



# Spontaneous Adrenal Hemorrhage—a Mixed Bag: 18 Cases from a Single Institution

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## Abstract

Spontaneous adrenal hemorrhage is a rare clinical entity which can lead to an adrenal crisis, shock, and death. We conducted this study to analyze the etiopathogenesis, clinical presentation, imaging modality, and treatment of patients with spontaneous adrenal hemorrhage. Retrospective analysis of 18 patients with spontaneous adrenal hemorrhage managed between 2005 and 2017 at a single institution was performed. The most common presenting symptom was abdominal pain in 10 (55.6%) patients. Contrast-enhanced computerized tomography (CECT) was the most commonly used diagnostic modality (16/18 [88%]). Bilateral adrenal hemorrhage was seen in 6 patients (33%). Adrenal insufficiency was detected in 7 (38.9%) and these patients received steroid therapy. Etiology of the bleed included idiopathic (5 [27.8%]), antiphospholipid antibody syndrome (APLA) (5 [27.8%]), and pheochromocytoma (4 [22.2%]), associated with pregnancy, anticoagulant use, pseudoaneurysm, and myelolipoma in 1 (5.5%) each. Nine (50%) patients could be managed conservatively, and 8 (44.4%) required adrenalectomy while embolization was performed in one (5.6%). There were no mortalities. In this series, the most common clinical presentation of a patient with spontaneous adrenal hemorrhage was abdominal pain. The detection of an unexplained adrenal hemorrhage should prompt one to look for predisposing conditions like APLA. Patients with adrenal hemorrhage should be evaluated for adrenal insufficiency and if present, steroid therapy needs to be initiated. As seen in this series, not all patients with adrenal hemorrhage require an adrenalectomy.

**Keywords** Adrenal hemorrhage · Adrenal crisis · Antiphospholipid antibody syndrome · Pheochromocytoma

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## Introduction

Spontaneous adrenal hemorrhage is a rare clinical entity which was previously diagnosed primarily at post-mortem. Reported incidence in various autopsy studies ranges from 0.14 to 1.1% [1]. The advancements in imaging technology and their increased usage have resulted in the increased frequency of diagnosis of adrenal hemorrhage (1.5–5%) [2]. The risk factors for adrenal hemorrhage are based on case reports/series and include trauma, sepsis, and severe stress, following major surgeries, anticoagulant therapy, chronic nonsteroidal anti-inflammatory abuse, antiphospholipid antibody (APLA) syndrome, tumors of the adrenal gland, and pregnancy [3–6]. The clinical presentation of these patients varies depending upon the rate and degree of hemorrhage and the volume of adrenal cortex affected by the bleed. If left untreated, this may lead to adrenal crisis, shock, and death. Therefore, a high level of suspicion for patients at increased risk for adrenal hemorrhage may lead to early diagnosis and improved survival.

## Material and Methods

This was an institution review board, and ethics committee approved the retrospective study of patients with spontaneous adrenal hemorrhage managed either in the departments of endocrinology, endocrine surgery, urology, and obstetrics or in the surgical intensive care unit (ICU) at a single institution between January 2005 and December 2017. Patients managed in general medical wards or in the medical ICU as well as those in whom complete data was unavailable were excluded. Data was collected from the computerized hospital information system and was summarized using mean ± SD/median (min, max) for continuous variables and frequency with percentage for categorical variables. The etiopathogenesis, clinical presentation, imaging modality used, treatment, and outcome were analyzed.

## Results

Eighteen patients with spontaneous adrenal hemorrhage were managed during the study period. The mean age of presentation was 39 years (range 27–59 years) with eight males and ten females. The clinical presentation and etiology of the bleed for these patients are depicted in Tables 1 and 2.

Contrast-enhanced computer tomography (CECT) was the most common imaging modality used for evaluation (16/18 [88%]) (Fig. 1) while in the remaining two patients, magnetic resonance imaging (MRI) was used. The average tumor size on imaging was 6.4 cm (range 3.8–15 cm). Imaging revealed bilateral adrenal hemorrhage in 6 patients (33.3%) (Fig. 2). Among them, four were diagnosed with APLA syndrome, one patient had an associated pregnancy, and one was associated with a pheochromocytoma. Twenty-four-hour urine catecholamines and 8 am cortisol levels were checked in all patients for functional assessment. The 8 am cortisol level was low in 8/18 (44.4%) patients, seven of whom were hyponatremic (S. sodium < 135 meq/L) and two were hyperkalemic (S. potassium > 5 meq/L). Seven (38%) of these patients required steroid replacement in view of adrenal failure. Nine out of 18 (50%) patients were managed with supportive therapy; this included 5 patients with bilateral hemorrhage. Eight patients (44.4%) underwent an adrenalectomy, and seven were unilateral while one patient with a bilateral pheochromocytoma underwent a

**Table 1** Depicting the clinical presentation

Clinical presentation	N (%)
Abdominal pain	10 (55)
Hypertensive crisis	4 (22)
Dyspepsia	2 (11)
Shock	1 (5.6)
Incidental	1 (5.6)

**Table 2** Enumerating the etiology of the bleed

Etiology	N (%)
Idiopathic	5 (28)
APLA	5 (28)
Pheochromocytoma	4 (22)
Myelolipoma	1 (5.5)
Pregnancy associated	1 (5.5)
Pseudoaneurysm	1 (5.5)
Anticoagulant use	1 (5.5)

bilateral operation—this was the only patient with bilateral hemorrhage that was surgically managed. The indications for surgery were pheochromocytoma (4), myelolipoma (1), and an extensive retroperitoneal hemorrhage (3). The surgical approach included transperitoneal laparoscopy in four, retroperitoneoscopic adrenalectomy in one, and transperitoneal open in three. One patient (5.6%) with uncontrolled hypertension and dialysis-dependent chronic kidney disease developed a right adrenal hemorrhage secondary to a bleed from a pseudoaneurysm. This patient was hemodynamically stabilized and underwent embolization of the pseudoaneurysm (Fig. 3). Twelve patients were reviewed following treatment. The mean duration of follow-up among them was 2.3 years (1–9 years). There were no deaths among any of the patients during the management of their acute episodes nor in the 12 patients reviewed.

## Discussion

The most common reported presenting symptom of adrenal hemorrhage is abdominal/flank pain [3, 7–9]. A similar presentation was witnessed in the majority of patients (55%) in



**Fig. 1** CECT of the abdomen depicting a heterogeneously enhancing mass lesion in the left suprarenal region with discontinuity in its margins and extension into the surrounding area suggestive of a left adrenal hemorrhage



**Fig. 2** CECT of the abdomen depicting thickening of bilateral adrenals with loss of shape suggestive of bilateral adrenal hemorrhage

this cohort. Hypertensive crisis defined as systolic blood pressure > 180 mmHg or diastolic blood pressure > 120 mmHg; a rare presentation of adrenal hemorrhage was seen in four patients (22%) [10]. Among these 4 patients, two were due to a pheochromocytoma, one was due APLA, and one was idiopathic. Adrenal hemorrhage leading to hypertensive crisis in the absence of a pheochromocytoma has been reported previously [1, 11]. The proposed etiology being intermittent excessive secretion of catecholamines due to the raised intra-adrenal pressure secondary to the hematoma [11].

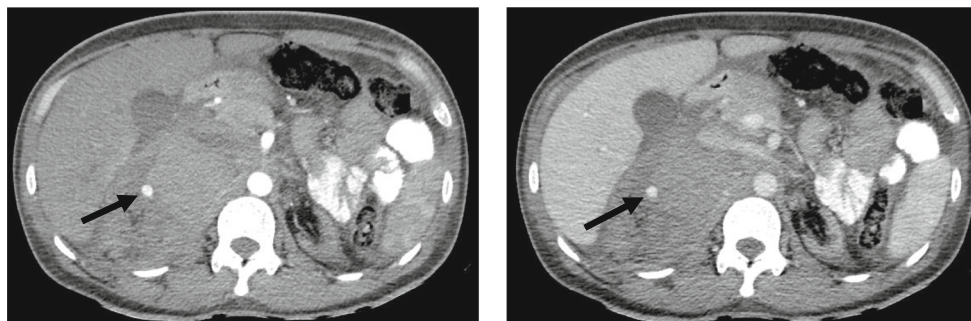
The largest series of spontaneous adrenal hemorrhage (141 cases) has been reported from Mayo Clinic [3]. Their series excluded hemorrhage secondary to an adrenal mass. In their cohort, sepsis/stress was the most common cause (39.7%); other causes included idiopathic (31.2%) and heparin-associated thrombocytopenia (HAT)/APLA (14.2%), following major surgery (9.9%) and patients on anticoagulant therapy/trauma (< 5%) [3]. Our patient cohort did not include patients admitted in medical intensive care units/medical wards. This may account for the majority of adrenal hemorrhages in this series being idiopathic (28%) while there were no hemorrhages due to sepsis. APLA accounted for 28% and among these five patients, four had bilateral adrenal hemorrhage. Spontaneous adrenal hemorrhage in

a preexisting adrenal mass is rare. A recent review of 133 cases reported the most common cause to be due to a pheochromocytoma (48%). Malignant adrenal lesions (20%), pseudocyst/adenoma (17%), and myelolipoma (10%) were the other causes detected [7]. Five (27.8%) patients in this series had an adrenal hemorrhage secondary to an underlying mass; among them, 4 (80%) were due to a pheochromocytoma while the remaining one (25%) was due to a myelolipoma.

CECT of the abdomen is a good modality to evaluate patients with an adrenal hemorrhage. Adrenal hemorrhage appears as a round to oval lesion with focal heterogenous high density (50–70 Hounsfield units) and a lack of contrast enhancement. Periadrenal fat stranding may also be seen. In addition, adrenal hematomas decrease in size and attenuation over time and hence, CECT is a useful imaging modality to assess the lesion on follow-up [12–16]. Magnetic resonance imaging (MRI) is another modality commonly used for the evaluation of patients suspected of having an adrenal hemorrhage. The appearance of hemorrhage on MRI depends on the age of the bleed with signal intensity changing with the progressive degradation of hemoglobin. Therefore, this modality is useful in differentiating acute from chronic bleeds. In the acute phase (< 2 days), hemorrhage is hypointense on T1-weighted image while in 2–7 days, it becomes hyperintense on T1. Chronic hematoma demonstrates a rim of low T1 and T2 signals due to intracellular hemosiderin with central T2 hyperintensity [17]. CECT was adequate modality in the majority of patients (88%) in this series. In view of pregnancy-related adrenal hemorrhage, MRI was performed in the remaining two patients.

Bilateral adrenal hemorrhage is associated with several predisposing factors such as stress caused by surgery, severe illness, overwhelming sepsis, burns, hemorrhagic diatheses, and thromboembolic disease (including antiphospholipid antibody syndrome) [18]. There were 6 patients with bilateral adrenal hemorrhage in this study. Four were due to APLA and one was associated with pregnancy. Interestingly one other patient had bilateral adrenal hemorrhage secondary to bilateral pheochromocytomas. Presotto et al. reported sixteen cases of adrenal hemorrhage due to APLA; fourteen were bilateral whereas

**Fig. 3** CECT of the abdomen depicting a large heterogenous hematoma in the right suprarenal region with a central arterial phase enhancing focus that shows no change in size and shape in the venous phase—suggestive of a pseudoaneurysm (black arrow) with right adrenal hemorrhage



Arterial Phase

Venous Phase



two were unilateral [19]. In addition, Espinosa et al. reported 40 patients with APLA and adrenal hemorrhage [20]. These reports indicate the increased risk of adrenal hemorrhage in patients with APLA. This is due to a hypercoagulable state leading to adrenal vein thrombosis. The unique vascular structure of adrenal glands with a rich arterial supply and a limited venous drainage predisposes this gland for secondary hemorrhagic infarction after venous thrombosis [21]. Hence, bilateral adrenal hemorrhages are commonly seen in these patients. Bilateral adrenal hemorrhage can be potentially life threatening as these patients may develop acute adrenal insufficiency. A mortality rate of 15% has been reported in spite of steroid therapy, and this rate varies according to the severity of the underlying predisposing illness [18]. Therefore, it would be prudent to evaluate for APLA in all patients with bilateral adrenal hemorrhage as well as those with spontaneous adrenal hemorrhage as these patients can avoid surgery. Further, work-up for associated rheumatological disorder can be initiated, and the patient can be started on anticoagulation to prevent further thrombotic episodes. Eight patients (44.4%) in this study developed adrenal insufficiency, seven of whom required steroid supplements.

The management of adrenal hemorrhage depends upon the etiology. Surgery is indicated in patients where the bleed is secondary to an underlying adrenal mass (pheochromocytoma, myelolipoma, adenoma, or malignancy), in whom the hemorrhage is due to trauma, in whom there is a fall in hematocrit or remains unstable despite resuscitation, and in those with extensive retroperitoneal hemorrhage. The surgical approach could be either laparoscopic or open depending upon the nature of the bleed/lesion, hemodynamic stability of the patient, and the experience of the surgeon. Eight patients in this series needed surgery; five were performed laparoscopically while three were open. All other causes of adrenal hemorrhage may be managed conservatively with supportive therapy and specific treatment for the underlying cause. Steroid replacement must be initiated in patients with bilateral adrenal hemorrhage and in those detected to have adrenal failure. Embolization is an alternative strategy reported in literature to control the hemorrhage. This modality has been described in patients with traumatic adrenal hemorrhage with a few cases reporting its use in those with an underlying tumor [22–26]. In our series, embolization was performed successfully in one patient with adrenal hemorrhage secondary to a pseudoaneurysm who presented in shock.

## Conclusion

The most common presenting symptom of adrenal hemorrhage is abdominal pain. A high index of suspicion of adrenal hemorrhage should be raised in the chronically ill, septic, postoperative patients and those on anticoagulant therapy presenting with severe acute abdominal pain. The detection of an

unexplained adrenal hemorrhage should prompt one to look for predisposing conditions like APLA. Patients with adrenal hemorrhage should be evaluated for adrenal insufficiency and if present, supplementary steroid therapy needs to be initiated. Abdominal CECT is a good imaging modality for evaluation of this condition. As seen in our cohort, not all patients with adrenal hemorrhage require an adrenalectomy and with multi-departmental coordination, mortality can be prevented.

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

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