Unusual association of diseases/symptoms

An endocrinological emergency masquerading as an overdose

Nihal Sinha,¹ Faisal Rahman,² Mirae Shin,¹ Peter Burbridge¹¹Acute General Medicine Department, University of Oxford, Oxford, Oxfordshire, UK;²Acute General Medicine Department, John Radcliffe Hospital, Oxford, UK

Correspondence to Dr Nihal Sinha, n.sinha35@gmail.com

Summary

Primary adrenocortical insufficiency (Addison's disease) is a potentially life-threatening endocrinological disorder caused by destruction of the adrenal cortex with consequent reduction in glucocorticoid and mineralocorticoid function. Although this is a rare condition, misdiagnosis can result in fatal consequences. Previous case reports have described the neuropsychiatric manifestations of Addison's disease which can result in misdiagnosis. Here the authors describe how a psychiatric history combined with atypical biochemical results can point towards a mistaken diagnosis of poisoning and hence disguise an Addisonian crisis.

BACKGROUND

Primary adrenal insufficiency is a rare disease but prompt diagnosis and immediate institution of treatment can prevent death.^{1 2} Treatment must often be initiated prior to confirmatory tests. The disease can present with neuropsychiatric features such as aggression, depression and personality change. The typical picture of hyperkalaemia, hyponatraemia and metabolic acidosis with a normal anion gap may not always be present due to factors such as vomiting. The case presented here highlights the importance of considering an Addisonian crisis despite atypical biochemical results.

CASE PRESENTATION

A 44-year-old, white woman presented to the emergency department at 0600 with behavioural disturbances, escorted by the police. She was reported to have been shouting and displaying aggressive behaviour at a local hotel. Upon assessment by the medical team the patient gave a history of recent social problems and admitted to having fallen out with her family. After several arguments with family and friends they had asked her to move out and she had been staying in a hotel. She could remember behaving strangely including shouting and throwing things around but was unable to recall why she was behaving in this way. On direct questioning she described a 2 month history of lethargy and weight loss and a 2 day history of vomiting. She mentioned that her skin had remained tanned since she had visited India 3 months previously. She denied taking any regular medication although she was discovered to have tricyclic antidepressants (TCA) (amitriptyline 10 mg) on her person by the nursing staff. She denied substance abuse or overdose and upon direct questioning said the antidepressants had recently been prescribed by her general practitioner. Family history included maternal thyroid problems and paternal type II diabetes.

On examination, the patient appeared dehydrated and in mild distress. Vital signs were as follows: blood pressure 94/52 mm Hg; heart rate 140 beats/min; temperature, 38.5°C; respiratory rate, 14 breaths/min and oxygen saturation 95% on room air. The woman was

thin with bronzed skin but no palmar or buccal pigmentation. There was no obvious focus of infection. The rest of the examination was unremarkable except that the patient was agitated with disorientation.

At 0800, her Glasgow coma score (GCS) dropped to 3/15 with a blood sugar of 0.9 mmol/l. She was resuscitated with 50 mls of 50% dextrose and her GCS recovered to 15/15 after approximately 10 min. The patient was commenced on intravenous fluids. Despite 3 litres of intravenous normal saline given over approximately 2 h, she remained tachycardic and hypotensive but had urine output exceeding 50 ml/h.

INVESTIGATIONS

Full blood count was unremarkable. Blood chemistry (taken prior to intravenous fluids starting) found normal sodium (135 mmol/l), normal potassium (3.7 mmol/l), hypochloraemia (98 mmol/l), normal urea (5.9 mmol/l), normal creatinine (67 µmol/l). Arterial blood gas results showed a metabolic acidosis (pH 7.178, bicarbonate 13.3 mmol/l, lactate 0.9 mmol/l, pCO₂ 4.2 kPa). From this the anion gap was calculated as 27.4 mmol/l (normal range 6–16 mmol/l). The electrocardiograph showed sinus tachycardia with narrow complexes. Urine dipstick and chest radiograph were unremarkable.

DIFFERENTIAL DIAGNOSIS

The combination of disturbed behaviour, metabolic acidosis with raised anion gap and the history of depression with antidepressants found on the patient led to a provisional diagnosis of poisoning including TCA overdose. Urgent reports were obtained from the patient's general practitioner: thyroid function performed 2 weeks prior to admission revealed mild subclinical hypothyroidism with thyroid stimulating hormone 4.54 (0.40–4.50), FT4 11.8 (10–24), sodium 130 mmol/l and potassium 5.4 mmol/l.

OUTCOME AND FOLLOW-UP

A potential diagnosis of Addisonian crisis was considered and a short synthetic adrenocorticotrophic hormone

(Synacthen) test was performed. Her baseline cortisol was <6 nmol/l (180–620) and 1 h level 7 nmol/l. The patient made an excellent clinical response to intravenous hydrocortisone (200 mg initially, then 100 mg intravenously 6 hourly) and further fluid replacement (further 3 litres) over the course of the next 24 h with complete resolution of her acidosis and hypotension (blood pressure increased to 112/96 within 8 h of starting steroids). Her behavioural disturbance resolved over the following 3 days. There was no clinical or laboratory evidence of infection and her fever continued for a further 48 h before resolving. Subsequent investigations confirmed primary adrenal insufficiency (Addison's disease). The patient had positive adrenal cortical antibodies. The adrenals had unremarkable appearance on CT.

DISCUSSION

The presenting biochemical picture in this patient supported an overdose as there was a metabolic acidosis with raised anion gap. This combined with a history of depression and agitated behaviour pointed towards an initial diagnosis of poisoning. In Addison's disease the failing adrenal gland leads to mineralocorticoid deficiency.² In the normal state, aldosterone causes sodium absorption, potassium secretion and H⁺ secretion.³ There are multiple mechanisms by which aldosterone contributes to acid base balance. First, aldosterone increases the secretion of H⁺ in the collection duct. Second, by increasing the tubular luminal sodium concentration it creates a negative potential needed for efficient secretion of H⁺. Third, aldosterone directly and indirectly increases the synthesis of ammonia. Consequently a deficiency in mineralocorticoid function produces hyperkalaemic, hyponatraemic metabolic acidosis with a normal anion gap.⁴

The reason for the absence of this typical biochemical picture in this case is likely to be due to vomiting which had caused a misleadingly normal potassium and reduced chloride thereby creating a falsely raised anion gap. A diagnosis of Addison's must be considered in all patients with hypoglycaemia and/or hypovolaemia even in the absence of typical electrolyte findings.

Although neuropsychiatric features of Addison's disease, hypoglycaemia and the associated electrolyte imbalance is well described⁵ the acute picture of Addisonian crisis may

not always be typical. A history of behavioural changes combined with a metabolic acidosis with other biochemical changes should alert the physician into considering primary adrenocorticoid deficiency. The importance of making a prompt diagnosis of Addison's disease is highlighted by a recent case⁶ in which a 22-year-old lady presented with fever, jaw pain, shock and hypokalaemia was discovered to have Addison's disease based on postmortem investigations.

Learning points

- ▶ Primary adrenal insufficiency is a rare disease but prompt diagnosis and immediate institution of treatment can prevent death. Treatment must often be initiated prior to confirmatory tests.
- ▶ The disease can present with neuropsychiatric features such as aggression, depression and personality change.
- ▶ The typical picture of hyperkalaemia, hyponatraemia and metabolic acidosis with a normal anion gap may not always be present particularly if significant vomiting has occurred during the Addisonian crisis.
- ▶ Treatment should be started immediately with isotonic fluid resuscitation and corticosteroids.

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Competing interests None.

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