Learning points
- Sweet's syndrome is acute febrile neutrophilic dermatosis.
- Sweet's syndrome is characterised by tender, erythematous, or violaceous nodules or plaques.
- It may be a harbinger of malignancy, either solid tumours or lymphoproliferative disorders.
- It may be seen in a variety of other conditions, including inflammatory bowel disease, sarcoidosis, and infections.
- It may be seen with subacute thyroditis, possibly as a result of immune mediated cytokine expression.

infectious agents, such as chlamydia, atypical mycobacteria, and *Yersinia enterocolitica*.[4] Several cases of Sweet's syndrome have resulted from exogenous causes, including exposure to hydralazine and jalapeno peppers.[5]

The association of thyroid disorders and Sweet's syndrome has been reported. Alcalay *et al* first reported the simultaneous occurrence of Sweet's syndrome and subacute thyroiditis in a 63 year old woman, and suggested that both disorders had a possible identical viral aetiology.[6] Of interest is the fact that the first report, as ours, came from Israel. O'Brien and Darling described a 33 year old woman with hypothyroidism and Sweet's syndrome,[7] and Nakayama and colleagues documented the interesting occurrence of Sweet's syndrome with Takayasu's arteritis and Hashimoto's thyroiditis in a 39 year old woman.[8]

The patient described in this report developed classical lesions of Sweet's syndrome one week after the onset of subacute thyroiditis. Although the relationship between these two disorders may have been fortuitous, it is tempting to consider a possible pathogenetic connection. The effect of treatment with interferon alfa on the occurrence of thyroiditis[9] and the development of dermatological inflammatory disorders, including Sweet's syndrome,[10] hints towards a possible connection via immune mediated side effects of cytokines. However, further cases will have to be reported in order to establish this observation.

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Addison's disease in type 1 diabetes presenting with recurrent hypoglycaemia

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Submitted 1 June 1999
Accepted 6 September 1999

Abstract

Primary adrenal insufficiency (Addison's disease) often develops insidiously. Although a rare disorder, it is more common in type 1 diabetes mellitus. A 19 year old male with type 1 diabetes and autoimmune hypothyroidism experienced recurrent severe hypoglycaemia over several months, despite a reduction in insulin dose, culminating in an adrenal crisis. Recurrent severe hypoglycaemia resolved after identification and treatment of the adrenocortical insufficiency. In type 1 diabetes, undiagnosed Addison's disease can influence glycaemic control and induce severe hypoglycaemia.

(*Postgrad Med J* 2000;**76**:230–232)

Keywords: type 1 diabetes; Addison's disease; hypoglycaemia; cortisol

Hypoglycaemia is a common side effect of insulin treatment for type 1 diabetes. However, people with diabetes are susceptible to other causes of spontaneous hypoglycaemia that can affect the non-diabetic population. A patient is described who developed recurrent severe hypoglycaemia associated with underlying glucocorticoid deficiency from undiagnosed Addison's disease.

Case report

A 19 year old male who had developed type 1 diabetes when aged 7 years, was treated with twice daily soluble and isophane insulins. Thyroid microsomal antibodies were present at diagnosis and at the age of 11 years he had developed hypothyroidism requiring thyroxine. There was no family history of autoimmune disease. As a teenager his attendance at the diabetic clinic was erratic and he seldom monitored his

Table 1 Features and treatment of Addison's disease

Common symptoms and signs	**Laboratory features**
Anorexia	Hyponatraemia
Weakness	Hyperkalaemia
Fatigue	Uraemia
Nausea and vomiting	Metabolic acidosis
Postural dizziness	Hypercalcaemia
Weight loss	Normochromic normocytic anaemia
Hypotension	Eosinophilia
Pigmentation	Lymphocytosis
Emergency treatment	**Maintenance therapy**
Measure plasma cortisol	Primary adrenal failure:
Intravenous hydrocortisone 100 mg with 0.9% saline	Hydrocortisone 15–20 mg am, 5–10 mg at 4 pm *or* Hydrocortisone 15–20 mg am, 5 mg at noon, 5 mg at 4 pm *and* Fludrocortisone 0.05–2 mg am
	Secondary adrenal failure: Hydrocortisone as above

Learning points

- In patients with type 1 diabetes who develop unexplained recurrent hypoglycaemia, the development of an associated endocrinopathy, such as Addison's disease, should be considered.
- An unexplained reduction of total insulin requirement of more than 15%–20% (in response to recording frequent low blood glucose values) should arouse suspicion of adrenocortical insufficiency. This may precede the clinical features.
- The development of abnormal pigmentation in a patient with type 1 diabetes merits investigation of adrenocortical function with dynamic tests.
- In children or teenagers with type 1 diabetes a clue to underlying Addison's disease is a decline in normal growth velocity.
- The diagnosis of adrenocortical insufficiency in a patient with type 1 diabetes requires simultaneous investigation of thyroid function and thyroid autoantibodies; biochemical evidence of hypothyroidism may resolve after glucocorticoid replacement.
- Plasma electrolyte abnormalities are not invariable in adrenal insufficiency until an advanced stage; 20%–30% of patients do not have hyponatraemia or hyperkalaemia at any time.

blood glucose. His overall glycaemic control was poor, with total HbA1 10.3% in February 1992 (non-diabetic range 5%–8 %). Body mass index (BMI) was 19 kg/m^2 with blood pressure of 120/70 mm Hg (seated). In May 1994, a hypoglycaemia induced seizure followed excessive consumption of alcohol, and 14 days later hypoglycaemic coma, the cause of which was not identified, was treated in hospital. In July 1994, he was detained and charged by the police after driving erratically and dangerously for four miles on the city bypass. In custody he was drowsy, incoherent, and verbally abusive. A venepuncture wound in the antecubital fossa of his right arm raised the suspicion that he may have injected drugs despite a drug screen being negative. However, after four hours his father arrived and immediately recognised that his son's aberrant behaviour was attributable to severe hypoglycaemia; complete recovery occurred rapidly after the ingestion of oral carbohydrate.

At outpatient review later that month, he reported experiencing twice weekly episodes of severe hypoglycaemia despite having reduced his insulin dose. HbA1c was 6.2% (non-diabetic range 4.0%–5.8%). His skin was mildly pigmented, his blood pressure (seated) was 98/58 mm Hg and BMI was 24 kg/m^2. Although plasma electrolytes were normal, a Synacthen test (intramuscular synthetic adrenocorticotrophic hormone (ACTH), 250 μg) was performed. The basal plasma cortisol concentration was 172 nmol/l but unfortunately the second sample was discarded by the laboratory. The patient did not attend for a repeat Synacthen test and was not seen until November 1994, when he was readmitted with acute vomiting. He was afebrile with a sinus tachycardia and blood pressure was 130/90 mm Hg. Although dizzy on standing, no postural hypotension was demonstrable. Truncal pigmentation and vitiligo on the arms were observed. Hyponatraemia (sodium 129 mmol/l), hyperkalaemia (potassium 5.2 mmol/l), and a modest metabolic acidosis (bicarbonate 14 mmol/l; hydrogen ion 49 nmol/l) were present, random blood glucose concentration was 11.7 mmol/l, and he had ketonuria. Intramuscular synthetic ACTH did not stimulate a rise in plasma cortisol (baseline 253 nmol/l; 30 minutes after injection, 265 nmol/l). Adrenal antibodies were positive. He recovered after intravenous administration of saline and hydrocortisone and was treated thereafter with oral hydrocortisone and fludrocortisone. His insulin dose returned to the premorbid level and no further severe hypoglycaemia occurred. At a subsequent court hearing, the driving charges were dismissed after presentation of medical evidence that unpredictable hypoglycaemia may be associated with undiagnosed Addison's disease.

Discussion

This patient with insulin dependent diabetes, who previously had prolonged suboptimal glycaemic control, developed recurrent severe hypoglycaemia without any change in treatment or physical activity. He was presumed to have increased insulin sensitivity secondary to underlying glucocorticoid deficiency, the treatment of which restored his usual total insulin requirement and abolished the hypoglycaemia.

Addison's disease is rare, with a reported incidence in the UK of about 5 cases/million population/year[1] and a prevalence of 110 per million, although it is at least five times more common in the diabetic population.[2] It often presents with non-specific features (see table 1), making the diagnosis elusive. An association with type 1 diabetes is well recognised with 10%–18% of patients with Addison's disease also having insulin dependent diabetes.[3 4] However, the prevalence of Addison's disease in type 1 diabetes is reported to be lower at 1.2%.[5] Diabetes precedes the development of adrenocortical insufficiency in most patients,

and often presents at a young age.[6] Addison's disease in patients with type 1 diabetes usually has an autoimmune aetiology, and the present patient had pluriglandular endocrine deficiencies. The association of Addison's disease with thyroiditis is known as Schmidt's syndrome and is a common manifestation of type 2 polyglandular autoimmune syndromes.[7]

Hypoglycaemia is not a common presenting feature of Addison's disease, either in patients with type 1 diabetes or in the non-diabetic population, although it has been reported to be associated both with primary and secondary glucocorticoid deficiencies,[8 9] and is considered to be caused by enhanced insulin sensitivity. Diminished secretion of other counter-regulatory hormones may also contribute and a combination of cortisol and growth hormone deficiencies has been associated with profound hypoglycaemia in diabetic patients treated with insulin.[8 9]

The much more common factors of excessive insulin, insufficient carbohydrate, and exercise that precipitate or predispose to acute hypoglycaemia in patients with type 1 diabetes, must not be overlooked despite evidence of glucocorticoid deficiency. Although in the present case contributory factors such as excessive alcohol consumption and delayed ingestion of meals could be identified in a few of the episodes of severe hypoglycaemia, the recurrence of severe hypoglycaemia in conjunction with a decline in total insulin dosage was suggestive of another underlying pathogenetic problem, unassociated with the patient's self management of his diabetes.

The classical features of adrenal failure such as anorexia, lethargy, and weight loss with deranged plasma electrolytes, were not prominent in the present case until the patient presented in adrenal crisis, although signs of hypotension, hyperpigmentation and vitiligo (which occurs in 4%–17% of patients with autoimmune Addison's disease) had been noted. The decreasing insulin requirement with a concomitant, but unexplained, improvement in glycaemic control heralded the change in endocrine status. This highlights the importance of maintaining an awareness that patients with established autoimmune disorders are at risk of developing other endocrinopathies.

A defence of automatism associated with insulin induced hypoglycaemia in people with insulin treated diabetes is usually not accepted by the courts, although evidence of contemporaneous hypoglycaemia may mitigate any penalty imposed. The law considers that the individual is responsible for allowing hypoglycaemia to occur (through careless or reckless behaviour),[10] even though many episodes of hypoglycaemia have no obvious precipitating factor. However, in the present case the hypoglycaemia could be considered to be truly "spontaneous" as it resulted from an unrecognised underlying endocrine disorder which directly influenced insulin sensitivity and blood glucose concentrations, and driving charges were dismissed.

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Galactorrhoea and pituitary mass: a typical prolactinoma?

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Submitted 27 April 1999
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Abstract

A 21 year old woman presenting with galactorrhoea, hyperprolactinaemia, and a pituitary mass on magnetic resonance imaging (MRI) is described who was referred to us before planned pituitary surgery. Although a thorough history did not suggest hypothyroidism, laboratory studies revealed profound primary hypothyroidism. At that time, pituitary MRI showed homogeneous enlargement of the pituitary gland consistent with pituitary hyperplasia due to primary hypothyroidism. With thyroid hormone replacement therapy the galactorrhoea resolved, concentrations of prolactin and thyroid hormones returned to normal, and the pituitary shrunk to normal size within two months. This case illustrates that primary hypothyroidism can present only with galactorrhoea and pituitary mass, and should therefore be considered in the differential diagnosis of hyperprolactinaemia and pituitary enlargement.
(*Postgrad Med J* 2000;**76**:232–234)

Keywords: primary hypothyroidism; galactorrhoea; pituitary mass