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Adrenal congestion preceding adrenal hemorrhage on CT imaging: a case series

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Abstract

Introduction: Adrenal hemorrhage is an uncommon but potentially life-threatening condition, particularly in cases of bilateral adrenal hemorrhage causing primary adrenal insufficiency. It is difficult to diagnose clinically, particularly in critically ill patients, given its non-specific symptoms and signs, which include abdominal pain, vomiting, fever, weakness, hypotension, and altered conscious state. Non-traumatic adrenal hemorrhage has been observed to occur in times of physiological stress, such as post-surgery, sepsis, burns, and hypotension. This is hypothesized to be due to a combination of increased arterial blood flow to the adrenal glands, the paucity of draining adrenal venules and adrenal vein thrombosis, leading to intra-glandular vascular congestion and subsequent hemorrhage.

Case series: We present four cases of non-traumatic adrenal hemorrhage, which demonstrated features of preceding adrenal congestion (adrenal gland thickening and peri-adrenal fat stranding) on computed tomography (CT) imaging. Comparison was made with 12 randomly selected intensive care patients to observe if these findings were prevalent in this subgroup of patients.

Conclusion: Non-traumatic adrenal hemorrhage is an uncommon condition that is difficult to diagnose clinically. As such, it may be useful to recognize CT features of adrenal congestion as a sign for potential adrenal dysfunction and subsequent adrenal hemorrhage, so early steroid replacement therapy can be commenced to prevent death from adrenal insufficiency.

Key words: Adrenal hemorrhage—Primary adrenal insufficiency—Adrenal congestion—Adrenal gland thickening—Peri-adrenal fat stranding

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Adrenal hemorrhage is a rare condition, with an estimated incidence of 0.14%–1.1% based on post-mortem studies [1, 2]. It is potentially life-threatening when bilateral adrenal glands are involved, leading to primary adrenal insufficiency, although at least 90% of each adrenal cortex must be compromised before this is clinically evident [3].

Non-traumatic adrenal hemorrhage is observed in times of physiological stress, such as recent surgery, hypotension, sepsis (e.g., fulminant meningococcaemia in Waterhouse–Friderichsen syndrome), and burns [4]. The risk of adrenal hemorrhage was also found to be increased in coagulopathic patients who were thrombocytopaenic or being anti-coagulated with heparin [5]. Interestingly, hypercoagulable conditions such as anti-phospholipid syndrome have also been linked with adrenal hemorrhage, presumably secondary to adrenal vein thrombosis [6]. In fact, adrenal vein thrombosis was identified in 33 of 78 cases of adrenal hemorrhage in a pathological study by Fox [7].

As implicated by the above risk factors, non-traumatic adrenal hemorrhage often occurs in critically ill patients. The clinical manifestations of acute adrenal hemorrhage with adrenal insufficiency are non-specific, including abdominal pain, vomiting, fever, weakness, hypotension, and altered conscious state, making it a difficult to diagnosis clinically, particularly in seriously ill patients with multiple concurrent illnesses [8]. Biochemical findings of hyponatremia, hyperkalemia, and fall in hemoglobin are also found in adrenal insufficiency, but may be attributed to other causes [8]. Given these difficulties, primary adrenal insufficiency secondary to adrenal hemorrhage was almost exclusively diagnosed on post-mortem examination in the past [8], as patients were not treated early enough with steroid replacement therapy. With the current widespread use of CT imaging, adrenal hemorrhage is most often identified serendipitously during investigation for other diagnoses, as demonstrated in a case review over 25 years at the Mayo Clinic [9]. As such, it is crucial for radiologists to rec-

ognize early signs of impending adrenal hemorrhage, so they can alert clinicians to the diagnosis. This will enable steroid replacement therapy to be commenced early, which is critical for preventing death from acute adrenal crisis.

We present four cases demonstrating CT features of adrenal congestion, namely adrenal gland thickening and peri-adrenal fat stranding, which can be used to diagnose impending adrenal hemorrhage. Our findings are based on a previous study by Vincent et al. [10], in which the individual limbs of normal adrenal glands in people without known endocrine disorders were found to measure less than 5 mm [95th percentile] on axial CT imaging.

Case series

Case 1

Case 1 is a 55-year-old male who underwent coronary artery bypass surgery, complicated by sternal wound infection and pulmonary embolism, requiring a 3-week intensive care unit (ICU) admission. The patient was commenced on therapeutic heparin anti-coagulation for pulmonary embolism. He was also taking 100 mg Aspirin daily for ischemic heart disease. In the post-operative period, he developed right flank pain. This was investigated with a non-contrast abdominal CT for renal calculi, which demonstrated bilateral peri-adrenal fat stranding and thickening of the adrenal glands (Figs. 1, 2, 3), with no other cause for abdominal pain identified. A repeat contrast-enhanced abdominal CT 4 days later for ongoing abdominal pain, revealed a rounded right adrenal mass, in keeping with right adrenal hemorrhage

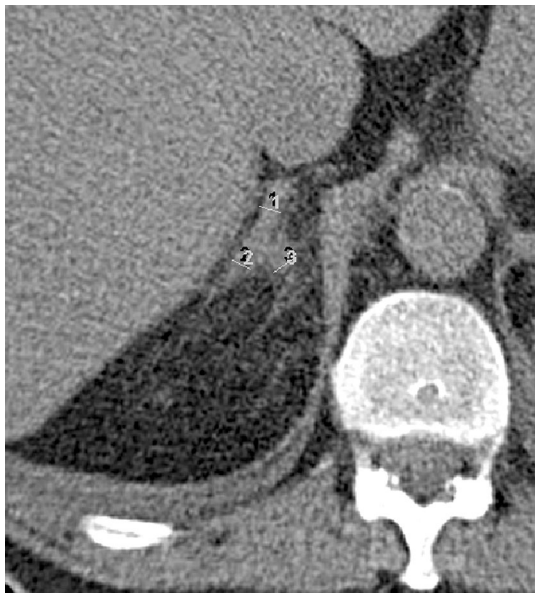

Fig. 1. Right adrenal gland. Right adrenal body [1]—6 mm, Right lateral limb [2]—5.5 mm, Right medial limb [3]—7 mm.

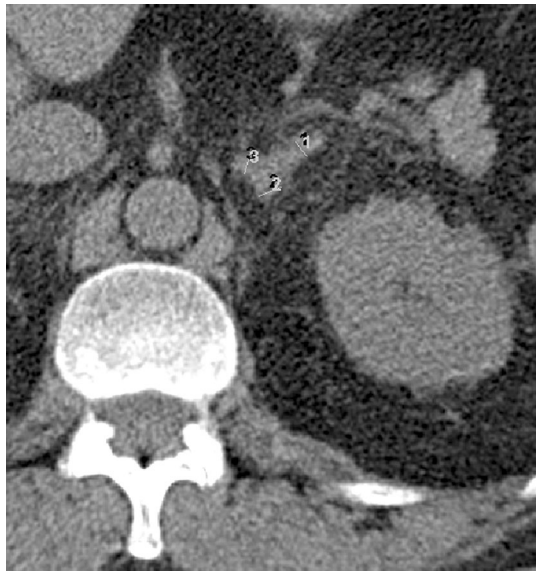

Fig. 2. Left adrenal gland. Left adrenal body [3]—6 mm, Left lateral limb [1]—5.3 mm, left medial limb [2]—7 mm.

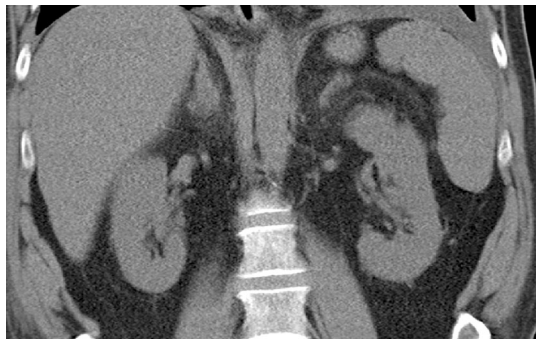

Fig. 3. Coronal CT image demonstrating bilateral peri-adrenal fat stranding.

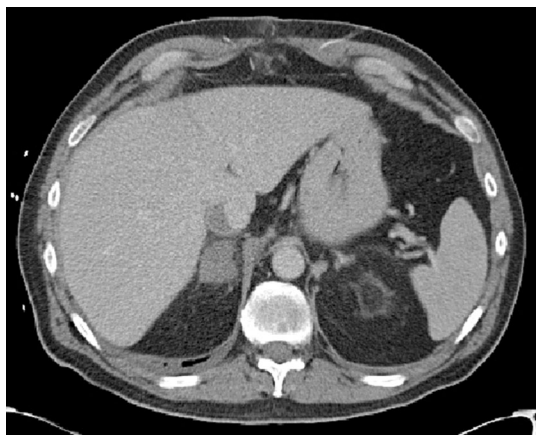

Fig. 4. Right adrenal hemorrhage. Crescentic filling defect within the right side of the suprarenal inferior vena cava, consistent with thrombosis.

as well as suprarenal inferior vena cava thrombosis (Fig. 4).

Bilateral peri-adrenal fat stranding and thickening of the adrenal glands.

Case 2

A 64-year-old male presented with spontaneous left upper quadrant abdominal pain. Initial non-contrast CT abdomen showed bilateral peri-adrenal fat stranding and thickened appearances of the glands (Figs. 5, 6, 7, 8). Repeat non-contrast CT abdomen 3 days later revealed an ovoid right adrenal mass, consistent with right adrenal hemorrhage (Fig. 9).

Case 3

A 63-year-old male with anti-phospholipid syndrome was admitted for treatment of left lower limb cellulitis. During his admission, he developed severe abdominal pain and was found to have a sigmoid volvulus, for which he underwent a sigmoid colectomy. The initial preoperative abdominal CT revealed inflammatory stranding surrounding bilateral adrenal glands with associated thickening of the glands. A repeat abdominal CT for investigation of fever 2 days post-surgery, revealed bilateral rounded adrenal masses, consistent with adrenal hemorrhages (Figs. 10, 11, 12, 13).

Case 4

Case 4 is a 78-year-old male who underwent a right total knee arthroplasty. During the post-surgical rehabilitation period, he developed acute epigastric pain. A CT

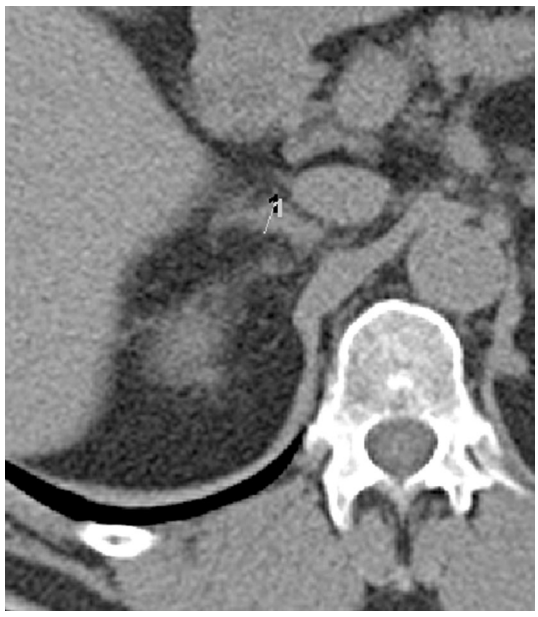

Fig. 5. Right lateral adrenal limb—8.3 mm.

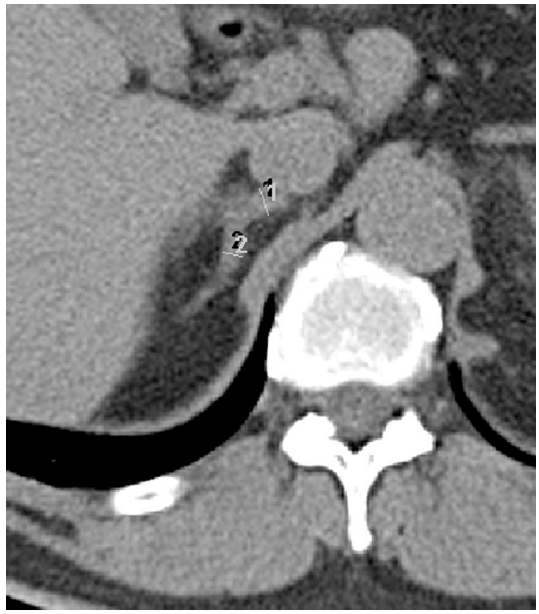

Fig. 6. Right adrenal body [1]—7.0 mm, Right medial adrenal limb [2]—5.5 mm.

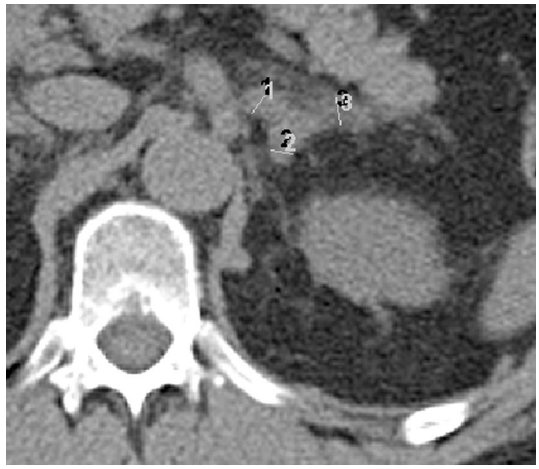

Fig. 7. Left Adrenal Gland. Left adrenal body [1]—8.4 mm, Left lateral limb [3]—7.0 mm, Left medial limb [2]—6.0 mm.

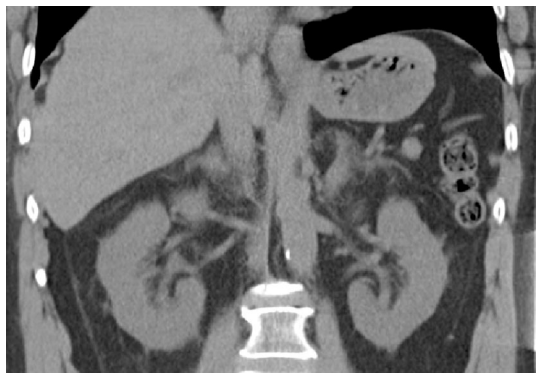

Fig. 8. Bilateral adrenal gland thickening and peri-adrenal fat stranding.

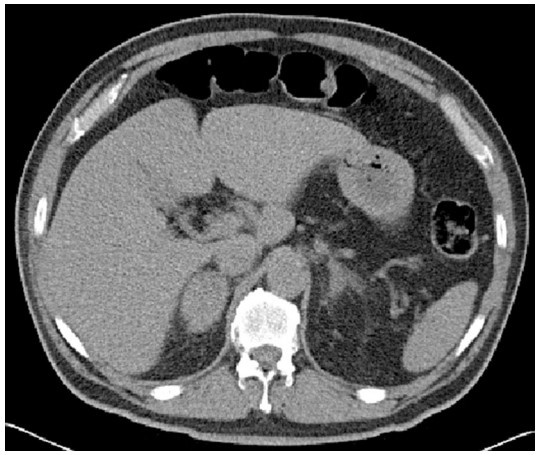

Fig. 9. Right adrenal hemorrhage.

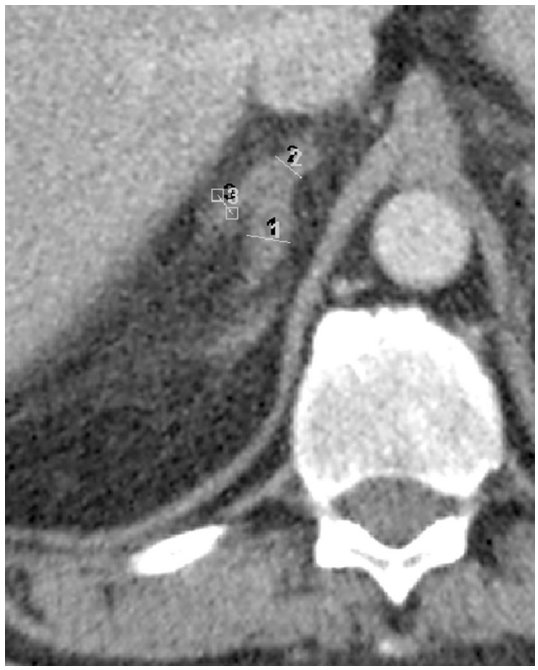

Fig. 10. Right adrenal gland. Right adrenal body [2]—7.2 mm, Right lateral limb [3]—5.5 mm, Right medial limb [1]—9.5 mm.

pulmonary angiogram and abdomen revealed a left lobar pulmonary embolus as well as inflammatory stranding surrounding bilateral adrenal glands, which appeared thickened (Figs. 14, 15, 16, 17, 18). The patient was then commenced on therapeutic heparin anti-coagulation for management of the pulmonary embolus. However, the patient continued to suffer from epigastric pain and sustained a hemoglobin drop from 122 to 101 g/L. Repeat abdominal CT revealed bilateral ovoid adrenal masses in keeping with adrenal hemorrhages (Fig. 19).

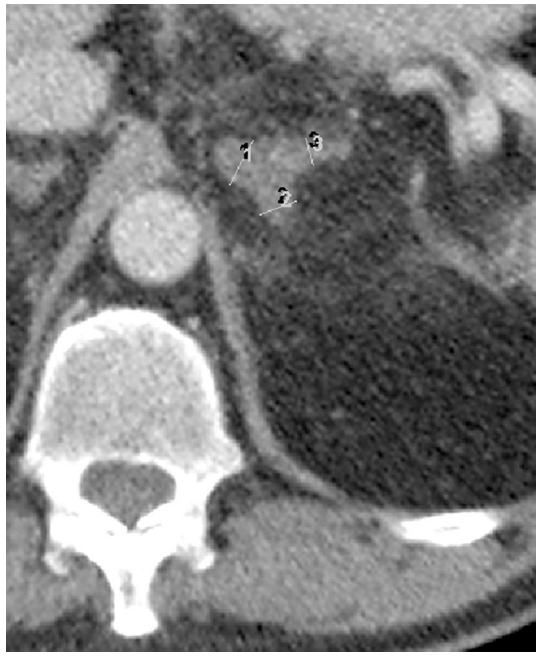

Fig. 11. Left adrenal gland. Left adrenal body [1]—11.5 mm, Left lateral limb [3]—6.5 mm, Left medial limb [2]—9.2 mm.

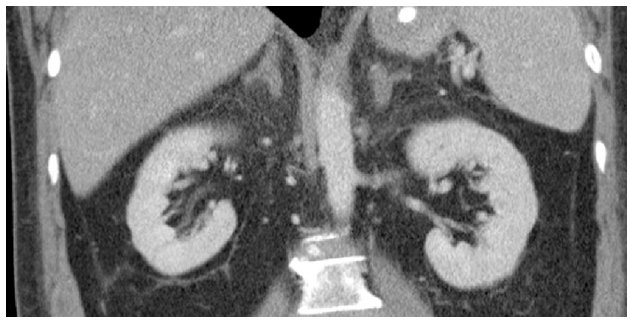

Fig. 12. Bilateral peri-adrenal fat stranding and adrenal gland thickening.

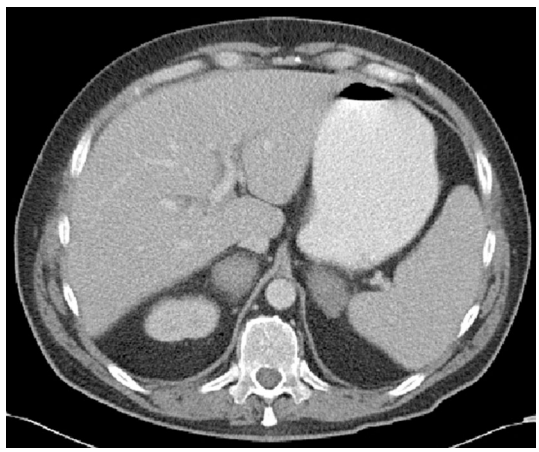

Fig. 13. Bilateral adrenal hemorrhage.

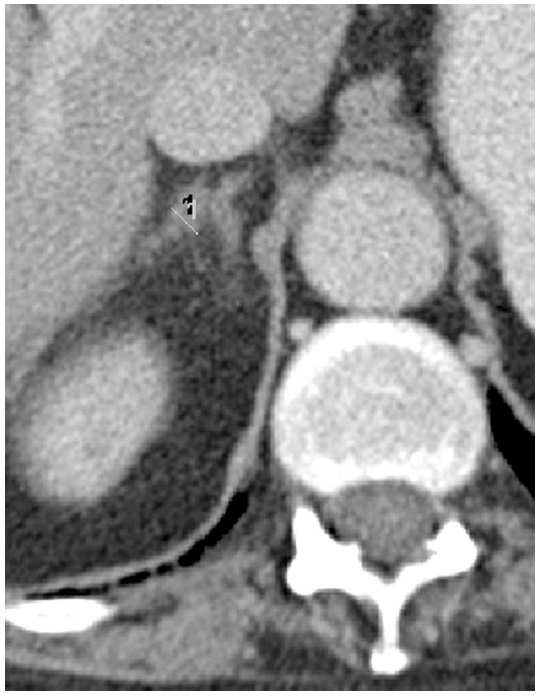

Fig. 14. Right lateral adrenal limb—7.2 mm.

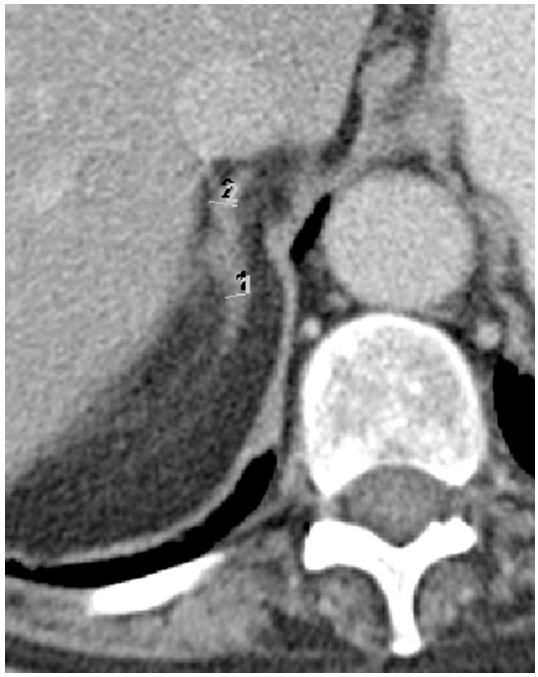

Fig. 15. Right adrenal body [2]—6.0 mm, Right medial adrenal limb [1]—5.3 mm.

Control cases

We also analyzed the CT images of 12 randomly selected intensive care unit patients, who underwent two abdominal CTs at least 2 weeks apart, to observe if features of adrenal gland thickening and peri-adrenal fat stranding often occurred in this subgroup of patients. None of the 12 patients analyzed demonstrated adrenal gland thickening or peri-adrenal fat stranding on their initial or subsequent CTs. We present images from a representative case as well as a table outlining our findings below (Table 21).

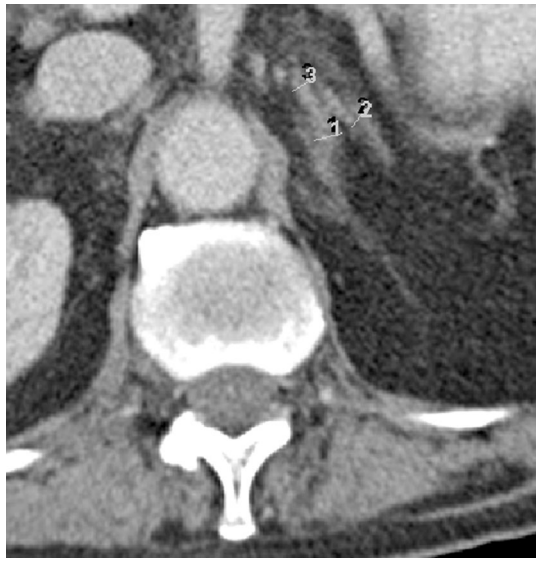

Fig. 16. Left adrenal gland. Left adrenal body [3]—6.0 mm, left lateral limb [2]—5.4 mm, left medial limb [1]—7.0 mm.

The representative control case illustrated below demonstrates thin adrenal limbs (less than 5 mm) bilaterally with no evidence of peri-adrenal fat stranding, although mild bilateral peri-nephric stranding is noted (Figs. 20, 21, 22, 23).

Discussion

The adrenal gland receives multiple branches from three main adrenal arteries but is drained by only relatively few venules, which flow into a single central adrenal vein, thus forming a 'vascular dam' [4, 8]. In times of physiological stress, the release of adrenocorticotrophic hormone (ACTH) and catecholamines increases arterial blood flow into the adrenal glands [9]. Catecholamine concentrations are highest within the adrenal veins, causing vasoconstriction of the draining venules [4]. Furthermore, the catecholamines promote platelet aggregation and cause turbulent venous blood flow through intense contraction of the asymmetrically arranged muscle bundles surrounding the adrenal veins, predisposing to adrenal vein thrombosis [5]. Overall, these processes work synergistically to cause increased pressure within the adrenal venous sinusoids, causing adrenal gland congestion and venous stasis. As adrenal venous pressure increases, there is a proportional increase in vascular wall tension, in keeping with Laplace's Law (Wall tension $\propto$ intravascular pressure $\times$ vessel radius). Hemorrhage occurs when the tensions within the

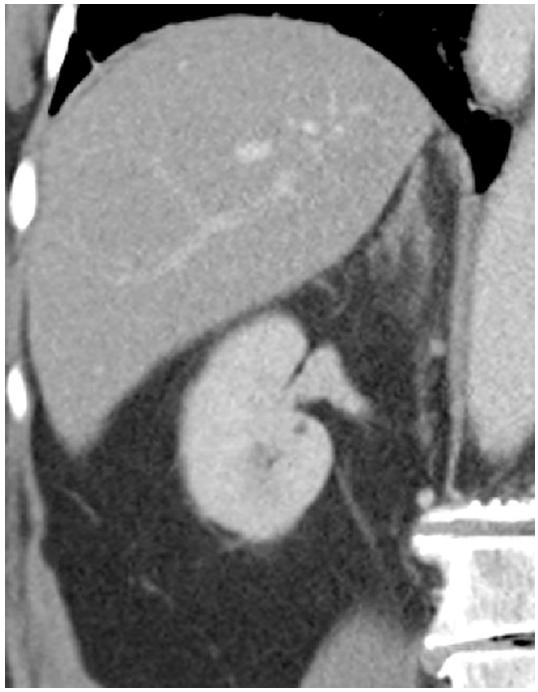

Fig. 17. Bilateral peri-adrenal fat stranding—Right adrenal gland.

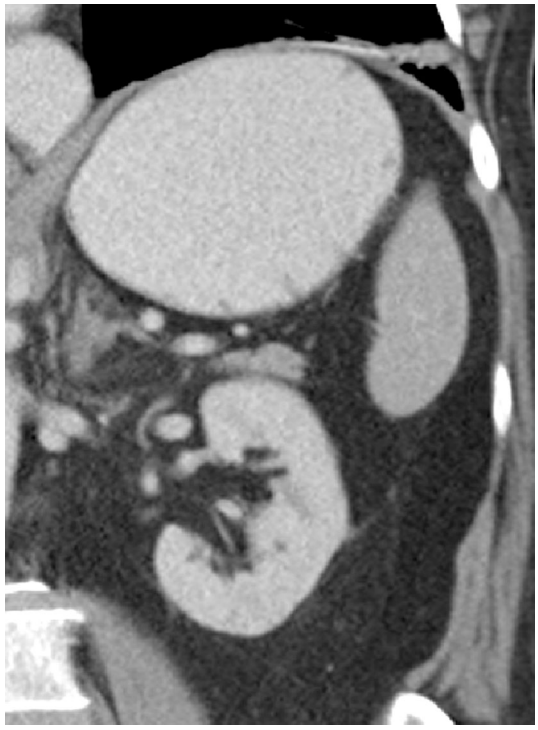

Fig. 18. Bilateral peri-adrenal fat stranding—Left adrenal gland.

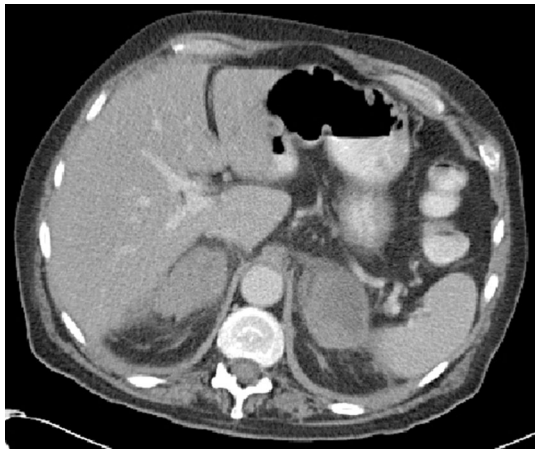

Fig. 19. Bilateral adrenal hemorrhage.

thin walls of the adrenal veins are overwhelmed as they cannot resist high intravascular pressures [8]. Furthermore, venous stasis results in venous ischemia, which further compromises vascular wall integrity, predisposing to hemorrhagic necrosis, as observed in other medical conditions such as testicular and ovarian torsion [8].

Multiple predisposing factors have been linked to non-traumatic adrenal hemorrhage including sepsis, hypotension, recent surgery, anti-coagulation, and anti-phospholipid syndrome [4]; various combinations of which were observed in the four cases we analyzed. In Cases 1 and 4, the patients were at even higher risk of hemorrhage as they had been commenced on therapeutic heparin anti-coagulation for management of pulmonary embolism. In addition, there was increased thrombotic tendency in these patients with pulmonary embolism, raising the possibility of associated adrenal vein thrombosis. In Case 2, however, the patient did not possess any risk factors and the adrenal hemorrhage was presumably idiopathic in nature, as has been described in previous case reports [11–14].

In the cases we have described, initial CT imaging demonstrated diffuse thickening of bilateral adrenal glands with peri-adrenal fat stranding. These features are thought to reflect the increased hydrostatic pressure within the adrenal capillary sinusoids, causing diffuse gland enlargement as well as fluid extravasation leading to peri-adrenal stranding. Subsequent CT imaging then revealed ovoid adrenal soft tissue masses, either unilateral or bilateral, consistent with acute adrenal hemorrhage. These findings support the current hypothesis of vascular congestion within the adrenal gland as the pathogenesis of non-traumatic adrenal hemorrhage. Interestingly, in Case 1, the patient was also found to have suprarenal inferior vena cava thrombosis on the right, ipsilateral to the right adrenal hemorrhage. This thrombosis would have obstructed the venous outflow of the right adrenal gland, leading to venous congestion and subsequent hemorrhage, further supporting the prevailing theory of adrenal congestion preceding hemorrhage.

In a recent pictorial essay by Sacerdote et al. [15], it was proposed that adrenal hemorrhage could present as

Table 1. Adrenal gland thickness measurements (mm)

	Initial CT						Subsequent CT					
	Right adrenal			Left adrenal			Right adrenal			Left adrenal		
	Body	Medial limb	Lateral limb	Body	Medial limb	Lateral limb	Body	Medial limb	Lateral limb	Body	Medial limb	Lateral limb
1	3.0	2.2	2.8	3.8	3.6	3.6	2.8	2.4	3.0	3.9	3.7	3.5
2	3.6	3.2	3.4	2.9	3.4	2.7	3.1	2.9	3.2	3.1	2.9	2.9
3	3.5	2.1	2.3	3.1	2.6	2.8	3.5	2.4	2.1	3.3	2.3	2.7
4	3.4	2.8	2.6	3.2	2.7	3.2	3.3	3.0	2.8	3.4	2.5	3.3
5	3.3	1.8	2.3	2.2	1.3	1.7	3.5	1.9	2.1	2.5	1.7	1.6
6	3.9	3.6	3.3	3.4	2.9	3.0	3.7	3.9	3.2	3.2	3.0	2.7
7	3.2	2.5	2.7	2.8	1.5	1.8	3.3	2.3	2.6	3.0	1.8	1.7
8	3.9	2.8	2.5	3.8	3.5	3.3	3.7	3.0	2.8	3.4	3.2	3.1
9	3.8	2.7	2.9	3.7	2.8	2.7	3.9	3.0	2.6	3.5	2.9	2.5
10	3.2	2.3	2.8	3.8	3.0	2.8	3.4	2.5	2.6	3.6	3.2	2.7
11	3.9	3.3	3.2	3.8	3.2	2.8	3.6	3.2	2.8	3.7	3.0	2.9
12	3.3	2.7	2.9	3.6	2.2	2.6	3.4	2.4	3.0	3.9	2.5	2.7

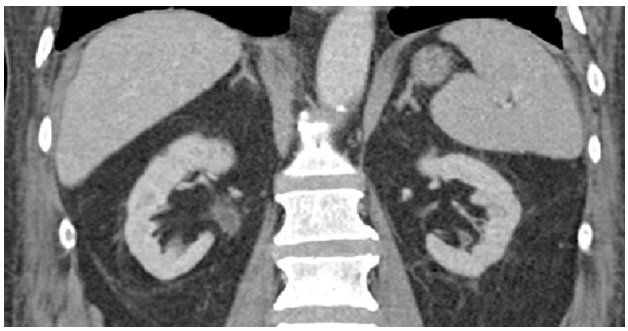

Fig. 20. Initial CT.

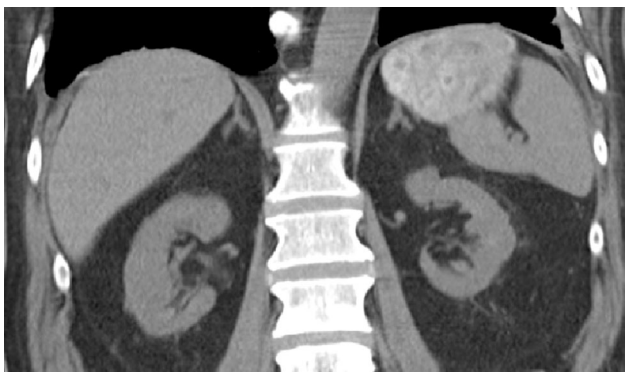

Fig. 21. Follow-up CT.

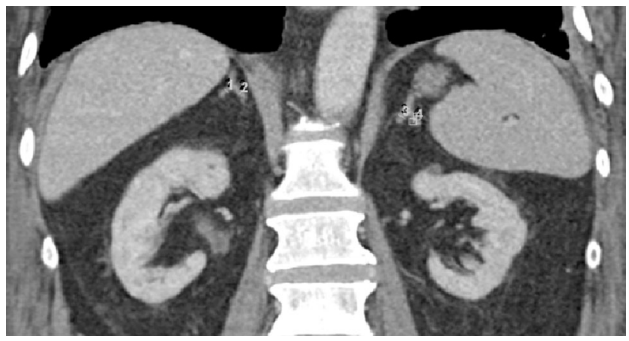

Fig. 22. Initial CT. Right lateral limb [1]—2.8 mm, Right medial limb [2]—2.2 mm, Left medial limb [3]—3.6 mm, Left lateral limb [4]—3.6 mm.

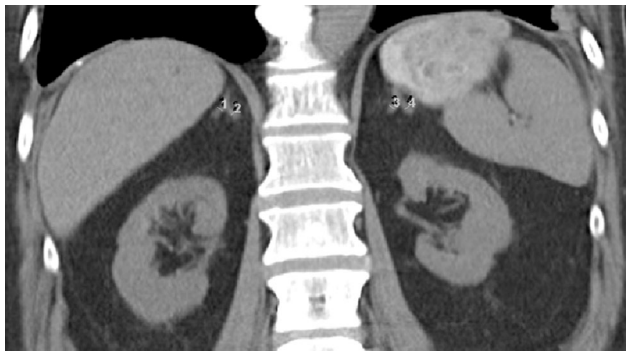

Fig. 23. Follow-up CT. Right lateral limb [1]—3.0 mm, Right medial limb [2]—2.4 mm, Left medial limb [3]—3.7 mm, Left lateral limb [4]—3.5 mm.

adreniform enlargement with thickening of the adrenal gland limbs. They supported this notion with a case of adrenal insufficiency associated with CT findings of adrenal gland thickening in the left adrenal gland and an ovoid hematoma in the right adrenal gland [15]. However, the progression of CT imaging appearances from adrenal gland thickening to ovoid adrenal masses in our cases suggests that adrenal gland thickening in fact represents a pre-hemorrhagic state of adrenal congestion. Nevertheless, it is likely that adrenal endocrine dysfunction can result from adrenal congestion, even prior to overt adrenal hemorrhage, due to cellular dysfunction from venous ischemia, thus explaining the findings described by Sacerdote et al. This is further exemplified by a case report by Dahiya et al. who described a patient in whom a CT performed for investigation of abdominal pain revealed 'diffuse enlargement of bilateral adrenal glands with adjacent inflammatory changes,' which was

reported to be not characteristic for adrenal hemorrhage [14]. Subsequent random serum cortisol test revealed severe adrenal insufficiency; however unfortunately, steroid replacement therapy was not commenced early enough to prevent the death of the patient [14].

As such, it may be useful to recognize the described CT features of adrenal congestion as they may indicate underlying adrenal dysfunction, enabling early recognition and treatment of adrenal insufficiency. This could be helpful given the difficulty in recognizing the clinical features of acute adrenal insufficiency in critically ill patients. Adrenal insufficiency is managed by correction of the salt, glucose, and steroid deficiencies [16]. Hydrocortisone is the preferred treatment in the acute stage, although some have argued that dexamethasone should be used as it does not interfere with serum cortisol measurement [17]. The importance of early treatment is demonstrated in cases described by Rao et al. [8], who showed complete recovery in patients who received early steroid replacement, compared to a patient in whom treatment was delayed, who suffered persisting neurologic deficits. Early treatment with exogenous steroids in patients demonstrating adrenal congestion with adrenal insufficiency may also reduce the physiological stress on the adrenal glands, potentially reducing the risk of adrenal hemorrhage and associated long-term adrenal insufficiency.

Conclusion

Non-traumatic adrenal hemorrhage is a rare clinical entity with potentially deadly consequences due to acute adrenal insufficiency. Adrenal gland thickening with surrounding fat stranding suggests adrenal congestion, which may also result in adrenal dysfunction. Early diagnosis of acute adrenal insufficiency is crucial to enable prompt steroid replacement therapy to prevent death from adrenal crisis.

As such, it may be useful to recognize the CT findings of adrenal congestion as indicators of potential adrenal dysfunction and adrenal hemorrhage. Follow-up CT imaging could be considered for patients in whom CT findings of adrenal congestion are identified, should they not appear to improve clinically, to exclude progression to adrenal hemorrhage. However, given the limitations of this case series of four patients, further prospective studies would be useful to validate these observations.

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