Adrenal insufficiency due to the development of bilateral adrenal haemorrhage following hip replacement surgery

Emily T Mudenha and Manjusha Rathi
Department of Diabetes and Endocrinology, Kings Mill Hospital, Mansfield Road, Sutton-in-Ashfield NG17 4JL, Nottinghamshire, UK
Corresponding author: Emily T Mudenha. Email: emily.mudenha@nhs.net

Case report

A 75-year-old man underwent a right total hip replacement for osteoarthritis. His comorbidities included atrial fibrillation and hypertension for which he was taking warfarin, sotalol 80 mg twice daily, co-amiloFruse 5/40, simvastatin 40 mg and paracetamol. One week prior to his surgery, warfarin therapy was stopped and his International Normalised Ratio on the day of operation was 1.1. No intra or post-operative problems were encountered. On Day 3 post operation, warfarin was reintroduced and on Day 7, his International Normalised Ratio was within therapeutic range (2.4) and he was discharged home.

A week later, he presented to the Emergency Department with symptoms of intermittent diarrhoea and vomiting. His blood pressure was 94/58 mmHg. Laboratory investigations revealed sodium 132 mmol/L (134–145), potassium 7.6 mmol/L (3.5–5.3), urea 14.8 mmol/L and creatinine 177 µmol/L and International Normalised Ratio 3.6. He was resuscitated with intravenous fluids, hyperkalaemia was treated with insulin and dextrose and regular calcium resonium. In order to investigate his symptoms and abnormal biochemistry, an ultrasound scan of his renal tract was arranged which did not reveal any abnormality. Sepsis screen was negative. Despite intravenous fluid resuscitation and stopping antihypertensive medication, he had persisting symptomatic hypotension. Therefore, a Short Synacthen test was organised which revealed baseline serum cortisol 62 nmol/L and post synacthen cortisol 63 nmol/L confirming a diagnosis of adrenal insufficiency. He was started on six hourly intravenous hydrocortisone therapy. His blood pressure and renal function improved and he was discharged on Hydrocortisone (10 mg am, 10 mg lunchtime 5 mg with evening meal) and fludrocortisone 50 micrograms once daily replacement regime. During this period, his warfarin therapy was continued and investigations to identify the cause for adrenal insufficiency were arranged as an outpatient.

His adrenal antibodies were negative, Magnetic Resonance Imaging scan adrenals showed enlarged adrenal glands and radiological features consistent with adrenal haemorrhage (Figures 1 and 2). He then had a follow-up Computerised Tomography scan of the abdomen three months after the initial MRI scan which revealed reduction in size of the adrenal masses (left adrenal mass measures 1.3 cm compared to 2.4 cm on the preceding MRI scan and the right adrenal mass measures 1.1 cm, previously 1.9 cm). However, despite reduction in the size of the adrenal masses, he has not recovered from adrenal insufficiency and there has been no improvement in his underlying cortisol reserve and hydrocortisone, fludrocortisone as well as the warfarin therapy is continued.
Discussion

The adrenal glands play a major role in the physiological response to stress, maintenance of blood pressure and electrolyte homeostasis. Adrenal failure due to bilateral adrenal haemorrhage is very rare.

The pathophysiology of bilateral adrenal haemorrhage is poorly understood. In the absence of trauma, existing scientific literature suggests that it may represent a multifactorial aetiology (Table 1). Due to the unique anatomy of the adrenal gland vascular supply, it is particularly vulnerable to haemorrhage. The adrenal gland receives a rich blood supply from the aorta and the inferior phrenic and adrenal arteries, which form a subcapsular plexus but only one vein is present for drainage. Several pathophysiological changes during the intraoperative and postoperative period make the adrenal gland susceptible to adrenal haemorrhage. These may include intra-operative hypotension, vascular engorgement and stasis which cause an increase in adrenal venous pressure. Platelet aggregation followed by venous thrombosis, vasoconstriction, and disruption of the vascular endothelium also has an important role in the pathogenesis of adrenal haemorrhage.

Other risk factors for developing postoperative bilateral adrenal haemorrhage are sepsis, presence of coagulopathy, thromboembolic disorders, antiphospholipid-antibody syndrome and increasing use of anticoagulation to prevent postoperative thromboembolic events.

The diagnosis of adrenal insufficiency secondary to adrenal haemorrhage is often delayed because of the nonspecific nature of the clinical presentation and low index of clinical suspicion. Until recently, most diagnoses of adrenal haemorrhage were made at post-mortem examination. Many cases do not have specific signs of adrenal insufficiency, which usually occurs in patients with damage of more than 90% of the adrenal cortex. However, with the increasing use of imaging modalities, estimated incidence of bilateral adrenal haemorrhage is 4.7–6.2 per million in developed nations.

In terms of the clinical presentation in this case, relevant findings included nausea, vomiting, diarrhoea and abdominal pain, and then the development

Table 1. Risk factors for non-traumatic bilateral adrenal haemorrhage.

| Risk Factor                                                                 |
|----------------------------------------------------------------------------|
| Postoperative (anti-coagulation, intraoperative hypovolaemia, pre-existing adrenal insult/insufficiency) |
| Sepsis – Waterhouse-Frederichson                                            |
| Coagulopathies – antiphospholipid syndrome, HIT                             |
| Anticoagulation therapy – Warfarin/heparin/ aspirin/ chronic NSAID use    |
| Prior steroid use/known adrenal insufficiency                               |
| Neoplastic – cyst/malignant – myoleiosarcoma, phaochromocytoma             |
| Essential thrombocytosis/thrombocytopenia                                  |
| Stress                                                                      |
| Adrenal aneurysms                                                           |
| Hypertension                                                                |
| ACTH administration                                                         |
| Pancreatitis                                                                |
| Burns                                                                       |
| Pregnancy, including pre-eclampsia and acutely postpartum                  |
of persistent hypotension despite stopping antihypertensive medication in a known hypertensive patient and hyperkalaemia which raised the clinical suspicion.

Once diagnosis is suspected, Adrenal insufficiency is readily diagnosed by the short synacthen test. These individuals should be treated with both glucocorticoid and mineralocorticoid therapy as with any other cause of primary adrenal insufficiency.

The usual physiological Glucocorticoid replacement dose is equivalent to 15–25 mg of hydrocortisone and fludrocortisone dose 50 and 250 µg OD. 8

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