Case Report

Diabetic ketoacidosis, a common disease with life-threatening pitfalls

C de Roquetaillade, JF Llitjos, M Paul, L Guillemet, OB Hadj Salem, JP Mira & A Cariou

Abstract

Diabetic ketoacidosis (DKA) is a common cause for admission in Emergency Department. Its treatment is well defined. Nevertheless, in some cases, type I diabetes combines with auto-immune polyendocrine syndrome, which can carry life-threatening consequences. Here we report the case of a young man with inaugural DKA who exhibited ventricular fibrillation and cardiac arrest due to significant hypokalaemia, following undiagnosed thyrotoxicosis with periodic paralysis.

Keywords

Cardiac arrest, Graves' disease, thyroid storm, type 1 diabetes, polyendocrine autoimmune syndrome, thyrotoxic periodic paralysis

Key points

- Diabetic ketoacidosis (DKA) is a frequent and life-threatening condition which can manifest itself in all ages albeit more common in younger patients. Despite improvement in its management, DKA's mortality rate ranges from 3% to 5%,
- The association of type I diabetes with autoimmune thyroid disease is not uncommon and can affect up to 23% of all patients during their lifetimes. Such association can combine with auto-immune polyendocrine syndrome type II, a clinical condition characterized by functional impairment of multiple endocrine glands.
- Hypokalaemic thyrotoxic periodic paralysis is a potentially life-threatening complication of hyperthyroidism, defined by association of thyrotoxicosis, hypokalaemia, and acute painless muscle weakness. It may be triggered by high glucose intake, intense effort or insulin administration.
- Treatment of TPP includes: emergency therapy, prevention of recurrence, determination of the cause of the hyperthyroidism and treatment of hyperthyroidism.

Case

A 34-year old man with no previous medical conditions was admitted to the Emergency Department (ED) for nausea and abdominal pain for two days. The patient reported fatiguability and weight loss, both of which had started 6 months prior to the consultation. In the ED, the patient reported polyuria and polydipsia for several days. His first clinical examination revealed blood pressure of 138/84 mmHg, heart rate of 140/min (sinus rhythm), and temperature of 36°C. He did not exhibit any neurological symptoms. Laboratory investigations revealed hyperglycaemia (blood glucose of 19 mmol/L), severe metabolic acidosis (arterial blood gas: pH 7.16, PaCO2 2.93kPa, PaO2 14.3kPa, HCO3- 7.9mmol/L, lactate 2.4mmol/L), and an elevated anion gap (36 mmol/L) associated with glycosuria and ketonuria on urinary strips. Serum potassium level was 4.3mmol/L, and serum phosphate level was 0.97mmol/L. Clinical and laboratory results were consistent with untreated type 1 diabetes, a diagnosis that was supported by a glycated haemoglobin (HbA1c) level of 96.7mmol/mol, and the detection of Glutamic Acid Decarboxylase (GAD) auto-antibodies in the blood.

After initial rehydration with crystalloids, intravenous insulin infusion and potassium supplementation were given starting at a rate of 7 units/h, according to the ED protocol, and the patient was transferred to the Intensive Care Unit, with protocolised evaluation for sequential blood sugar, electrolyte tests and urinary strips. A few hours after admission, he suddenly exhibited ventricular fibrillation with cardiac arrest. Cardiopulmonary resuscitation was undertaken immediately and the patient underwent endotracheal intubation. Spontaneous circulation returned following 2 minutes of external chest compressions and defibrillation. Biological examination revealed profound hypokalaemia (1.4 mmol/L) despite an overall amount of administrated potassium of 10 grams during the previous 6 hours in accordance with DKA management guidelines. During the following hours, regular tachycardia persisted despite adequate fluid loading and correction of acidosis with no concomitant administration of inotropic drug. As the tachycardia could no longer be explained by isolated hypovolemia, a possible thyroid disease was suspected. Biological exams revealed a severe hyperthyroidism due to Graves' disease with undetectable TSH serum levels (N= 0.48–5.08 mIU/mL), and T3 and T4 serum levels of 17.5nmol/L (N= 0.8-2.7nmol/L) and 67pmol/L

Charles de Roquetaillade[1]

Jean-François Llitjos[1]

Marine Paul[1]

Lucie Guillemet[1]

Omar Ben Hadj Salem[1]

Jean-Paul Mira[1]

Alain Cariou[1]

[1] Medical Intensive Care Unit, Cochin Hospital, Hôpitaux Universitaires Paris Centre, Assistance Publique des Hôpitaux de Paris, 27 rue du Faubourg Saint-Jacques, 75014 Paris, France and Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, 15 rue de l'école de Médecine, 75006 Paris, France

Correspondence
Charles de Roquetaillade
Medical Intensive Care Unit, Cochin Hospital, Hôpitaux Universitaires Paris Centre, Assistance Publique des Hôpitaux de Paris, 27 rue du Faubourg Saint-Jacques, 75014 Paris, France
Email: deroquetaillade.charles@gmail.com

(N= 11-27pmol/L) respectively. Serum TSH receptor auto-antibodies were strongly positive at 9IU/L (N < 4 IU/L). Despite significant potassium infusion, the serum level remained extremely low due to substantial urinary leakage (10g/day), with no alteration in glomerular filtration rate. Kidney injury was attributed to the severe hyperadrenergic state associated with thyrotoxicosis and in a lesser extent acute tubular necrosis consecutive to cardiac arrest. Such tubular injury was assessed by the presence of an important aminoaciduria with tubular proteinuria (180mg/L, 0.7g/24h).

The patient exhibited profound lethargy and muscle weakness for several days. Because of possible cerebral anoxia consecutive to cardiac arrest, further neurological investigations using MRI imaging was performed, which revealed neither brain oedema nor any other intracranial pathology. The final diagnosis was a thyrotoxic periodic paralysis (TPP), an acquired form of hypokalaemic paralysis, responsible for ventricular fibrillation. The patient was treated with a high dose of carbimazole (60mg daily), as well as propranolol (160mg/day). While his hormonal levels normalised, he fully recovered and could be discharged without sequelae.

Discussion

Diabetic ketoacidosis (DKA) is an extreme metabolic status caused by insulin deficiency. It is a relatively common cause for admission in emergency department. Data from national diabetes audit shows a number of DKA episodes per 100 patient year of 4.8, with 6% of cases occurring in patients with newly presenting type 1 diabetes.[1] DKA might carry life-threatening consequences in itself and is recognised as a situation with high risk of hypokalaemia consecutive to insulin supplementation.[2] Despite considerable improvement in management of the disease, DKA's mortality rate persist between 3% to 5%, mostly associated with precipitating illness (cardiovascular disease or infection).[1]

Association between diabetes and thyroid disease is not a rare condition: Patients with type 1 diabetes may have other autoimmune disorder such as thyroid disease, coeliac disease, and Addison's disease. Auto-immune thyroid disease is detected in 3-5% of the general population, but may affect up to 23% in patients with diabetes.[3] Association between type 1 diabetes and Grave's disease, an autoimmune form of hyperthyroidism caused by thyroid-stimulating autoantibodies, is less frequent.[4] Its association with type 1 diabetes may occur in auto-immune polyendocrine syndromes (APS).

APS comprise a heterogeneous group of disease characterised by autoimmune activity against more than one endocrine organs. These syndromes can be dichotomised in two categories: (1) rare monogenic forms such as APS type 1 – characterised by the association of Addison's disease, hypoparathyroidism and chronic candidiasis – and (2) a more common, polygenic form, APS type 2, which involves association, to varying degrees, of Graves' disease, type 1 diabetes and Addison's disease.[5]

The coexistence of type 1 diabetes and Graves' disease is therefore not that uncommon in patients, and several factors may lead to misdiagnosis of such association in patients presenting with DKA. In our case for example, the significant tachycardia the patients presented on admission, was misinterpreted as a clinical sign of dehydration consecutive to osmotic polyuria.

Thyrotoxic periodic paralysis (TPP) is an endocrine channelopathy and the most common cause of acquired periodic paralysis, it is most commonly a complication of Graves' disease but it was also associated with toxic adenoma, toxic multinodular goitre and amiodarone-induced thyrotoxicosis.[6] In patients with TPP, paralysis attack has been associated with various precipitating factors such as high glucose intake, unusual physical exercise, but exceptionally in association with inaugural ketoacidosis.[7] The exact pathophysiology of TPP remains uncertain, but might involve a rapid and massive intracellular influx of potassium into muscles responsible for hypokalaemia. It appears that thyroid hormones can directly stimulate Na-K adenosine triphosphatase (ATPase) activity. Thyroid hormones also increase both number and sensitivity of beta-receptors, resulting in an increased catecholamine-mediated potassium uptake. This last condition might explain why cases are described after exercise.[8] Hyperinsulinism seems to play also an important role by promoting potassium uptake into muscle which might explain cases related to high carbohydrate meal ingestion. In our case, insulin supplementation undoubtedly triggered the acute event.

The association between type 1 diabetes and Grave's disease is not uncommon and may integrates into auto-immune polyendocrine syndrome of various type. Several studies highlighted the importance of obtaining screening TSH level in patients newly diagnosed with type 1 diabetes.[4] A part from biological screening, careful examination of patient presenting with DKA is of primary importance and might alert the clinician to the possibility of associated thyrotoxicosis. Such signs include goitre at inspection, exophthalmia, hyperthermia and persistent tachycardia despite rehydration. As demonstrated in our case, failure to reach a correct diagnosis in such patients might

carry life-threatening consequences, assuming that treatment of one endocrinopathy might decompensate another. In a similar manner, it is interesting to note that treatment of thyroid disease with thyroxine among patients suffering from undiagnosed Addison's disease, has been associated with severe adrenal crisis.[9]

Declaration of competing interests

Nothing to declare.

References

1. Misra S, Oliver NS. Diabetic ketoacidosis in adults. *BMJ* 2015;**351**:h5660. doi:10.1136/bmj.h5660.
2. Davis SM, Maddux AB, Alonso GT, Okada CR, Mourani PM, Maahs DM. Profound hypokalemia associated with severe diabetic ketoacidosis. *Pediatr Diabetes* 2016;**17**:61–5. doi:10.1111/pedi.12246.
3. Cerai LMP, Weber G, Meschi F, Mora S, Bognetti E, Siragusa V, *et al.* Prevalence of Thyroid Autoantibodies and Thyroid Autoimmune Disease in Diabetic Children and Adolescents. *Diabetes Care* 1994;**17**:782–3. doi:10.2337/diacare.17.7.782.
4. Fleiner HF, Bjøro T, Midthjell K, Grill V, Åsvold BO. Prevalence of Thyroid Dysfunction in Autoimmune and Type 2 Diabetes: The Population-Based HUNT Study in Norway. *J Clin Endocrinol Metab* 2016;**101**:669–77. doi:10.1210/jc.2015-3235.
5. Husebye ES, Anderson MS, Kämpe O. Autoimmune Polyendocrine Syndromes. *N Engl J Med* 2018;**378**:1132–41. doi:10.1056/NEJMra1713301.
6. Maciel RMB, Lindsey SC, Silva MRD da. Novel etiopathophysiological aspects of thyrotoxic periodic paralysis. *Nat Rev Endocrinol* 2011;**7**:657–67. doi:10.1038/nrendo.2011.58.
7. Osada E, Hiroi N, Sue M, Masai N, Iga R, Shigemitsu R, *et al.* Thyroid storm associated with Graves' disease covered by diabetic ketoacidosis: A case report. *Thyroid Research* 2011;**4**:8. doi:10.1186/1756-6614-4-8.
8. Ko GTC, Chow CC, Yeung VTF, Chan HHL, Li JKY, Cockram CS. Thyrotoxic periodic paralysis in a Chinese population. *QJM* 1996;**89**:463–8. doi:10.1093/qjmed/89.6.463.
9. Murray JS, Jayarajasingh R, Perros P. Deterioration of symptoms after start of thyroid hormone replacement. *BMJ* 2001;**323**:332–3.