Important Symptoms

Intractable hiccups – an early feature of Addison's disease

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Summary: Hiccups has not been previously reported as a manifestation of Addison's disease. We report two cases where persistent hiccups was an early feature of Addison's disease. Steroid replacement cured the symptoms in both patients with no recurrence.

Introduction

Hiccup is an intermittent spasmodic contraction of the diaphragm, often accompanied by similar contraction of the accessory muscles of inspiration. It may be central in origin; due to excitation of the motor cortex and brainstem respiratory centre, or peripheral, due to phrenic, vagus, or upper spinal nerve irritation.¹

Hiccups are usually transient, but when persistent, they may be a symptom of a metabolic, abdominal thoracic, or central nervous system disease.²

Case reports

Case 1

A 49 year old man presented to his doctor with a 3-month history of frequent and prolonged hiccups, epigastric pain and nausea. He was treated symptomatically. However, the symptoms persisted. Over the 12 months he had consulted a number of doctors. Gastroscopy was performed and reported normal. He became depressed and withdrawn; he felt very tired, lost weight, his short term memory was impaired and he could not cope with work. Clinical depression was diagnosed and imipramine was prescribed by the psychiatrist, which helped but did not completely abolish the hiccups. Despite anti-depressant therapy, his symptoms progressed and he developed painful muscles and cold hands and feet.

Thyroid function tests showed total thyroxine (T4) 13 nmol/l (normal 50–150), triiodothyronine (T3) 1.4 nmol/l (1.0–2.9) and thyroid stimulating hormone (TSH) 75.2 mU/l (0.5–6.5). L-Thyroxine was prescribed and the dose was gradually increased to 300 µg daily. His symptoms remained unchanged and he

became progressively weaker, vomited continuously, his hearing became sensitive and he could not sleep. He was admitted to hospital as an emergency. On examination, he was thin and tanned; alopecia totalis was noted, pulse was 90 per minute and blood pressure 90/60 mmHg with postural drop. He was resuscitated with intravenous hydrocortisone and fluid replacement, with excellent response and the hiccups were cured.

Investigations on arrival showed plasma sodium 134 mmol/l, potassium 4.2 mmol/l, blood sugar 5.2 mmol/l, haemoglobin 10.2 g/dl and urea 14.3 mmol/l. The electrocardiogram showed small voltage and inverted T waves in leads V1–V3, which reverted to normal after steroid therapy. Serum cortisol was 10 nmol/l (180–600) and did not rise after an injection of tetracosactrine. Thyroid and adrenal antibodies were present. He made a full recovery, taking cortisol, fludrocortisone and L-thyroxine 100 µg daily.

Case 2

A 60 year old man had been on replacement therapy for Addison's disease for 5 years. On direct questioning he clearly remembered several month's history of intractable hiccups with abdominal discomfort before the diagnosis was confirmed.

His symptoms, including hiccups, resolved completely following steroid therapy.

Discussion

Addison's disease is an uncommon condition, caused by autoimmune adrenalitis, or less commonly, due to adrenal destruction by tuberculosis, malignant disease, syphilis, amyloid, and haemochromatosis.³ In the age group 25 to 65 years, it affects 39 per million.⁴

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However, the condition is probably under diagnosed due to the fact that the clinical presentation is often non-specific. A combination of Addison's disease and hypothyroidism may occur in multiple autoimmune disease.⁵ Treatment with thyroxine alone in such cases may lead to Addisonian crisis.⁶

Hiccups has not been described in Addison's disease before. In the two cases hiccups presented early, were very disturbing and exhausting, particularly in the first case. In both cases abdominal symptoms were prominent too. Protracted hiccups may lead to serious complications including vomiting, dehydration, debilitation and even death.⁷ Several metabolic conditions are associated with hiccups: uraemia, diabetes mellitus,⁸ hypocalcaemia,⁹ and hyponatraemia.¹⁰

It is difficult to explain the aetiology of hiccups in Addison's disease. Hypersensitivity of taste, smell and hearing are uncommonly associated with Addison's disease; symptoms which are reversible by steroid replacement.¹¹

If we postulate that these symptoms are due to

cranial nerve irritation, then hiccups and vomiting in Addison's disease can be explained by phrenic and vagus nerve irritation or hypersensitivity, and this may explain how the anti-cholinergic effect of imipramine partially helped the hiccups in the first patient.

However, a central cause for hiccups due to the underlying metabolic changes cannot be ruled out, since abnormal changes in the electroencephalogram are observed in a high proportion of patients with Addison's disease.¹² The treatment of hiccups is often unsatisfactory. Manoeuvres such as repeated swallowing, local irritation of the oropharynx, or tickling the nasopharynx with a nasogastric tube have been recommended.¹³ When these measures fail, drugs such as atropine, chlorpromazine, metoclopramide, nifedipine,¹⁴ amitriptyline,¹⁵ and anti-epileptic drugs¹⁶ may be tried, depending on the cause. Our patients' hiccups were cured by steroids.

We, therefore, suggest that in an unexplained case of hiccups, particularly when associated with abdominal symptoms, Addison's disease should be excluded.

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