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Rhabdomyolysis-Associated Acute Kidney Injury Complicated by Heparin-Induced Thrombocytopenia and Bilateral Adrenal Hemorrhage

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Abstract

A 49-year-old woman with developmental delay and no known chronic kidney disease presented with left lower extremity cellulitis after an unwitnessed fall. Her hospitalization was complicated by severe rhabdomyolysis, with a peak creatine kinase level of 87,696 U/L, and anuric stage 3 acute kidney injury requiring intermittent hemodialysis. Following heparin exposure, she developed profound thrombocytopenia, positive platelet factor 4/heparin antibody testing, and venous thromboses. Heparin was discontinued, and treatment with argatroban was initiated.

After an initial increase in urine output, she developed abdominal pain, nausea, poor oral intake, relative hypotension, and reduced urine output. Computed tomography demonstrated bilateral adrenal hemorrhages. A baseline serum cortisol concentration of 2.08 µg/dL, with an inadequate response to cosyntropin stimulation (post-stimulation cortisol 2.28 µg/dL), supported the diagnosis of adrenal insufficiency. Stress-dose hydrocortisone was initiated, followed by maintenance hydrocortisone and fludrocortisone. Blood pressure and urine output subsequently improved. Kidney function gradually recovered, with the final hemodialysis session occurring on hospital day 26. Serum creatinine decreased to 1.71 mg/dL by discharge but remained above the previous baseline.

This case highlights the importance of reassessing new hemodynamic deterioration during recovery from severe acute kidney injury. In patients with heparin-induced thrombocytopenia, new abdominal symptoms or otherwise unexplained hypotension should prompt consideration of bilateral adrenal hemorrhage and adrenal insufficiency. Improvement after corticosteroid replacement supported an adrenal contribution to the clinical deterioration, although its effect on the duration of dialysis dependence could not be established.

Categories: Hematology, Nephrology, Endocrinology/Diabetes/Metabolism
Keywords: acute kidney injury, acute tubular injury, adrenal insufficiency, bilateral adrenal hemorrhage, hemodialysis, heparin-induced thrombocytopenia, hypotension, renal recovery, rhabdomyolysis, thrombosis

Introduction

Rhabdomyolysis can cause acute kidney injury (AKI) through myoglobin-associated tubular toxicity, intrarenal vasoconstriction, and tubular obstruction [1,2]. Severe injury may require kidney replacement therapy, which meets the Kidney Disease: Improving Global Outcomes (KDIGO) criteria for stage 3 AKI [3]. Resolution of muscle injury does not necessarily coincide with recovery of kidney function, and subsequent systemic or hemodynamic disturbances may complicate recovery from established acute tubular injury (ATI) [4].

Heparin-induced thrombocytopenia (HIT) is an immune-mediated complication of heparin exposure that produces a prothrombotic state despite thrombocytopenia [5]. Bilateral adrenal hemorrhage is an uncommon complication associated with severe illness, coagulopathy, and HIT [6,7]. In patients with HIT, adrenal venous thrombosis resulting in venous congestion and hemorrhagic infarction is a proposed mechanism, although direct evidence of adrenal vein thrombosis may be absent [7]. Adrenal injury may result in adrenal insufficiency, presenting with nonspecific symptoms such as abdominal pain, nausea, weakness, and hypotension [8].

We describe a patient with dialysis-requiring rhabdomyolysis-associated AKI whose recovery was complicated by HIT, bilateral adrenal hemorrhage, and clinically diagnosed adrenal insufficiency. The case illustrates the diagnostic challenges of recognizing an additional reversible complication during recovery from severe kidney injury.

Case Presentation

A 49-year-old woman with developmental delay and limited verbal communication presented with progressive left thigh pain, swelling, erythema, and inability to ambulate approximately 1 week after an unwitnessed fall. Initial examination and imaging raised concern for a severe soft tissue infection, including possible necrotizing fasciitis. Urgent surgical exploration and debridement were performed on admission. No deep necrotizing infection was identified, and the lower extremity infection was managed as cellulitis.

She had no known chronic kidney disease, and her previous serum creatinine was approximately 0.77 mg/dL. Admission creatinine was 3.98 mg/dL (reference range: 0.60-1.60 mg/dL) and subsequently increased. Creatine kinase peaked at 87,696 U/L (reference range: 33-211 U/L) on hospital day 2. By hospital day 4, serum creatinine had reached 10.31 mg/dL, accompanied by anuria, metabolic acidosis, and hyperphosphatemia. The clinical presentation was consistent with severe rhabdomyolysis-associated AKI, with presumed pigment-associated ATI. Intermittent hemodialysis was initiated.

Heparin was administered early during hospitalization. The platelet count subsequently declined from approximately 288 × 10^3/μL to a nadir of 11 × 10^3/μL (reference range: 150-400 × 10^3/μL). The retrospective 4Ts score was estimated at 6, indicating high clinical probability of HIT when subsequently confirmed thrombotic events were included. Laboratory testing demonstrated a strongly positive platelet factor 4 (PF4)/heparin antibody assay (>16.0 U/mL; reference range: 0.0-0.9 U/mL) and a positive functional heparin-induced platelet activation assay (WP-HIPA), with 63% platelet activation (reference range: <20%). Thrombotic complications included a left peroneal deep vein thrombosis and bilateral internal jugular catheter-associated thromboses. Heparin was discontinued, and argatroban was subsequently initiated.

Creatine kinase levels declined substantially, but the patient continued to require hemodialysis. During hospital days 14-17, urine output began to improve. On hospital day 19, she developed new abdominal pain, nausea, poor oral intake, tachycardia, relative hypotension, eosinophilia, and reduced urine output. Subsequent computed tomography of the abdomen and pelvis demonstrated bilateral adrenal hematomas measuring approximately 4.0 × 2.2 cm on the right and 4.1 × 2.3 cm on the left (Figure *1*).

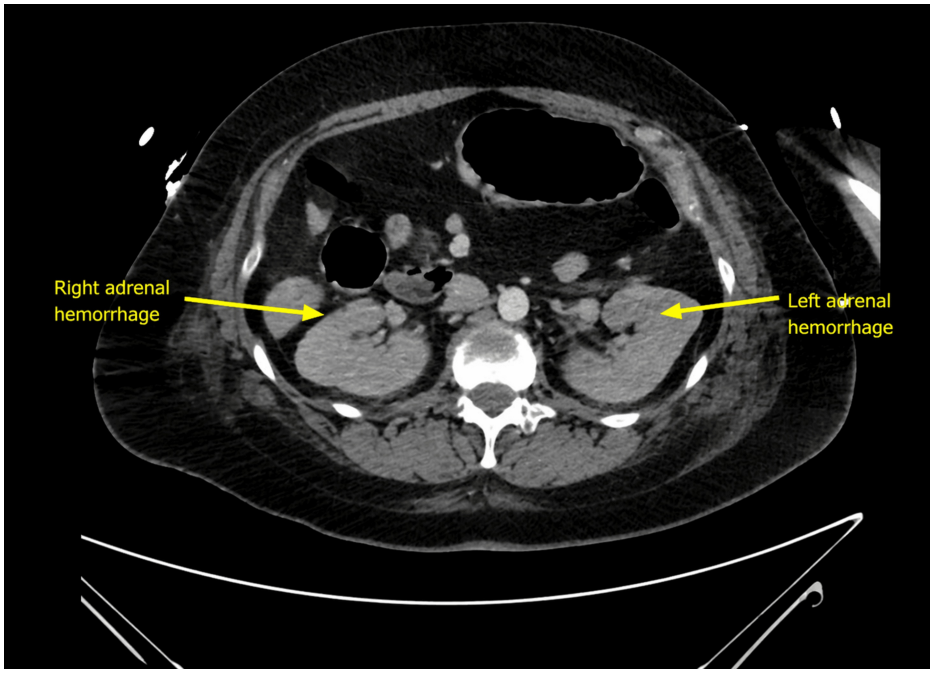


FIGURE 1: Bilateral adrenal hemorrhage on abdominal computed tomography

Axial computed tomography image demonstrating bilateral adrenal hematomas. Arrows indicate the right and left adrenal hemorrhages.

An early morning serum cortisol concentration was markedly low at 2.08 μg/dL (reference range: 3.09-22.4 μg/dL). A standard-dose (250 μg IV) cosyntropin stimulation test demonstrated an inadequate adrenal response, with serum cortisol increasing to only 2.28 μg/dL at 68 minutes after administration. Intravenous hydrocortisone was subsequently initiated. Plasma ACTH measured two days later was low at 5.2 pg/mL; however, this sample was obtained after hydrocortisone exposure. In the setting of bilateral adrenal hemorrhage, compatible symptoms, and hemodynamic deterioration, these findings supported the diagnosis of adrenal insufficiency.

Intravenous hydrocortisone was administered at 50 mg every six hours for the first three days, followed by oral maintenance hydrocortisone 15 mg each morning and 5 mg each evening. Fludrocortisone 0.05 mg orally daily was added.

Following hydrocortisone initiation, blood pressure improved, and urine output increased to more than 3 L/day. Serum creatinine remained elevated, and hemodialysis continued while kidney function was reassessed. Repeat imaging demonstrated stability and subsequent improvement of the adrenal hemorrhages. Anticoagulation was resumed after bleeding stability was established and was later transitioned to apixaban.

Kidney function progressively improved, and the final hemodialysis session occurred on hospital day 26. By discharge, serum creatinine had decreased to 1.71 mg/dL, representing substantial but incomplete recovery relative to the previous baseline. The patient remained clinically stable on maintenance hydrocortisone and fludrocortisone, with outpatient follow-up arranged. Selected clinical events and laboratory results are summarized in Table *1*.

Day	Key event	Serum creatinine (mg/dL; reference range: 0.60–1.60)	Platelet count (×10³/μL; reference range: 150–400)	CK (U/L; reference range: 33–211)	Key clinical findings	Management	Clinical interpretation
Day 1	Admission after fall; cellulitis	3.98	270–288	Not yet resulted	Oliguria	Supportive care	Early AKI from rhabdomyolysis
Day 2	Peak rhabdomyolysis	5.66	288	87,696	Severe muscle injury	Supportive care	Pigment-induced acute tubular injury
Day 4	Peak acute kidney injury with anuria, heparin initiated	10.31	270	10,777	Anuria and metabolic acidosis	Hemodialysis initiated	Dialysis-dependent acute tubular injury
Day 6	Ongoing severe AKI	8.34	283	3,462	Persistent anuria	Continued hemodialysis	No renal recovery yet
Day 9	Worsening thrombocytopenia	5.83	200	500	Platelet drop after heparin exposure	Heparin discontinued	High suspicion for HIT
Day 12	HIT diagnosed clinically with positive antibody testing	5.79	17	438–459	PF4/heparin antibody >16.0 U/mL (positive; reference range: 0.0–0.9 U/mL)	Argatroban initiated	HIT with thrombotic complications
Day 13	Platelet nadir	6.71	11	371	Severe thrombocytopenia	Continued anticoagulation	Severe thrombocytopenia in the setting of HIT
Day 14–17	Early renal recovery phase	around 5	around 60	272–191	Urine output increased to 0.5–0.7 mL/kg/h.	Continued hemodialysis	Early diuresis; dialysis dependence persisted
Day 19	Clinical deterioration	5.74	95	272	Reduced urine output, relative hypotension, abdominal pain, and nausea	Evaluation for hemodynamic deterioration	New hemodynamic instability during AKI recovery
Day 20	Bilateral adrenal hemorrhage identified	4.79	110	183	Bilateral adrenal hematomas on CT	Evaluation for adrenal insufficiency	Suspected adrenal insufficiency contributing to hemodynamic deterioration
Day 21–25	Adrenal insufficiency confirmed; diuretic phase	around 5	Improving	143–349	Day 21: baseline cortisol 2.08 μg/dL; post-cosyntropin cortisol 2.28 μg/dL. Subsequently, urine output increased to >3–4 L/day	Hydrocortisone initiated on Day 21; continued supportive care	Inadequate adrenal response; subsequent hemodynamic improvement and polyuria
Day	Final dialysis	3.92	136	123	Sustained urine output, clinical	Hemodialysis	Renal recovery sufficient

26	session				improvement	discontinued	to stop dialysis
Day 31+	Recovery and discharge	1.71	186	91	Stable clinical status, no further dialysis needed	Apixaban, maintenance hydrocortisone & fludrocortisone.	Sustained renal and hematologic recovery

TABLE 1: Timeline of kidney injury, thrombocytopenia, adrenal hemorrhage, and treatment

Selected laboratory results, clinical events, and treatments during hospitalization. Days are numbered from admission. Reference ranges are provided in the laboratory column headings or alongside individual results. Serum creatinine values were influenced by intermittent hemodialysis and should be interpreted in relation to dialysis timing. Improvement after hydrocortisone was temporally associated with hemodynamic stabilization and increased urine output; its effect on the duration of dialysis dependence could not be determined.

Abbreviations: AKI, acute kidney injury; CK, creatine kinase; CT, computed tomography; HIT, heparin-induced thrombocytopenia; PF4, platelet factor 4. Units: mg/dL, milligrams per deciliter; ×10³/μL, thousands per microliter; U/L, units per liter; U/mL, units per milliliter; μg/dL, micrograms per deciliter; mL/kg/h, milliliters per kilogram per hour; L/day, liters per day.

Discussion

Rhabdomyolysis-associated AKI results from overlapping mechanisms, including myoglobin-mediated tubular toxicity, intrarenal vasoconstriction, and tubular obstruction [1,2]. In this patient, marked creatine kinase elevation, rapidly increasing creatinine, and anuria supported a clinical diagnosis of pigment-associated AKI. The requirement for hemodialysis established stage 3 AKI according to KDIGO criteria [3]. Declining creatine kinase levels indicated improvement in muscle injury but did not establish recovery of kidney function. Established tubular injury and subsequent systemic disturbances could continue to influence the recovery trajectory [4].

HIT introduced an additional thrombotic complication. Antibody-mediated platelet activation and thrombin generation produce a hypercoagulable state despite a falling platelet count [5]. Adrenal hemorrhage may occur in the setting of severe illness, coagulopathy, and anticoagulant exposure [6]. In HIT, adrenal venous thrombosis with subsequent hemorrhagic infarction is a proposed mechanism. The adrenal glands have a rich arterial supply and relatively restricted venous drainage, making them susceptible to congestion and hemorrhage when venous outflow is impaired [7]. Bilateral adrenal injury may cause adrenal insufficiency, with abdominal pain, nausea, weakness, and hypotension serving as potential clinical clues [8].

Increasing urine output complicated the assessment of kidney recovery. Urine volume alone does not establish adequate solute clearance, and serum creatinine changes gradually after alterations in filtration under nonsteady-state conditions [9]. Intermittent hemodialysis further affects creatinine concentrations. Consequently, polyuria with a persistently elevated creatinine cannot independently establish separate phases of tubular and glomerular recovery. In this case, sustained dialysis independence and the subsequent decline in creatinine provided stronger evidence of improving endogenous kidney function.

Severe illness, HIT, and anticoagulant exposure may have contributed to adrenal hemorrhage through overlapping mechanisms. Adrenal vein thrombosis was not demonstrated, and HIT-associated hemorrhagic infarction remained a plausible rather than confirmed mechanism.

Bilateral adrenal hemorrhage, compatible symptoms, markedly reduced baseline cortisol, and an inadequate response to cosyntropin stimulation supported the diagnosis of adrenal insufficiency. Although bilateral adrenal hemorrhage suggests primary adrenal insufficiency, the subsequently measured low ACTH concentration was obtained after hydrocortisone exposure and may reflect glucocorticoid-mediated suppression. Therefore, this ACTH result could not reliably distinguish primary from central adrenal insufficiency. The traditional peak cortisol threshold following standard-dose cosyntropin stimulation is approximately 18 μg/dL, although assay-specific thresholds may be lower [10]. In patients with suspected adrenal crisis, hydrocortisone treatment should not be delayed while awaiting diagnostic confirmation [10].

Cortisol deficiency can impair vascular responsiveness and contribute to hemodynamic instability. Associated mineralocorticoid deficiency may further compromise effective circulating volume. Corticosteroid replacement can also restore free-water excretion, meaning that an increase in urine output after treatment does not necessarily indicate a corresponding increase in glomerular filtration [11]. The improvement in blood pressure and urine output after hydrocortisone supported an adrenal contribution to the deterioration, but it did not establish that treatment accelerated renal repair or shortened dialysis dependence.

The HIT diagnosis and anticoagulation decisions also require clinical and laboratory context. American Society of Hematology (ASH) guidance recommends estimating pretest probability with the 4Ts score and interpreting PF4/heparin immunoassay results alongside that assessment. Functional testing is generally

suggested when available, although it may be unnecessary with a high clinical probability and a very strongly positive immunoassay. Treatment of HIT with thrombosis requires heparin avoidance and a non-heparin anticoagulant, with agent selection guided by kidney and liver function, clinical stability, and bleeding risk [12].

The association between HIT, bilateral adrenal hemorrhage, adrenal insufficiency, and renal dysfunction has previously been described [7]. A more recent report also illustrates the difficulty of managing adrenal hemorrhage in a patient with active thrombosis and HIT [13]. The present case adds the clinical setting of recovery from severe rhabdomyolysis-associated ATI. Its educational value lies in recognizing a new adrenal complication during an evolving course of kidney recovery and balancing anticoagulation against bleeding risk.

This report cannot determine whether adrenal insufficiency prolonged dialysis dependence. Recovery from severe ATI, improvement in systemic illness, and concurrent supportive treatment could also explain the subsequent course. Although the patient achieved dialysis independence, creatinine remained above baseline at discharge. Continued follow-up was therefore necessary, particularly given the association between severe AKI and subsequent chronic kidney disease [14].

Conclusions

Bilateral adrenal hemorrhage and adrenal insufficiency should be considered when patients with HIT develop new abdominal symptoms or otherwise unexplained hypotension during recovery from AKI. In this case, hydrocortisone replacement was followed by improved blood pressure and urine output, with subsequent recovery sufficient to discontinue hemodialysis. This temporal relationship supported an adrenal contribution to clinical deterioration, but its effect on the duration of kidney recovery remained uncertain. Declining creatine kinase levels and increasing urine output should be interpreted alongside metabolic stability, solute clearance, and ongoing dialysis requirements.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Divya Akella, Virin Ramoutar

Acquisition, analysis, or interpretation of data: Divya Akella, Virin Ramoutar

Drafting of the manuscript: Divya Akella, Virin Ramoutar

Critical review of the manuscript for important intellectual content: Divya Akella, Virin Ramoutar

Supervision: Divya Akella, Virin Ramoutar

Disclosures

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