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New onset type 1 diabetes presenting as ketoacidosis simultaneously presenting with autoimmune hyperthyroidism—a case report☆,☆☆

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Abstract

Autoimmune conditions are common with an estimated prevalence in the UK of 2.5%. The presence of one condition should always prompt the clinician to look for others if new symptoms arise. Autoimmune polyglandular syndromes are well described. However, it is unusual for two or more autoimmune conditions to present simultaneously. We describe a case of two autoimmune conditions—type 1 diabetes and Graves' disease—being diagnosed for the first time in the same individual at the same visit to the emergency department. We suggest that thyrotoxicosis be added to the list of potential precipitants for diabetic ketoacidosis.

Keywords: Ketoacidosis; Autoimmune hyperthyroidism

1. Case

A previously well 24-year-old male healthcare assistant presented with a 3-week history of polydypsia, polyuria, and a 1-week history of vomiting. He had also experienced weight loss of approximately 12 kg over the past 2 months despite describing himself as 'ravenously hungry'. His only other symptom of note was his tremor that has been present for the preceding 2 weeks. The only significant family history was of type 1 diabetes in his maternal grandmother.

On examination, he was cachectic; neck examination showed he had a smooth, non-tender, enlarged thyroid, with no associated lymphadenopathy. He had no evidence of thyroid eye disease. His pulse rate was 105 bpm, in sinus rhythm. His blood pressure was 148/93 mmHg, his respiratory rate was 20 breaths per minute, and his temperature was 37.3°C. His admission haematological and biochemical data are shown in Table 1. An ECG showed a sinus tachycardia, with voltage criteria for left ventricular hypertrophy.

He was diagnosed with newly presenting type 1 diabetes mellitus and diabetic ketoacidosis. He was treated with insulin, fluids, and potassium, all given intravenously.

Further blood tests taken at the time of admission showed a free thyroxine (fT4) of 48 pmol/l (8–21), a free triiodothyronine (fT3) of 16.7 pmol/l (3.8–6.0), and thyroid-stimulating hormone of <0.01 mIU/l (0.35–3.5). A coeliac screen was negative; vitamin B_{12} and random cortisol levels were normal. Anti-thyroid peroxidise antibodies were positive, and his anti-glutamic acid decarboxylase antibody levels were >2000 U/ml (1–5). Anti-pancreatic islet cell antibodies were also weakly positive. Our institution does not perform anti-thyroid receptor antibodies as a matter of routine, but our laboratory performs anti-thyroid peroxidise antibodies as the thyroid autoantibody of choice.

Following treatment for his ketoacidosis with an intravenous infusion of regular human insulin given at 6

☆ We declare that we have no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

☆☆ Dr. Mercer and Dr. Burt drafted the initial versions of the manuscript. All three authors looked after the patient. Dr. Dhatariya was in charge of the patients' care and finalised the manuscript. He acts as the guarantor for this article.

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Table 1
Haematology and biochemistry values on admission

	Value on admission	Reference range
Serum sodium	130 mmol/l	134–145 mmol/l
Serum potassium	4.6 mmol/l	3.6–5.0 mmol/l
Serum urea	3.6 mmol/l	1.7–7.1 mmol/l
Serum creatinine	77 μmol/l	55–125 μmol/l
Haemoglobin	14.9	13.5–18.0 g/dl
Haematocrit	0.429	0.400–0.540
Arterial pH (room air)	7.250	7.35–7.45
Serum bicarbonate	11.0 mmol/l	22–30 mmol/l
Serum glucose	26.1 mmol/l	3.5–7.8 mmol/l
Haemoglobin A_{1c}	12.1% (109 mmol/mol)	<7.0% (<53 mmol/mol)

U/h until he was ketone free and 6 l of 0.9% sodium chloride solution, his observations 24 h after admission—by which time he was ketone free—were a pulse rate of 110 bpm, in sinus rhythm, blood pressure of 130/65 mmHg, and a respiratory rate of 18 breaths per minute. His temperature was 37.6°C and he had remained slightly pyrexial throughout his admission, however, with no other objective evidence to suggest an infection. A further diagnosis of new onset thyrotoxicosis due to Graves' disease was made for which he was started on carbimazole.

2. Discussion

Autoimmune diseases are common. The prevalence of type 1 diabetes in the UK is 0.34% and that of Graves' disease is 0.65% (Gatling et al., 1998; Tunbridge et al., 1977). An association between thyroid disease and type 1 diabetes is well recognised. Over 13% of patients with type 1 diabetes have thyroid dysfunction, rising to over 30% in women (Perros, McCrimmon, Shaw, & Frier, 1995). The coexistence of two or more autoimmune endocrine disorders in the same patient is described as an autoimmune polyglandular or polyendocrine syndrome (APS) and can be categorised according to the specific disorders. These are described in Table 2. This case was an example of an APS type II (sometimes known as type III), as it included both autoimmune diabetes and thyroid disease, but Addison's disease had been excluded.

Polyglandular syndromes are autoimmune and inherited. In APS II, mutations in the CTLA-4 gene on chromosome 2 have been identified. Mutations in this gene often lead to type 1 diabetes, Graves' disease, or Hashimoto's thyroiditis. However, the manifestation of APS II may also depend on other genetic factors: for example, the presence of defects in the loci of HLA-DR/DQ on chromosome 6. In addition, it has been suggested that environmental factors play a role in triggering the autoimmunity in those who are genetically susceptible (Vaidya & Pearce, 2004).

This case is unusual because both the disorders presented for the first time together. While there are a few known cases of simultaneous new presentation of two endocrine diseases, it is much more usual for one to significantly predate the other. In most of the cases of APS IIb which have been described, the patients were previously known to have either

Table 2
Overview of autoimmune polyglandular syndromes and their component features

	Autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED)		
	PAS I	PAS II (A) (Schmidt's syndrome)	PAS II (B) (or III)
Central clinical feature	Autoimmune adrenal failure (Addison's disease)	Autoimmune adrenal failure (Addison's disease)	Autoimmune thyroid disease (Hashimoto, Graves)
Other clinical features (one or more)	Hypoparathyroidism Chronic candidiasis Gondal failure Hypopituitarism Coaliac disease Pernicious anaemia Vitiligo Alopecia Immune mediated diabetes (type 1) Autoimmune thyroid disease	Autoimmune thyroid disease(Hashimoto, Graves) Pernicious anaemia Vitiligo Alopecia Immune mediated diabetes (type 1) Coeliac disease Gonadal failure	Pernicious anaemia Vitiligo Alopecia Immune-mediated diabetes (type 1) Coeliac disease Gonadal failure
Genetics	Autosomal recessive Defect of AIRE gene	Likely to be an autosomal dominant, with variable expression CTLA-4 gene HLA-DR3 and/or HLA-DR4 haplotypes, chromosome 6	Likely to be an autosomal dominant, with variable expression CTLA-4 gene HLA-DR3 and/or HLA-DR4 haplotypes, chromosome 6
Prevalence	Rare	More common	More common
Onset	Childhood onset	Adult onset	Adult onset

the diabetes or hyperthyroidism (Yeo, Yang, Chen, Peng, & Huang, 2007). Moreover, although cases of DKA and thyrotoxicosis can occur simultaneously, it is much less common for them to be both new presentations of the underlying autoimmune diseases.

A literature search on Medline found just three cases of previously well patients who presented, as this patient did, with DKA and thyrotoxicosis simultaneously: two in 1980 in England (Bridgman & Pett, 1980) and one in New Zealand in 2004 (Lim, Lunt, Ojala, & Turner, 2004). In all of these cases, as with our patient, the DKA was the most prominent clinical feature, and the simultaneous thyrotoxic crisis became apparent afterwards. None of these patients had been previously diagnosed with either diabetes or autoimmune thyroid disease. However, the two English cases were slightly more complex. The patients both presented with a pyrexia, with concurrent infections, and both were managed by the surgeons because abdominal pain and vomiting were the central symptoms. In contrast, our patient presented more classically with the features of diabetic ketoacidosis. The other notable difference between the previously reported cases and ours was that all the other patients were female. As with most autoimmune conditions, APS type II is more common in women than in men (Baker, 1997).

This case illustrates the fact that thyrotoxicosis can precipitate DKA. It worsens glycaemic control in people with diabetes by various mechanisms, such as increasing production of basal glucose (and reducing the effectiveness of insulin in suppressing it) and increasing absorption of exogenous glucose. It is also thought to increase peripheral insulin resistance (Battacharyya & Wiles, 1999). Conversely, it is also known that poor glycaemic control can mask some of the signs of hyperthyroidism (Wu, 2000), demonstrating the importance of considering concomitant diagnoses in a patient presenting with DKA.

In summary, although this case is unusual, it demonstrates the need to be aware that the symptoms of thyrotoxicosis can be masked by DKA. Secondly, this case also reinforces the need to exclude other associated conditions when making a diagnosis of one autoimmune endocrine disease. Finally, while thyrotoxicosis is not traditionally considered a precipitant for DKA, it is clear that the changes in glycaemic control that result from thyrotoxicosis could result in ketoacidosis. Hence we feel that thyrotoxicosis should be added to the list of potential precipitants for DKA.

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