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Letter to the Editor

ADRENAL CRISIS MAY OCCUR EVEN IN PATIENTS WITH ASYMPTOMATIC COVID-19

To the Editor:

The outbreak of COVID-19 (coronavirus disease 2019), an infectious disease caused by the severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), led to major anxiety in patients with primary and secondary adrenal insufficiencies. Indeed, concern has been raised on the risks of severe forms of SARS in patients treated by high dose glucocorticoids (1). For now, for patients presenting with continuous dry cough and/or fever, it is recommended to remind patients of the “sick day rules,” that is, the absolute need to double their daily oral glucocorticoid dose and to maintain this regimen until fever has subsided (2,3). However, to the best of our knowledge, no case of COVID-19 in patients with adrenal insufficiency has been reported to judge the safety of this approach.

We report here the cases of 3 patients with a history of secondary (idiopathic combined hormone pituitary deficiency in patient 1; Sheehan syndrome in patient 2)

or primary adrenal insufficiency (after bilateral adrenalectomy in patient 3 for right adrenalectomy 30 years ago, and left enlarged nephrectomy in 2019 in the management of a urothelial carcinoma) followed in our institution, and infected with SARS-CoV-2. The patient’s main characteristics and outcomes are depicted in Table 1. All 3 cases were women (aged 34, 61, and 85 years, respectively) with only few associated comorbidities. Interestingly, none of the patients presented with severe infectious signs despite an increased dose of hydrocortisone. Patient 1 exhibited typical signs of COVID-19 (fever, coughing, myalgia); she had no sign of adrenal crisis; she doubled her daily oral dose of hydrocortisone for 3 days, and remained paucisymptomatic. The other 2 patients were admitted to the emergency room with typical signs of adrenal crisis. Patient 2 presented with diarrhea, abdominal pain (signs also known to be associated with COVID-19) and hypotension, but she also complained of anosmia. Since she had no sign of severity, she was treated for a few hours with intravenous saline infusion, her daily oral dose of hydrocortisone was doubled, and the symptoms decreased very rapidly. Patient 3 was admitted to the emergency room for a severe adrenal crisis without fever, cough, or anosmia.

Table 1
Main Characteristics and Outcomes of the 3 Patients

Patient Number	Cause of adrenal insufficiency	Age (years)	Gender	Comorbidities	Usual hydrocortisone dose (mg per day)	Clinical presentation	Chest CT findings	Outcome
1	Secondary (combined pituitary hormone deficiency)	34	Female	None	30	Fever, coughing, myalgia	Bilateral and peripheral ground-glass opacities	Paucisymptomatic and favorable
2	Secondary (Sheehan syndrome)	61	Female	Type 2 diabetes	20	Diarrhea, hypotension, abdominal pain, anosmia	One limited ground glass opacity	Paucisymptomatic and favorable
3	Primary (bilateral adrenalectomy in a context of urothelial carcinoma)	85	Female	Arterial hypertension	20	Adrenal crisis	One limited ground glass opacity	Symptomatic and favorable

Abbreviation: CT = computed tomography.

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She was systematically tested with reverse transcriptase polymerase chain reaction (RT-PCR) assessment which turned out to be positive for COVID-19. She was first treated intravenously with 100 mg hydrocortisone per 24 hours for 48 hours; the dose was then rapidly decreased, and she became rapidly asymptomatic. In all 3 patients, the RT-PCR test remained positive for 12 days and, to date, they completely recovered. Interestingly, in patients 2 and 3, a complete etiologic workup was performed (including electrocardiogram, blood, and urine cultures) and did not show any reason other than COVID-19 for adrenal crises.

Three main lessons can be learned from these cases. First, the “sick day rules” seems an efficient management strategy for adrenal insufficient patients affected with COVID-19. Second, physicians should be informed that signs of adrenal crisis (mainly gastro-intestinal) may be the only clinical expression of COVID-19. Third, patients with adrenal insufficiency may present in adrenal crisis in the setting of asymptomatic COVID-19 infection. We thus consider that COVID-19 assessment should be performed in any such patient presenting with clinical signs of adrenal insufficiency, even in the absence of the typical symptoms of COVID-19.

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

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REFERENCES

1. **Ruan S-Y, Lin H-H, Huang C-T, Kuo P-H, Wu H-D, Yu C-J.** Exploring the heterogeneity of effects of corticosteroids on acute respiratory distress syndrome: a systematic review and meta-analysis. *Crit Care.* 2014;18:R63.
2. **Kaiser UB, Mirmira RG, Stewart PM.** Our response to COVID-19 as endocrinologists and diabetologists. *J Clin Endocrinol Metab.* 2020;105:dgaal48.
3. **Isidori AM, Pofi R, Hasenmajer V, Lenzi A, Pivonello R.** Use of glucocorticoids in patients with adrenal insufficiency and COVID-19 infection. *Lancet Diabetes Endocrinol.* 2020;8:472-473.