Journal of Case Reports and Clinical Studies

Bille D, J Case Rep Clin Stud. 2026;2(1):14-17.

Case Report

Divergent outcomes in twins with bilateral adrenalectomy and COVID-19: importance of stress-dose steroids

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Received date: March 02, 2026
Accepted date: March 21, 2026

Abstract

Patients with primary adrenal insufficiency require stress-dose glucocorticoids during acute illness to prevent adrenal crisis. We report twin patients with von Hippel–Lindau syndrome status post bilateral adrenalectomy who presented concurrently with symptomatic SARS-CoV-2 infection but experienced markedly different clinical courses based on adherence to stress-dose steroid recommendations. Twin 1 appropriately increased her glucocorticoid dose at symptom onset and remained hemodynamically stable, requiring only brief observation before discharge. Twin 2 did not initiate stress dosing and developed adrenal crisis with hypotension, hypoglycemia, and altered mental status, requiring hospitalization and parenteral glucocorticoids. This case highlights the physiologic importance of stress-dose glucocorticoids in patients without adrenal reserve and illustrates the consequences of delayed dose escalation during systemic infection. The contrasting outcomes underscore the critical role of patient education, early recognition of illness, and adherence to sick-day management protocols in reducing preventable morbidity.

Keywords: Adrenal crisis, Glucocorticoid replacement, Stress-dose steroids, Sick-day rules

Introduction

Patients with primary adrenal insufficiency lack the ability to mount an endogenous cortisol response to physiologic stress and are therefore at risk for adrenal crisis during acute illness [1]. Adrenal crisis is a potentially life threatening endocrinologic emergency condition caused by low serum cortisol often a result of acute adrenal insufficiency. Stress-dose glucocorticoids are recommended during infections, trauma, or other stressors to mitigate this risk. Despite established guidelines, adherence to sick-day management remains variable. We present a novel and to our knowledge previously undocumented case of twin patients with von Hippel-Lindau syndrome who were both status-post bilateral adrenalectomy who presented simultaneously with COVID-19 infection but experienced markedly different clinical courses due to variation in adherence to stress-dose steroid use prior to emergency department arrival.

Case Presentation

Middle-aged identical twin sisters with a shared history of von Hippel-Lindau syndrome status post bilateral adrenalectomy presented concurrently to the emergency department with symptoms of acute viral illness. Due to their history of adrenalectomy both twins were prescribed chronic glucocorticoid and mineralocorticoid replacement therapy in the outpatient setting. Twin 1 was prescribed prednisone 5 mg and fludrocortisone 0.1 mg daily and Twin 2 was prescribed hydrocortisone 10 mg every morning and 5 mg every evening with fludrocortisone 0.1 mg daily. In the days preceding their arrival, both twins developed progressive constitutional and respiratory symptoms consistent with a viral illness.

Twin 1 presented with shortness of breath, nausea, and flu-like symptoms. She had been evaluated in the emergency department eight days earlier, diagnosed with right upper lobe pneumonia, and discharged home on oral antibiotics. Since her evaluation she had been taking prednisone at three times her maintenance dose in accordance with stress-dose guidance provided at her prior emergency department visit. Following that encounter, she experienced worsening symptoms and returned for further evaluation due to concern for lack of clinical improvement.

Twin 2 presented at the same time in extremis. She was noted to have marked lethargy and altered mental status on arrival and was unable to provide further history; her sister reported they had both been experiencing symptoms of upper respiratory infection. Unlike her twin, she had not increased her glucocorticoid dosing after the onset of viral symptoms in the days prior to presentation.

Diagnostic Assessment

Twin 1 was afebrile and hemodynamically stable on arrival, with mild hypotension consistent with her documented outpatient baseline and adequate oxygen saturation on room air. Physical examination revealed no acute respiratory distress, normal lung auscultation, and no focal neurologic deficits. Laboratory evaluation was notable for a positive SARS-CoV-2 test and borderline-low glucose of 71 mg/dL (3.94 mmol/L) (reference range: 70–99 mg/dL; 3.9–5.5 mmol/L), which corrected with oral intake. Venous blood gas analysis was within normal limits, including a pH within the normal range of 7.32–7.43. No acute electrolyte abnormalities were identified. Chest imaging demonstrated no acute cardiopulmonary findings and interval improvement of her previously diagnosed right upper lobe pneumonia. Given her stable clinical status, reassuring diagnostic studies, and reported adherence to stress-dose glucocorticoid therapy prior to presentation, adrenal crisis was considered unlikely.

Twin 2 arrived in critical condition with altered mental status and lethargy. Initial vital signs were notable for hypotension to 90/50 mmHg. Physical examination demonstrated tachycardia, rales in the bilateral lower lung fields, and hyperpigmentation of the hands. Point-of-care glucose testing revealed significant hypoglycemia with a serum glucose of 52 mg/dL (2.89 mmol/L) (reference range: 70–99 mg/dL; 3.9–5.5 mmol/L), necessitating immediate intravenous dextrose administration. Laboratory evaluation demonstrated metabolic acidosis with a venous pH of 7.29 (reference range: 7.32–7.43), partial pressure of carbon dioxide (pCO_2) of 38 mmHg (5.1 kPa) (reference range: 38–50 mmHg; 5.1–6.7 kPa), and bicarbonate level of 18 mmol/L (18 mEq/L) (reference range: 22–26 mmol/L; 22–26 mEq/L). Serum sodium was 135 mmol/L (135 mEq/L) (reference range: 135–145 mmol/L; 135–145 mEq/L). Random serum cortisol was markedly low at 0.9 µg/dL (25 nmol/L) (reference range for morning cortisol: 5–25 µg/dL; 138–690 nmol/L). SARS-CoV-2 testing was positive. In the context of known bilateral adrenalectomy, absence of stress-dose glucocorticoid use, and clinical findings of hypotension, hypoglycemia, mild hyponatremia, and altered mental status, adrenal crisis was strongly suspected. Diagnostic evaluation was necessarily limited by the urgency of resuscitation, and empiric treatment was initiated without delay.

Treatment

Twin 1 was managed in the emergency department with continuation of her home oral stress-dose glucocorticoid regimen, consisting of prednisone 15 mg daily, three times her home maintenance dose, consistent with stress-dosing principles in adrenal insufficiency. She was also continued on her maintenance fludrocortisone at 0.1 mg daily for mineralocorticoid support. Given her mildly low blood pressure she was provided with 2 liters of isotonic therapy with improvement in her blood pressure. Given her stable hemodynamics and lack of evidence for adrenal crisis or significant respiratory compromise, no escalation to parenteral hydrocortisone was required and she was admitted to the observation unit.

In contrast, Twin 2 presented with findings highly suggestive of adrenal crisis, including hypotension, hypoglycemia, and hyponatremia in the setting of acute SARS-CoV-2 infection and failure to initiate stress-dose steroids prior to presentation. Consistent with established management recommendations from the Endocrine Society Clinical Practice Guideline that emphasize prompt parenteral glucocorticoid administration in suspected adrenal crisis, she was treated emergently with a 100 mg intravenous hydrocortisone bolus, followed by 50 mg of hydrocortisone every six hours for four additional doses, to approximate stress coverage [2]. Intravenous isotonic fluid resuscitation was provided, totaling three liters, to address hypotension. Given her risk of immunosuppression secondary to chronic steroid use and current high dose steroid regimen, remdesivir was administered for treatment of COVID-19. After completion of the hydrocortisone regimen, she was transitioned to an oral stress-dose glucocorticoid regimen, including hydrocortisone 30 mg each morning and 15 mg at bedtime, triple her prescribed outpatient maintenance glucocorticoid dose along with her baseline fludrocortisone 0.1 mg daily.

Table1. Clinical course comparison of twin patients with adrenal insufficiency during Covid-19 infection.

Variable	Twin 1	Twin 2
Stress-dose steroid prior to presentation	Yes, prednisone 15 mg daily, 3x maintenance dose	No
Initial presentation	Flu-like symptoms	Altered mental status
Serum glucose	71 mg/dL (3.94 mmol/L)	52 mg/dL (2.89 mmol/L)
Serum cortisol	n/a	0.9 µg/dL (25 nmol/L)
Adrenal Crisis	No	Yes
Initial steroid treatment	Continued oral stress dose	100 mg IV hydrocortisone
Level of care	Observation (<24 hours)	Progressive care unit (48 hours)
Length of stay	<24 hours	72 hours

Outcome and Follow-up

Twin 1 remained hemodynamically stable throughout her observation stay without progression of respiratory symptoms or evidence of adrenal crisis. She tolerated oral intake and medications without difficulty and did not require escalation of care. She was observed for 24 hours and discharged in stable condition with a planned glucocorticoid taper consisting of prednisone 10 mg daily for three days, followed by 7.5 mg daily for three days, and then a return to her baseline maintenance dose of 5 mg daily until outpatient follow-up. She continued her usual fludrocortisone dose of 0.1 mg daily. At follow-up, she reported continued clinical improvement, and no outpatient endocrinology medication adjustments were required. No adverse events occurred following discharge.

Twin 2 demonstrated gradual improvement following aggressive intravenous glucocorticoid therapy and fluid resuscitation, with resolution of hypotension and hypoglycemia and normalization of mental status after 24 hours. She required admission to the progressive care unit for 48 hours for close monitoring and was hospitalized for a total of 72 hours. Once clinically stable, she was transitioned from intravenous to oral glucocorticoids and discharged on a stress-dose taper consisting of hydrocortisone 30 mg in the morning and 15 mg in the evening for three days, followed by 20/10 mg daily for three days, and then 10/5 mg daily (AM/PM respectively) until outpatient follow-up, in addition to fludrocortisone 0.1 mg daily. No further episodes of hemodynamic instability or hypoglycemia occurred prior to discharge. At last follow-up, she continued to improve clinically, required no outpatient endocrinology medication adjustments, and experienced no adverse events after discharge.

To decrease the risk for future readmission both twins were given urgent referrals to outpatient adult endocrinology. Both patients were provided with individualized materials regarding their specific dosing for stress dosing, along with written instructions detailing indications and emergency room return precautions.

Discussion

This report illustrates the divergent clinical courses of two twins with von Hippel-Lindau syndrome status post bilateral adrenalectomy who presented simultaneously with SARS-CoV-2 infection yet experienced markedly different outcomes based on adherence to outpatient glucocorticoid stress dosing. Twin 1, who appropriately increased her glucocorticoid dose at the onset of symptoms, required only brief observation and was discharged in stable condition. In contrast, Twin 2, who did not initiate stress dosing prior to presentation, developed clinical features consistent with adrenal crisis, including hypotension, hypoglycemia, and altered mental status. As such, she subsequently required intensive supportive care, high-dose parenteral glucocorticoids, and significantly longer hospitalization when compared to her sister.

Adrenal crisis is a life-threatening complication of adrenal insufficiency precipitated by physiologic stressors such as acute infection and represents a major source of morbidity and mortality in this population. Prompt recognition and immediate administration of parenteral hydrocortisone combined with fluid resuscitation remain cornerstones of emergency management to reverse shock and prevent fatal outcomes. Existing clinical guidance strongly emphasizes that diagnostic evaluation should never delay treatment once adrenal crisis is suspected. Stress-dose glucocorticoids should be administered immediately when needed, as high-dose hydrocortisone in suspected crisis is not harmful and may be lifesaving. Beyond acute stabilization, long-term management following recovery should include reassessment of maintenance glucocorticoid dosing, reinforcement of individualized sick-day plans, routine endocrinology follow-up, and confirmation that patients have access to emergency injectable hydrocortisone. Structured post-discharge review provides an opportunity to evaluate adherence, clarify tapering schedules, and prevent recurrent hospitalization.

Prevention efforts to stop progression to adrenal crisis rely on rigorous patient education regarding sick-day rules, clear guidance on when and how to adjust glucocorticoid dosing, and strategies to recognize early physiologic stress. Patient-focused educational resources developed by endocrinology societies underscore the importance of understanding steroid medication and "sick-day rules," including increasing doses during fevers, infections, or other stressors and maintaining emergency supplies of injectable steroids [3]. Effective education empowers patients to act preemptively, potentially preventing adrenal crisis and associated hospitalizations. Detailed patient information references such as the one developed by the Society for Endocrinology can be lifesaving for patients and families [4]. Of note, these resources also provide patients with emergency documentation that can be provided in the case that the patient is too obtunded to provide medical history as Twin 2 was in our case. These materials include written sick-day algorithms, dosing tables, emergency injection instructions, printable steroid emergency cards, and guidance for family members or caregivers. Incorporating these tools into routine clinic visits, hospital discharge planning, and community pharmacy counseling may enhance patient confidence and adherence.

Twin 1's early adherence to stress-dose escalation likely mitigated the onset of adrenal crisis in the setting of her viral illness, consistent with sick-day guidance recommending increased glucocorticoid replacement during physiologic stress. Conversely, Twin 2's presentation exemplifies adrenal crisis precipitated by infection and exacerbated by failure to adjust chronic glucocorticoid therapy, resulting in significant morbidity and need for emergent therapy and admission. Published cohort studies have consistently identified infection as the most common precipitating factor for adrenal crisis, with retrospective analyses demonstrating that intercurrent illnesses, particularly viral and gastrointestinal infections, account for a substantial proportion of crisis episodes in patients with primary adrenal insufficiency [5]. These reports also highlight that delayed or omitted stress-dose glucocorticoid escalation is frequently associated with preventable hospital admissions [5]. Observational data collected during the COVID-19 pandemic further supports this association. European multicenter surveys and retrospective cohorts have reported favorable clinical outcomes among patients with adrenal insufficiency who implemented recommended sick-day dose adjustments [6,7], whereas patients who did not appropriately increase glucocorticoid dosing were at greater risk of clinical deterioration and need for acute medical intervention [6].

While specific literature on adrenal insufficiency management during COVID-19 remains limited, emerging observational data and expert opinion suggest that outcomes are more favorable when stress dosing is implemented appropriately and when patient education on stress management is emphasized. COVID-19 presents additional risks for patients with adrenal insufficiency, including high fevers, gastrointestinal symptoms impairing oral medication absorption,

systemic inflammatory response, and increased metabolic demand. Furthermore, social isolation and reduced access to routine medical care during pandemic surges may delay reinforcement of sick-day education and follow-up. These factors underscore the importance of proactive counseling during viral outbreaks. Regular reinforcement of sick-day strategies, access to emergency hydrocortisone, and clear action plans are essential components of outpatient and preventative care. In addition, psychological stress associated with chronic disease management and acute infection may impair adherence. Integrating psychological support, peer support groups, or counseling services into chronic endocrine care may improve patient engagement and self-management behaviors, particularly in high-risk populations.

Limitations of this report include its reliance on a single twin pair and subsequent biases that result from this single case study approach, it is further limited by the absence of long-term adrenal axis assessment post-COVID-19. Nonetheless, the presentation under similar stressors but with differing management prior to presentation provides a natural experiment highlighting how patient education and proactive self-management can influence outcomes. In patients with adrenal insufficiency, structured repeated education on stress-dose management, access to practical written resources, integration of psychological support, and clear sick-day action plans represent low-cost, high-impact interventions capable of preventing adrenal crisis and reducing avoidable hospitalizations.

In summary, this case highlights how adherence to stress-dose glucocorticoid recommendations can significantly influence clinical outcomes in patients with primary adrenal insufficiency during acute infection. Despite shared genetic background and similar infectious exposure, these twins experienced markedly different trajectories based on pre-presentation management. Infection remains a common precipitating factor for adrenal crisis, yet timely dose escalation and structured patient education can mitigate morbidity and reduce hospitalization risk. This report reinforces that proactive sick-day planning, access to emergency hydrocortisone, regular endocrinology follow-up, and ongoing patient education are critical components of long-term management. Strengthening preventive strategies in this high-risk population represents a practical and impactful opportunity to reduce avoidable adrenal crises.

Learning Points

- Patient education regarding sick-day rules and stress-dose steroid management is critical and should be reinforced regularly to prevent avoidable morbidity.
- Comparative cases involving genetically similar patients highlight the impact of adherence to established management guidelines and underscores opportunities for improved preventive care.
- Patients with primary adrenal insufficiency are at high risk for adrenal crisis during acute infections such as SARS-CoV-2 and require prompt stress-dose glucocorticoid therapy.
- Early initiation of stress-dose glucocorticoids during acute illness may prevent progression to adrenal crisis and reduce the need for hospitalization.
- Failure to increase glucocorticoid dosing during physiologic stress can result in life-threatening complications, including hypotension, hypoglycemia, and altered mental status.

Acknowledgments

None.

Funding

No public or commercial funding.

Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent obtained directly from both patients.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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