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lesson of the month (2)

A young man with a dizzy spell and acute abdominal pain

Isolated adrenocorticotropic hormone (ACTH) deficiency is a rare cause of secondary adrenal insufficiency and its presentation with adrenal crisis is rather rare. Acute adrenal insufficiency (adrenal crisis) can be an elusive diagnosis, particularly in previously undiagnosed patients. As in this patient, the presentation of adrenal crisis with acute abdominal pain was misdiagnosed as an acute surgical abdomen, leading to a delay in the diagnosis and in the initiation of life saving treatment.

Lesson

A 30-year-old male was admitted to the emergency department with a one-day history of acute, generalised abdominal pain which was dull and aching in nature and associated with nausea, vomiting and sweating. One day prior to the onset of pain he experienced a dizzy spell associated with brief loss of consciousness for a few seconds. His past medical history was unremarkable, his appetite was good and his weight steady.

On examination, he was in hypovolaemic shock with a pulse of 116/min and blood pressure (BP) of 66/48 mmHg with no postural drop. He was pale and fully conscious with a normal Glasgow coma scale. His temperature was subnormal at 35.2°C, but there was no evidence of goitre or any other endocrinopathy. Abdominal examination revealed a diffusely tender abdomen with normal bowel sounds and no organomegaly. Other systems were unremarkable.

Blood investigations showed a moderately raised serum creatinine of 153 µmol/l (71–115) with normal urea and electrolytes (U&E) and normal blood count, except for mild leucocytosis, with normal C-reactive protein (CRP). Blood glucose levels were low at 2.5 mmol/l. Liver function tests, calcium profile and pancreatic enzymes were all unremarkable. A chest X-ray (CXR) proved normal and an abdominal computed tomography (CT) scan suggested mild to moderate ascites and small bilateral pleural effusions.

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A diagnosis of acute surgical abdomen was made by emergency room staff and therefore the patient was admitted under the surgical team. His BP remained low, despite resuscitation with fluids and inotropes, and he later developed a seizure due to documented hypoglycaemia. Subsequent endocrine evaluation confirmed adrenal insufficiency with a flat response on a standard short corticotropin (Synacthen) test (baseline cortisol = 0.5 nmol/l, at 30 minutes cortisol = 5.76 nmol/l and at 60 minutes cortisol = 6.93 nmol/l). Adrenocorticotropic hormone (ACTH) levels were very low at <0.22 pmol/l. Other anterior pituitary hormones were normal except for a significantly raised thyroid stimulating hormone (TSH) of >100 mu/l and a moderately raised prolactin of 640 mu/l (86–390). Full thyroid function tests confirmed primary hypothyroidism with strongly positive thyroid antibodies. Insulin antibodies were positive with negative autoimmune profile including adrenal cortical antibodies. A vasopressin stimulation test (Table 1) showed lack of response in keeping with isolated ACTH deficiency at the pituitary level. A pituitary magnetic resonance imaging (MRI) scan was suggestive of partially empty sella (Fig 1).

The patient was treated with steroids and thyroxine replacement therapy, resulting in a full clinical recovery and complete resolution of the ascites and pleural effusions, and normalisation of renal function and prolactin levels.

Discussion

Adrenal insufficiency is a rare disease with non-specific presenting symptoms such as fatigue, weight loss and anorexia. Because of these non-specific symptoms the disease is easily overlooked and may escape detection for a long time, but it can be life threatening when it presents with acute adrenal insufficiency (acute adrenal crisis).

Primary adrenal insufficiency is caused by diseases of the adrenal glands, whereas secondary and tertiary adrenal insufficiency is due to disruption of the hypothalamic-pituitary-adrenal axis. The symptoms of primary and secondary adrenal

Table 1. Vasopressin stimulation test.

Time (min)	Cortisol (nmol/l)	ACTH (pmol/l)
0	<0.50	<0.22
30	<0.50	<0.22
60	<0.50	<0.22
90	<0.50	<0.22
120	<0.50	<0.22
150	<0.55	<0.22

ACTH = adrenocorticotropic hormone.

insufficiency are similar, although primary adrenal insufficiency is associated with features of mineralocorticoid deficiency such as salt craving and electrolyte abnormalities. Patients with secondary adrenal insufficiency are often able to function very well during unstressed periods and may manifest cardiovascular instability or hypoglycaemia when they undergo physical stress.[1]

Isolated ACTH deficiency is a rare disorder characterised by secondary adrenal insufficiency with low or absent cortisol production, normal secretion of pituitary hormones (other than ACTH) and absence of structural pituitary defects.[2] The defect is usually at the pituitary level and most cases are secondary to an autoimmune process such as lymphocytic hypophysitis.[3] It may also occur after traumatic head injury[4] and pituitary irradiation.[5] Genetic causes are encountered in neonatal and childhood isolated ACTH deficiency.[6]

The presenting symptoms of isolated ACTH deficiency are generally non-specific and similar to those seen in adrenal insufficiency of any cause. Patients with this disorder usually remain asymptomatic during unstressed periods and only present with adrenal crisis when subjected to major stress such as infection. They may also present with hypoglycaemia, which is the presenting feature in over one-third of patients.[7] The association of isolated ACTH deficiency with empty sella,[8] primary hypothyroidism and transient hyperprolactinaemia[9] is well recognized.

Acute adrenal insufficiency is a rare presentation of isolated ACTH deficiency.[10] Patients with acute adrenal insufficiency typically present with severe hypotension, abdominal pain and vomiting. Such individuals are sometimes misdiagnosed as having an acute abdomen.[1] Hypotension is not solely due to mineralocorticoid deficiency, as pure glucocorticoid deficiency also plays a contributory role by causing catecholamine dysfunction.[7] This could account for the relative unresponsiveness to catecholamines in unrecognised adrenal crisis.[1]

In this patient, the combination of hypoglycaemia and refractory hypotension were suggestive of adrenal crisis, which was overlooked and misdiagnosed as an acute surgical abdomen. Surgical exploration in his case could have been catastrophic in the setting of unrecognised adrenal crisis. The most likely cause of isolated ACTH deficiency and empty sella is lymphocytic hypophysitis. This possibility is supported by the presence of autoimmune hypothyroidism and positive insulin antibodies.

All physicians, in particular those dealing with emergency admissions, should be able to suspect, diagnose and manage acute adrenal insufficiency. The simple treatment with glucocorticoid replacement therapy is lifesaving, whereas missing or delaying the diagnosis could result in a fatal outcome.

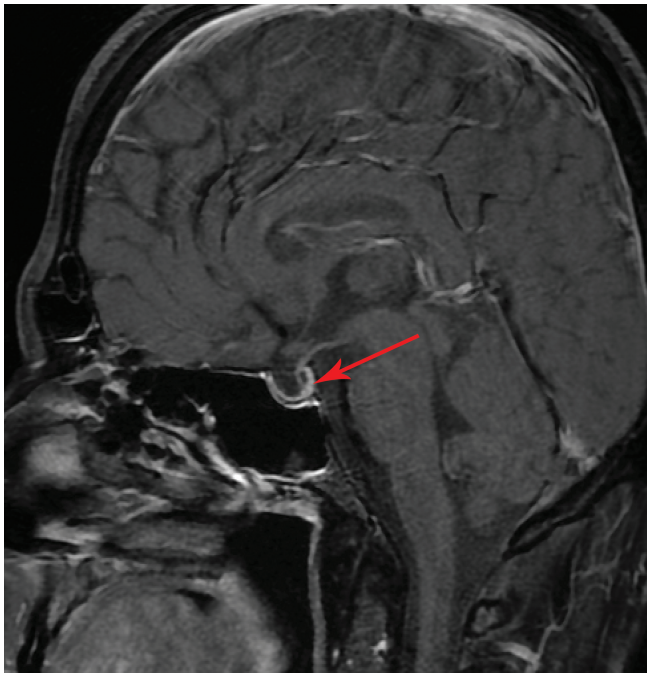

Fig 1. Sagittal view of pituitary MRI scan showing partially empty sella tursica (arrow). MRI = magnetic resonance imaging.

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