CASE REPORT

'Diabetic ketoacidosis may not always be the answer...'

Deirdre Philbin, Edina Moylett

Department of Paediatrics,
University College Hospital
Galway, Co Galway, Ireland

Correspondence to

Dr Deirdre Philbin,
philbind@tcd.ie

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SUMMARY

We present the interesting case of a 9-year-old boy with type 1 diabetes mellitus. He presented to the emergency department extremely unwell and the diagnosis of diabetic ketoacidosis was promptly performed. He was started on the local diabetic ketoacidosis (DKA) protocol, but his recovery remained slow. The possibility of an underlying pathology was later addressed and led to the diagnosis of primary adrenal insufficiency. This case highlights the difficulty in diagnosis of childhood Addison's disease due to its vague and non-specific symptoms and the importance of a high degree of clinical suspicion. This case also highlights the existence of autoimmune polyendocrine syndromes and the ongoing need to increase awareness and screening of these conditions.

BACKGROUND

This case demonstrates a presentation of primary adrenal insufficiency which was initially treated as a diabetic ketoacidosis.

Primary adrenal insufficiency is known to have wide variations in presentation which unfortunately, can frequently lead to delayed and misdiagnoses. We aim to highlight one such presentation.

This case also emphasises the need for clinicians to be aware of autoimmune polyendocrine syndromes and thus, to consider coexisting autoimmune conditions in their differential diagnoses.

CASE PRESENTATION

A 9-year-old boy, presented to the emergency department with a 1-day history of nausea, lethargy and mild headache. He had a known history of type 1 diabetes mellitus which was diagnosed when he was aged 2.

His blood sugar readings at home had all been within normal limits and he was fully compliant with his insulin regime. The patient mother reported that he woke up feeling unwell and had one episode of vomiting prior to his presentation to the emergency department.

His initial blood sugar reading on arrival was 13.6 mmol/L and urinalysis showed 4+ ketones.

The patient did not have any diarrhoea, respiratory nor urinary symptoms. His current insulin regime was insulin detemir (Levemir) 14 units at night and insulin aspart (Novorapid) 5 units three times daily.

He had a medical history of diabetic ketoacidosis (aged 7 years) secondary to gastroenteritis. He had also required intensive care unit admission (aged 5 years) due to pneumococcal sepsis.

Of note, his father had died from sudden adult death 1 year previously.

The patient had been seen in the diabetic outpatients 2 months prior to this presentation. His glycated haemoglobin reading at this time was 8%.

INVESTIGATIONS

Physical examination revealed a confused and restless state. He had dry mucous membranes. His vital signs demonstrated hyperthermia (temperature 38.7°C) with tachycardia (pulse rate=135 bpm) and tachypnoea (respiratory rate=35 breaths/min). A thready pulse was noted. His oxygen saturations were 99% on room air.

Cardiovascular examination revealed a soft pansystolic murmur at the left lower sternal edge. Respiratory examination demonstrated grossly clear lungs despite poor inspiratory effort. His abdomen was soft but mild tenderness was elicited in all four quadrants. There was no rigidity or rebound tenderness.

Neurological examination revealed a Glasgow coma score of 14/15 with equal and reactive pupils. Tone, power, coordination and reflexes were normal in all four limbs. No meningeal signs were elicited.

His venous blood gas demonstrated a metabolic acidosis with respiratory compensation. pH=7.3, pCO₂=5.25 kPa and pO₂=3.41 kPa. HCO₃⁻ was 17.8 mmol/L and base excess was 6.7 mmol/L. His lactate was elevated at 3.4 mmol/L. Glucose was 13.4 mmol/L (table 1).

His serum electrolytes demonstrated hyponatraemia (sodium =124 mmol/L). Serum potassium was 4.8 mmol/L.

His full blood count revealed normal white cell and platelet counts. Renal function tests showed urea=9.7 mmol/L and creatinine=76 µmol/L. Liver function tests were normal. C reactive protein was elevated at 45 mg/L (table 2).

Table 1 Venous blood gas results at presentation: (reference ranges for child aged 6–12 years)

pH	7.30	(7.33–7.43)
pCO ₂	5.25 kPa	(5.5–6.8 kPa)
pO ₂	3.41 kPa	(4–5.3 kPa)
HCO ₃ ⁻	17.8 mmol/L	(22–26 mmol/L)
Base excess	6.7 mmol/L	(–3 to +3 mmol/L)
Lactate	3.4 mmol/L	(0.5–2.2 mmol/L)
Glucose	13.4 mmol/L	(3.0–6.0 mmol/L)

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Table 2 Laboratory results at presentation: (reference ranges for child aged 6–12 years)

Haemoglobin	14.5 g/L	(11.5–15.5 g/L)
White cell count	8.5×10^9 /L	(4.5– 14.5×10^9 /L)
Platelets	317×10^9 /L	(150– 450×10^9 /L)
C Reactive protein	45 mg/L	(<10 mg/L)
Na ⁺	124 mmol/L	(133–145 mmol/L)
K ⁺	4.8 mmol/L	(3.5–5.0 mmol/L)
Cl [−]	89 mmol/L	(96–110 mmol/L)
Urea	9.7 mmol/L	(2.5–6.5 mmol/L)
Creatinine	76 μ mol/L	(20–80 μ mol/L)

A full septic workup was completed, including blood cultures, urinalysis and chest X-ray.

A repeat venous blood gas showed a worsening acidosis (pH=7.28) and he was transferred to the intensive care unit.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis at this point included: diabetic ketoacidosis secondary to infection (source unclear), hypovolaemic shock and possibly, pseudohyponatraemia secondary to hyperglycaemia.

TREATMENT

Emergency department management included fluid administration –10 mL/kg bolus of 0.9% NaCl. Three fluid boluses were required. This was followed by start of maintenance fluids, with an estimated 8% dehydration.

He was also started on an insulin infusion as per diabetic ketoacidosis protocol at 0.1 units/kg and empiric intravenous ceftriaxone.

While in the intensive care unit, the patient remained very drowsy and confused. He had hourly blood sugar monitoring and arterial blood gas analysis. Sodium levels remained low at 126–128 mmol/L despite normalisation of other parameters.

He had intermittent episodes of agitation overnight with associated urinary incontinence. His mother felt that he did not recognise her. Owing to the deterioration in his neurological status, suspicion arose for the development of cerebral oedema or possibly encephalopathy. He underwent CT and MRI scans of his brain, both of which were normal.

Urine output was maintained at 2 mL/kg/h. He was very slow to recover with a poor oral intake, but over the following days, an improvement was noted. He was transferred to the paediatric ward once stable.

A review of his medical history revealed five hospital admissions since diagnosis. He was noted to be very unwell at each presentation and always had a slow recovery. Sodium levels were persistently low, ranging from 127 to 135 mmol/L.

The possibility of an underlying pathology was addressed. His urinary sodium was 164 mmol/L. A tanned complexion was present which had previously been disregarded as his mother had always reported that the child's colour was 'similar to his father's'. An early morning cortisol was low at 102 μ g/dL with no diurnal variation, midnight cortisol=103 μ g/dL.

A short synacthen test was subsequently performed—the results of which were consistent with primary adrenal insufficiency.

He was started on hydrocortisone therapy—a single stat dose of 25 mg intravenous was administered, followed by 40 mg/m²/

day in three divided doses (to taper to 20 mg/m²/day when well). He was also started on fludrocortisone 0.1 mg daily.

OUTCOME AND FOLLOW-UP

The patient responded very well to steroid therapy and blood sugars remained well controlled. He was discharged home well, wearing a medi-alert bracelet highlighting his Addison's diagnosis.

The patient's mother was provided with emergency advice regarding double dosing of his hydrocortisone for moderate infection and triple dosing if severely unwell and emergency (intramuscular hydrocortisone 50 mg was prescribed in case of severe vomiting/collapse).

He continues to be closely monitored in the outpatient setting.

DISCUSSION

Diabetic ketoacidosis is diagnosed by hyperglycaemia (blood glucose >11 mmol/L) and metabolic acidosis (venous pH <7.3 and/or plasma bicarbonate <15 mmol/L) as defined by consensus statements from European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society (ESPE/LWPES) in 2004, the American Diabetes Association (ADA) in 2006, and the International Society for Pediatric and Adolescent Diabetes (ISPAD) in 2007.

The symptoms of diabetic ketoacidosis may include polyuria, polydipsia, weight loss and fatigue. Nocturia and daytime enuresis may also be present. Neurological findings include lethargy, reduced level of consciousness and coma. Cerebral function in diabetic ketoacidosis is thought to be related to the severity of acidosis rather than blood glucose concentration.¹

In a child with known type 1 diabetes mellitus who presents extremely unwell, the diagnosis, or exclusion of, diabetic ketoacidosis is a priority. However, this case highlights the importance of considering underlying pathology in such children and the difficulties in the diagnosis of childhood Addison's disease.

Despite significant advances in molecular genetics of congenital and acquired causes of adrenal insufficiency in the paediatric population, the clinical diagnosis is frequently delayed or missed because of its vague and non-specific symptoms.²

In 5 of 16 children in Melbourne, Australia, diagnosed with primary adrenal insufficiency over a 10-year period, there was a median of 2 years' delay between the onset of the first symptoms and the diagnosis.³

Patients with acute adrenal insufficiency generally present with acute dehydration, hypotension, hypoglycaemia or altered mental status. Acute adrenal insufficiency may be triggered by infection or trauma but may also be seen without an obvious concomitant illness or stress. Hypoglycaemia is most common in young children.

Altered mental status may occur at any age with or without hypoglycaemia.

Hyperkalaemia is not a consistent presenting sign of primary adrenal insufficiency in childhood and its absence cannot rule out the condition.⁴ As in this case, the presence of hyponatraemia should raise suspicion.

Case reports of unusual paediatric presentations of Addison's disease in the literature vary from acute mesenteric ischaemia⁵ to an acute abdomen, complicated by cardiomyopathy.⁶

The importance of a high degree of clinical suspicion must be emphasised.

This case also highlights the existence of autoimmune polyendocrine syndromes and the ongoing need to increase awareness and screening of these conditions.

The two major autoimmune polyendocrine syndromes (APS-1 and APS-2), both have Addison's disease as a prominent component.

APS type 1 involves chronic mucocutaneous candidiasis, chronic hypoparathyroidism+autoimmune adrenal insufficiency. APS type 2 involves autoimmune adrenal insufficiency with autoimmune thyroid disease and/or type 1 autoimmune diabetes mellitus.

It is well recognised that more than 20 years may elapse between the onset of one endocrinopathy and the diagnosis of the next.⁷

The presence of one autoimmune condition should encourage clinicians to be vigilant for others and to consider the possibility of autoimmune polyendocrine syndromes. Children with type 1 diabetes are known to be at increased risk of autoimmune thyroiditis and coeliac disease and are regularly screened for these

conditions. Approximately 1% of children with type 1 diabetes have autoimmune adrenalitis.⁸

We aim to increase awareness of the association of type 1 diabetes with Addison's disease in children. In doing so, we hope to promote a higher degree of clinical suspicion, potentially preventing a life-threatening adrenal crisis.

Contributors DP wrote the case report and completed the literature review; EM edited the case report prior to submission.

Competing interests None.

Patient consent Obtained.

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Learning points

- The diagnosis of Addison's disease is frequently delayed due to its vague and varied presentation. A high index of suspicion is required to aid diagnosis and prevent adrenal crisis.
- Autoimmune polyendocrine syndromes, type 1 and 2, both have Addison's disease as a prominent component.
- The presence of one autoimmune condition should encourage clinicians to be vigilant for others.

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