positive clinical dynamics, she was subsequently discharged from the hospital on the 17th day and was recommended to undergo radioiodine therapy after achieving compensation for hyperthyroidism.

Written informed consent for publication of this case was obtained from the patient.

DISCUSSION

The simultaneous occurrence of TS and DKA in our patient represented a rare yet potentially life-threatening clinical situation. To date, only a few cases involving this combination have been described, with only one published systematic review on this subject.[4] An important conclusion arising from these observations was the extreme complexity of TS diagnosis, mostly due its overlapping clinical symptoms with DKA. There are two main reasons for developing such a combination, i.e., progression of thyrotoxicosis or uncontrolled hyperglycemia. The specificity of our clinical case was that severe hypoglycemia probably contributed to the development of TS and DKA.

Under these conditions, the timely recognition of the prerequisites for TS and DKA is crucial. Prerequisite recognition depends on the presence of thyrotoxicosis and/or DM in a patient's history as well as any potential triggering factors.[5] Triggering factors may ultimately lead to decompensating thyrotoxicosis or DM. The relationship between hyperglycemia and thyrotoxicosis is often discussed and realized by involving mechanisms such as increased gluconeogenesis and glycogenolysis as well as reduced peripheral insulin sensitivity. Insufficient compensation for carbohydrate metabolism and thyrotoxicosis are common triggers for the development of both TS and DKA.[5,6]

In our case, the development of TS and DKA in our patient with T1DM and Graves' disease was preceded by the unusual occurrence of hypoglycemia. Indeed, there have been very few documented clinical scenarios in which severe thyrotoxicosis, including TS, co-manifested with severe hypoglycemia; this may have been caused by anorexia, liver dysfunction, heart issues, or adrenal insufficiency, either primary or as a result of ß-blocker therapy.[7,8]

We hypothesized that the development of severe hypoglycemia in our patient was likely provoked by a prolonged reduction in daily caloric intake due to decreased appetite and lack of insulin therapy adjustment. Poorly controlled latent hyperthyroidism may also have contributed to this effect, thereby potentially masking hypoglycemia by accelerating basal metabolism as well as facilitating the peripheral transport and utilization of glucose by various tissues.[10]

Our patient was initially admitted with acute neurologic deficits, thus necessitating an investigation to exclude stroke; this was successfully ruled out. It was highly probable that these symptoms, including quadriparesis, vestibular symptoms, and confusion, were primarily associated with thyrotoxicosis rather than hypoglycemia.[10] Additionally, the presence of thyrotoxicosis upon hospitalization was further supported by the unexplained hyperthermia and increased vascularity of the thyroid gland. However, the patient's confusion and absence of pathognomonic symptoms of Graves' disease, i.e., exophthalmos, goiter, and tremors, posed challenges in approaching the differential diagnoses. Upon hospitalization, the probability of developing TS appeared to be low (BWPS=20 points) as CNS changes did not fully meet the criteria; only elevated body temperature and tachycardia were observed. Consequently, thiamazole was resumed at a dose of 10 mg, which was later found to be insufficient.

Between the 4th and 5th day of hospitalization, despite a brief period of improvement and management of glycemia with insulin, there was a resurgence of hyperglycemia and severe DKA. Moreover, the recurrence of unexplained fever and severe tachycardia, even during DKA treatment and in the absence of infection or other causes, led to reconsidering a high probability of TS (BWPS=75 points). Several indirect indicators suggested the simultaneous development of DKA and TS. First, a significant improvement in the patient's condition was observed after increasing the doses of thiamazole and metoprolol as well as adding Prednisolone in accordance with the recommended TS treatment protocols. Second, the laboratory results confirmed the presence of primary hyperthyroidism.

The present case not only demonstrated the complexity and importance of timely diagnosing TS against the background of DKA, but also illustrated another scenario for TS development. It is likely that more severe-than-usual hypoglycemia in a patient with unstable remission of Graves' disease leads to thyrotoxic decompensation by activating contra-insular (stress) mechanisms. Subsequently, a well-known cascade of metabolic disorders may be triggered, thus culminating the onset of DKA.[6]

Currently, the diagnostic scales for TS have not been validated for use in patients with DKA, owing to the rarity of such co-existing conditions. Therefore, gathering information regarding the features of such clinical situations remains of paramount importance for enhancing diagnostic algorithms. Therefore, if our assumption about the role of hypoglycemia as a precipitating factor is accurate, it suggests that our patient might have had a higher risk for TS according to the BWPS (+10 points) from the outset; earlier correction of thyrostatic therapy could have prevented the development of DKA.

In conclusion, the simultaneous development of thyrotoxicosis and DKA is an uncommon yet potentially life-threatening clinical scenario, thereby rendering prompt TS and DKA assessments difficult even in patients with a known history of T1DM and Graves' disease. Severe hypoglycemia can also lead to the development of TS. Therefore, it may be a compelling reason to further re-evaluate and provide adjustments to the thyroid status.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Alena Aleksashina: https://orcid.org/0000-0001-8391-9802
Svetlana Rachina: https://orcid.org/0000-0002-3329-7846
Gayrat Kiyakbaev: https://orcid.org/0000-0002-8882-6143
Girindu Hewathanthirige: https://orcid.org/0000-0003-0317-9547
Yulia Cherdantseva: https://orcid.org/0000-0002-4900-2926

REFERENCES

1. Huber A, Menconi F, Corathers S, Jacobson EM, Tomer Y. Joint genetic susceptibility to type 1 diabetes and autoimmune thyroiditis: from epidemiology to mechanisms. Endocr Rev 2008;29:697-725.
2. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32:1335-43.
3. Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, Tsuboi K, et al. 2016 Guidelines for the management of thyroid storm from the Japan Thyroid Association and Japan Endocrine Society (first edition). Endocr J 2016;63:1025-64.
4. Rathish D, Karalliyadda S. Concurrent presentation of thyroid storm and diabetic ketoacidosis: a systematic review of previously reported cases. BMC Endocr Disord 2019;19:49.
5. Iino T, Akatsuka M, Yamamoto S. Case report: occurrence of thyroid storm in a young patient with recurrent diabetic ketoacidosis. Front Endocrinol (Lausanne) 2022;13:834505.
6. Potenza M, Via MA, Yanagisawa RT. Excess thyroid hormone and carbohydrate metabolism. Endocr Pract 2009;15:254-62.
7. Nakatani Y, Monden T, Sato M, Domeki N, Matsumura M, Banba N, et al. Severe hypoglycemia accompanied with thyroid crisis. Case Rep Endocrinol 2012;2012:168565.
8. Lee CW, Mathew H, Steenkamp D. A case of profound hypoglycemia in the setting of starvation and beta-adrenergic blockade in a patient with hyperthyroidism. AACE Clin Case Rep 2018;4:e353-7.
9. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis: thyroid storm. Endocrinol Metab Clin North Am 1993;22:263-77.
10. Cicatiello AG, Di Girolamo D, Dentice M. Metabolic effects of the intracellular regulation of thyroid hormone: old players, new concepts. Front Endocrinol (Lausanne) 2018;9:474.

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