Bilateral adrenal haemorrhage

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DOI:
10.1093/qjmed/hcw212

The heterogeneous presentation and causes of adrenal haemorrhage

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Key points for clinicians regarding Adrenal Haemorrhage (AH)
• AH should be considered in anticoagulated patients with new-onset back pain. • Acute AH should be managed as an acute adrenal crisis with intravenous hydrocortisone [(1)]. • Underlying neoplastic pathology of the adrenal gland must be considered in the context of acute AH, interval imaging may reveal the diagnosis.

Introduction

Adrenal haemorrhage (AH) is a rare condition with an unknown incidence. Due to non-specific symptoms at presentation, it can present to many specialities (e.g. general

medicine, urology, emergency medicine etc.), clinicians require a high clinical suspicion to avoid missing the diagnosis.

AH has potentially life threatening consequences and historically was often diagnosed at autopsy [(2)]. AH has been reported to occur spontaneously, but is associated with additional predisposing factors. Those reported include anticoagulation, underlying adrenal lesion (e.g. metastatic disease or primary adrenal tumour), trauma, severe sepsis (e.g. Waterhouse-Frederichson's syndrome associated with meningococcal septicaemia), antiphospholipid antibody syndrome, burns, or the early postoperative period, including unrelated procedures (e.g. joint arthroscopy, laparotomy) [(1–3)].

Clinical cases

In Table 1 we summarise key points of three cases of AH presenting to our institution, demonstrating the heterogeneous presentation, management and underlying pathologies associated with this condition.

Discussion

Hypotension, shock and non-specific abdominal pain are commonly reported presenting features for significant AH [(2)]. Others can include weakness, vomiting, palpable abdominal masses, and tenderness. Unilateral or minor AH may go undetected. Although reported in unilateral AH, adrenal insufficiency (AI) is more common with bilateral AH, as 90% of the adrenal tissue must typically be destroyed before hormone deficiency is clinically apparent. Biochemical investigations may demonstrate hyponatraemia and hyperkalaemia but this is not uniform in all cases.

AI resulting in adrenal crisis is a medical emergency and treatment should not be delayed in cases of high clinical suspicion. Treatment with high dose intravenous (IV) hydrocortisone should be commenced immediately to prevent rapid clinical deterioration and

shock. Ideal treatment regimen is 100 mg IV bolus of hydrocortisone, followed by a 200 mg infusion over 24 hours, or 50 mg boluses every 6 hours [(1)]. IV rehydration should also be initiated according to clinical need.

A recognised method for reliably diagnosing glucocorticoid deficiency is to carry out a short Synacthen test (Cosyntropin test), measuring serum cortisol at baseline and 30 minutes post intramuscular or IV injection with 250 micrograms of synthetic ACTH [(1)]. Due to assay inter-variability, cut off values for cortisol will depend on your local hospital assays derived from unselected normative data [(4)]. Diagnostic measures should never delay treatment and hence in the case of strong clinical suspicion of acute adrenal insufficiency, hydrocortisone treatment should be initiated without awaiting laboratory results. A diagnosis of concurrent mineralocorticoid deficiency is made by an elevated plasma renin and low aldosterone levels on a paired sample. Once confirmed synthetic mineralocorticoid replacement should be added, once the oral hydrocortisone dose is reduced below a total daily dose of 50 mg (e.g. fludrocortisone 100-150 micrograms per day) [(3)].

Due to the acute nature of AH, computed tomography (CT) is often the first modality of imaging to be performed. A diagnosis of AH may be suspected by the presence of enlargement and distortion of the adrenal glands, with hyperdense areas pre-contrast; pre-adrenal fat stranding is also a recognised feature. Contrast enhanced magnetic resonance imaging (MRI) has higher sensitivity and specificity for identifying underlying haemorrhagic pathology, and may help delineate the acuteness of AH by haemoglobin breakdown products. [(5)]. Ideally, follow-up imaging should demonstrate a reduction in the size of the bilateral masses.

Whilst most cases are self-limiting, adrenalectomy or embolisation may be required in occasional refractory cases of AH [(6)]. A diagnosis of AH should raise the suspicion of underlying overt or occult primary or secondary adrenal malignancy in patients without a

history of recent anticoagulation, as demonstrated in Case 3. Equally, underlying connective tissue disease or vasculitis should be excluded.

AH associated AI has the potential to recover, and ongoing assessment with 9am cortisol and/or short Synacthen tests as per local protocols to assess adrenal reserve should be undertaken at appropriate intervals.

Table 1

	Case 1	**Case 2**	**Case 3**
Age, Sex	63 year old male	70 year old male	79 year old female
Past medical history at time of diagnosis	Thromboembolic disease (recently anticoagulated) Rheumatoid arthritis with interstitial lung disease	Pulmonary embolism October 2015 COPD	Coeliac disease Diverticular disease. Type 2 diabetes. Hypertension. Upper GI bleed. Congestive cardiac failure
Medication	**Warfarin,** Sulfasalazine, Methotrexate, Simvastatin	Sodium Docusate, Ranitidine, Salbutamol & Tiotropium Inhaler.	**Clopidogrel**, Doxazosin. Ramipril. Bisoprolol. Frusemide. Atorvastatin. Insulin, Calcium/Vit D, Dosulepin, Metformin.
Symptoms	Acute right flank pain. Night sweats with weight loss.	Breathlessness; underwent CTPA showed bilateral adrenal masses. Further investigations arranged.	Acute and severe left-sided back pain located close to the spine
Initial working diagnosis	Possible metastatic lung cancer new lesion identified in lung.	Pulmonary embolus	Renal colic
Imaging	CT: bilateral adrenal abnormalities measuring 3.1 cm on the right and 2.6 cm on the left (not demonstrated on scan 18 months prior).	CT with contrast: Rapid bilateral adrenal enlargement between October and December 2015, density of adrenal gland 30HU.	CT: 2 x 4 cm Left adrenal mass 2014, appearances consistent with AH. Subsequent right adrenal bleed on clopidogrel 2015
Adrenal work up (Plasma renin normal range 5.1-38.7)	Glucocorticoid deficiency (morning cortisol 150 nmol/l) Plasma renin: 96.7 ng/l Aldosterone: <30 pmol/l	Glucocorticoid deficiency (SST 0 min 165, 30 min 176 nmol/L) Plasma renin 122 ng/l; aldosterone: <30 pmol/l	Glucocorticoid deficiency (SST 0 min 341nmol/l, 30 min 414nmol/l) Plasma renin 174.8 ng/l Aldosterone 60 pmol/l
Initial working diagnosis	Bilateral AH with AI secondary to recent anticoagulation. Lung lesion requires further investigation.	Bilateral AH with AI secondary to recent anticoagulation.	AH (initially left, with subsequent right AH)
Outcome	Significant and progressive reduction in size of lesions on 6 month interval imaging. Lung lesion subsequently diagnosed as inflammatory change	MRI: right adrenal gland reduced in size from 4.3 x 2.9 cm to 3.2 x 1.9 cm. Left adrenal gland also reduced in size from 4.3 x 2.9 cm to 2.8 x 2.4 cm.	Further bilateral adrenal enlargement on follow-up imaging. CT-guided biopsy confirmed metastatic hepatocellular carcinoma (HCC).
Final diagnosis	AI secondary to bilateral AH.	AI secondary to bilateral AH.	Metastatic HCC with bilateral adrenal metastases. Died 2015

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