Original Article

Acute non-traumatic adrenal haemorrhage—management, pathology and clinical outcomes

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Background: Acute adrenal haemorrhage is a rare medical emergency. The aim of the series was to study the clinical presentation and management of patients presenting with acute non-traumatic adrenal haemorrhage.

Methods: The records of patients presenting with an acute abdomen secondary to adrenal haemorrhage and treated in a tertiary endocrine surgical unit over a period of 6 years were reviewed.

Results: Of the 11 included patients, there were 4 males and 7 females; the median [range] age at presentation was 58 [27–89] years. All were initially managed conservatively for bleeding, except one who underwent angioembolisation to ensure hemodynamic stability. Two patients underwent percutaneous drainage of persistent collection and suspected sepsis. Biochemical workup showed hyper function with metanephrine excess in 1 patient. Adrenalectomy was performed in 5 patients after a median [range] of 10 [7–11] weeks. Histology showed benign pathology in 2 patients, malignant in 2 patients and necrotic tumour in 1 patient. Two patients died of disseminated metastatic disease at 5 and 2 months after presentation with bleeding. Conservative management in the other 3 patients was successful at a median follow up of 26 [6–66] months.

Conclusions: Acute adrenal haemorrhage is usually associated with an underlying pathology; which may be benign or malignant; functional or non-functional. Initial conservative management is preferred as it allows determination of functional status and elective surgery, if necessary.

Keywords: Adrenal haemorrhage; adrenalectomy; management

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Introduction

Adrenal haemorrhage is an uncommon condition, with reported incidence of 0.14–1.1% on post-mortem studies (1,2). It is difficult to recognize clinically as the presentations are non-specific and vary in severity, particularly in patients with other concurrent illnesses. Failure in early diagnosis of bilateral adrenal haemorrhage may lead to death as a result of untreated primary adrenal insufficiency (3,4). Primary adrenal insufficiency becomes clinically profound only after 90% of the adrenal cortex is compromised (4).

Non-traumatic adrenal haemorrhage has been reported in association with underlying stress like sepsis, pregnancy, and after abdominal surgery (5-14). During this period, there is a surge of circulating catecholamines and adrenocorticotrophic hormone (ACTH) that leads to vasoconstriction of the draining venules (15). Increased platelet aggregation as a result of high level of catecholamines predispose to adrenal vein thrombosis (4). Subsequently, venous stasis and increase in adrenal venous pressure leads to rupture of the thin walled adrenal venules (3). Other conditions reported to be linked with

spontaneous adrenal haemorrhage are anti-phospholipid syndrome, anticoagulant and haematological disorders (16-18).

Spontaneous adrenal haemorrhage has been defined variably in the literature. Some authors refer to this as the absence of trauma or anti-coagulant use while others restrict its use to cases where there is no obvious predisposition other than adrenal pathology (19,20). Bleeding in the absence of any adrenal pathology (i.e., normal adrenals on imaging after resolution of bleeding) and without other predisposing factors is thought to be very rare.

Literature on the management of adrenal haemorrhage is limited. In the published case reports, most patients are initially treated conservatively (5,10-14). Surgical resection has been performed electively by either the open or laparoscopic approach (9,21). CT scan may be performed during follow-up to monitor the size of the haematoma and evaluate any underlying lesion (22). Other options of treatment reported are urgent surgical resection (23) and angioembolisation of the adrenal arteries (8,23,24). However, both emergency treatments were reserved in patients with hemodynamic instability.

The objective of this study is to evaluate the clinical presentation, underlying predisposition and management strategies in adult patients who were referred to a single tertiary unit with acute abdominal pain secondary to non-traumatic adrenal haemorrhage.

Methods

This study was a retrospective review of the medical records of consecutive adult patients presented with acute adrenal haemorrhage and referred to the endocrine surgery unit at Sheffield Teaching Hospitals from 2012 to 2018. Patients who had evidence of recent bleed on radiology but did not present acutely with features consistent with bleeding and those with adrenal bleeding following trauma were excluded.

In addition to routine assessment and monitoring, computed tomography was performed in all patients at the time of the acute episode. Biochemical investigations such as serum cortisol, renin and aldosterone level and plasma or urine assessment for catecholamine/metanephrine excess were performed following resolution of the acute event.

Information on demographics, presentation, diagnosis and management was retrieved by one observer and validated by another. As this was a case series, no formal ethics application or informed patient consent was deemed necessary. Patient details were kept in secure electronic servers within the hospital intranet and the data was anonymised prior to analyses and reporting.

Results

In total, 11 patients were referred following a recent admission for spontaneous adrenal haemorrhage between 2012–2018. Of this, 7 (63.6%) patients were female and 4 (36.4%) were male. The median (range) age was 58 years (range, 27–89 years). Four (36.4%) patients were on anticoagulants (2 on rivaroxaban and 2 on warfarin) for atrial fibrillation.

Five (45.5%) patients underwent definitive surgical treatment after a median [range] of 10 [7–11] weeks. One patient who underwent surgery and another patient managed conservatively died of disseminated non-adrenal malignant disease at 5 and 2 months respectively after presentation with bleeding. Two other patients died of non-adrenal disease at 28 and 12 months after initial presentation. Conservative management in the other 3 patients was successful at a median follow up of 26 [6–66] months. *Table 1* showed the summary of demographic factors, initial management and follow up of patients presenting with acute, non-traumatic adrenal haemorrhage.

Discussion

Acute adrenal haemorrhage presents mostly with abdominal and flank pain (25,26), as noted in all our patients. Other symptoms like neuropsychiatric presentations, hypotension and anaemia are uncommon (27). A number of conditions are reported to be associated with non-traumatic adrenal haemorrhage as mentioned previously (3,5-18). Recognition of these existing predisposing factors (in particular anti-coagulant use) may help determine the initial management plan in this group of patients. In the patients on anti-coagulants in our series; bleeding appeared to resolve in all four patients.

Although pregnancy is a known risk factor for adrenal haemorrhage (10,11), the risk is unclear (28). It may occur without additional factors and is reported in complicated pregnancies such as hyperemesis gravidarum and difficult labour (11,28,29). One patient in our case series had history of post-partum haemorrhage 15 weeks before presentation.

Regardless of underlying risk factors, biochemical testing for hyperfunction and repeat cross-sectional imaging after the acute event is required to exclude underlying adrenal

Table 1 Clinical features, initial management and follow up of patients presenting with acute, non-traumatic adrenal haemorrhage

No.	Age/ gender	Clinical features and predisposing factors (other than abdominal pain)	Urgent intervention	Functionality	Follow up/status	Final diagnosis/pathology	Outcomes
1	77/M	Hypertension, on rivaroxaban	No	No	Repeat CT—reduced size with benign features; no surgery	Likely benign	Died of non-adrenal cause 28 months after presentation
2	89/F	INR 4.5, on warfarin	No	No	Repeat CT—increased size with features of malignancy; no surgery	Likely malignant	Died of non-adrenal cause 12 months after presentation
3	68/M	Hypertension, excessive sweating and feeling unwell, on rivaroxaban	No	No	Repeat MRI—reduced size with benign features; no surgery	Likely benign	Well at 26 months after presentation
4	44/F	Not reported	No	No	Repeat CT—'normal' adrenal; no surgery	Likely benign	Discharged well at 66 months after presentation
5	27/F	Shoulder tip pain, post-partum haemorrhage 6 weeks prior resulting in anemia	US guided drainage after resolution of bleeding	No	Repeat CT—infected collection; further percutaneous drainage and antibiotics done	Likely benign	Well at 6 months after presentation
6	64/F	Not reported	Left adrenal artery embolization	Pheochromocytoma	Repeat CT—persistent lesion; laparoscopic adrenalectomy done	Infarcted tumour—possible phaeochromocytoma	Well at 7 months after presentation
7	45/F	Not reported	US guided aspiration of collection after resolution of bleeding	No	Repeat CT—recurrent bleeding and progression; open adrenalectomy done for palliation of symptoms and bleeding	Adrenal metastasis (from breast cancer)	Died of metastatic breast cancer 5 months after presentation
8	72/M	Pain radiating to the back, sweating and clamminess, on warfarin	No	No	Subsequent admission for disseminated lung cancer; no surgery	Likely malignant	Died of metastatic lung cancer 2 months after presentation
9	27/F	Associated back pain	No	No	Repeat CT—persistent lesion; laparoscopic adrenalectomy done for persistent pain	Neurilemmoma with cystic degeneration	Well at 12 months after presentation
10	58/M	Not reported	No	No	Repeat MRI—reduced size, but persistent; hand-assist laparoscopic adrenalectomy to establish diagnosis	Cortical hyperplasia	Discharged well at 8 months after presentation
11	41/F	Nausea and vomiting	No	No	Repeat CT—persistent lesion, possibly malignant; open adrenalectomy and nephrectomy done	Oncocytic adrenal cortical neoplasm uncertain malignant potential	Well at 4 months after presentation

pathology. In a systematic review, 80% of bleeding adrenal tumours were benign (26). Common benign tumours underlying bleeding include phaeochromocytoma (15), cortical lesions, adrenal pseudo cysts and lipomas (21,30). Malignant adrenal tumours associated with adrenal haemorrhage include adrenocortical carcinoma and metastasis (26). Nevertheless, in around 13% of patients with adrenal haemorrhage, no significant underlying pathology was detected and follow up imaging demonstrated regression of the hematoma without no evidence of an underlying adrenal mass (26). In this presented case series, four patients had resolution of bleeding with either benign looking or 'normal sized' adrenals on repeat imaging. These four patients along with two others with adrenal metastases in the context of disseminated disease did not undergo surgery. Of those who had surgery, one had a phaeochromocytoma (n=5), the pathology included a possible phaeochromocytoma, a benign cortical lesion, a metastasis, a neurilemmoma and a lesion of uncertain malignant potential.

The definitive management of the non-traumatic adrenal haemorrhage is still uncertain and debatable. Initial conservative management has now replaced the trend of early surgery in early years due to increasing availability of CT scan (31). In patients with evidence of persistent bleeding and hemodynamic instability despite supportive care, angioembolisation has been used with good results in the acute setting (8,24). In the presented case series, angioembolisation was done in one patient and two patients required aspiration and drainage for infected hematoma soon after the acute episode.

In the systematic review, the majority of patients who presented with adrenal haemorrhage eventually had interval adrenalectomy (26). Interval adrenalectomy will allow the resolution of inflammatory process, thereby reducing the morbidity of surgery and facilitating minimally invasive approaches. In the presented case series (n=11), five patients had undergone adrenalectomy for either persistent symptoms, hyper function or indeterminate lesions on imaging. The laparoscopic approach was used in two patients, hand-assist laparoscopy in one and open approach in two.

In conclusion, initial conservative management is the preferred treatment as the surgery may be avoidable in some instances. Further investigations after resolution of bleeding will allow the clinician to determine the functional status and reassess the lesion on imaging. This will ensure that the patients are well-optimized before elective surgery and minimally invasive approaches may be used in an elective setting, if appropriate.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: As this was a case series, no formal ethics application or informed patient consent was deemed necessary.

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