Case Report

Adrenal crisis in a patient with APS2 due to COVID-19: A case report

Varun Suryadevara, Chandhana Merugu, Nandhini L. Perumal, Jayaprakash Sahoo, Sadishkumar Kamalanathan, Dukhabandhu Naik

Department of Endocrinology, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry, India

Abstract

COVID-19 (corona virus disease 2019), caused by the severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), has spread throughout the globe and affected millions of people worldwide. Here, we report a patient with autoimmune polyglandular syndrome type 2 who presented with adrenal crisis, precipitated by COVID-19. We intend to highlight the importance of stress dosing in preventing adrenal crisis in patients with adrenal insufficiency (AI). A uniform structured education programme is needed to improve knowledge and practices in patients with AI in our country.

Keywords: Addison's disease, adrenal crisis, adrenal insufficiency, COVID 19, steroid card

Introduction

Nearly one and a half years have elapsed since the first case of COVID-19 (corona virus disease 2019), caused by the severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), reported in Wuhan, China, in December 2019. It has currently evolved into a full-blown pandemic. Although the respiratory system is the primary organ system affected, SARS-CoV-2 also affects the endocrine system at multiple levels.[1] Hypothalamo-pituitary-adrenal (HPA) axis has been reported to be involved in patients suffering from COVID-19. Clinical practice guidelines from the Endocrine Society for primary adrenal insufficiency (AI) recommend doubling the usual oral glucocorticoid dose in fever or illness requiring bed rest.[2] Here, we report a patient with primary AI who presented with adrenal crisis due to COVID-19 despite compliance with therapy. We intend to highlight the importance of educating patients regarding stress dosing and recognising acute illness in patients with AI.

Address for correspondence: Dr. Dukhabandhu Naik, Department of Endocrinology, JIPMER, Puducherry, India.
E-mail: drnaik2000@gmail.com

Received: 14-07-2021 **Revised:** 16-12-2021
Accepted: 21-12-2021 **Published:** 14-05-2022

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_1405_21

Case Description

A 65-year-old man, a known case of primary hypothyroidism and vitiligo, presented in mid-2019 with complaints of recurrent vomiting and easy fatiguability for 1 year. Evaluation revealed low basal cortisol (<0.5 μg/dl), elevated adrenocorticotropic hormone (ACTH- 861 pg/ml), anti-thyroid peroxidase antibody positivity and atrophied adrenals [Figure 1]. He was diagnosed with autoimmune polyglandular syndrome type 2 (APS2-Addison's disease + primary hypothyroidism + vitiligo) and was started on prednisolone and fludrocortisone. His thyroxine dose was optimised. He was on regular follow-up for the past 2 years. Recently, he was brought to out patient department (OPD) with a history of easy fatiguability for 1 week and dizziness for 1 day. He was compliant with medications. However, he did not increase the prednisolone dose as he did not have fever or any other specific symptoms and was carrying on his routine activities. He was drowsy and lethargic at the presentation. Physical

How to cite this article: Suryadevara V, Merugu C, Perumal NL, Sahoo J, Kamalanathan S, Naik D. Adrenal crisis in a patient with APS2 due to COVID-19: A case report. J Family Med Prim Care 2022;11:2228-30.

examination revealed hypotension with tachycardia. He was immediately started on intravenous fluids and hydrocortisone after admission and was managed along the lines of adrenal crisis. Work up to evaluate the precipitant factor of the adrenal crisis revealed positive RTPCR for COVID. Chest X-ray did not show any significant opacities [Figure 2]. He was maintaining normal saturation without oxygen supplementation and recovered with supportive treatment. Hydrocortisone dose was tapered and converted to prednisolone, and fludrocortisone was restarted. He was discharged after 5 days. On the follow-up visit, he was doing well and was compliant with medications.

Discussion

In this report, we present a known patient of APS2 who developed acute adrenal insufficiency due to COVID-19 despite compliance with therapy. In a case report by Castinetti *et al.*,[3] adrenal crisis was reported in a patient with AI due to COVID-19, similar to the index case, who had very minimal symptoms of SARS-CoV-2 infection. The involvement of the HPA axis by the COVID-19 virus has been described in few cross-sectional studies. In a study by Alzahrani *et al.*,[4] 32% of the subjects with COVID-19 had serum cortisol levels <10.8 μg/dl on day 1 or 2 of hospital admission. Tan *et al.*[5] measured baseline cortisol concentration within 48 h of hospital admission and correlated with survival outcome. They demonstrated a marked cortisol stress response with higher cortisol concentrations being associated with increased mortality.

The possible mechanisms by which COVID-19 causes adrenal insufficiency are multifarious, ranging from cytokine storm producing HPA axis suppression[6] to bilateral adrenal hemorrhage causing primary AI.[7] Patients with AI are predisposed to an increased risk of infections due to inadequate innate immune responses. The physiological rise of glucocorticoid secretion in the acute phase is necessary for priming the immune response. Lack of such response may cause progression to severe infection. Considering these implications of COVID-19 in patients with AI, various endocrine societies throughout the world have given new clinical practice guidelines about managing AI patients in current times.[8,9] For patients with mild symptoms, either doubling of the replacement dose in circadian fashion or oral hydrocortisone 20 mg every 6 h was suggested. In patients requiring hospitalization or critically ill, the dose should be an equivalent of 200 mg/d intravenous hydrocortisone either as an infusion or in divided doses every 6 h.

Although clinicians understand the importance of educating patients about AI, it is not easy to transfer knowledge and induce behavioural changes. The status of health education nationwide was assessed in Germany recently.[10] Only 30% of the patients possessed a glucocorticoid emergency kit, and 10% never increased their glucocorticoid dose. A structured education programme was designed in Germany and was operational in 77 endocrine centres by 2018. This programme was highly effective in improving patient education and behaviour.[11] Such a programme is the need of the moment for patients with AI in India. Increasing cases of mucormycosis after COVID-19 have resulted in fear among patients with AI. Few of our patients had even stopped medication when they came for follow-up due to misinformation spread through social media. Apart from a lack of resources, we are currently fighting a battle of misinformation widespread through various sources nowadays. It is imperative in this group of patients, as delay in recognizing adrenal crisis can lead to poor outcomes and can even be fatal. Health education for patients with AI involves education regarding the need for the treatment, identifying special situations and critical situations, carrying a steroid card and self-injection of parenteral glucocorticoid when access to healthcare is delayed. Such health education requires a great deal of effort from endocrinologists and physicians of our country. Self-help groups may improve patients' knowledge better by interaction with other patients.

Conclusion

This pandemic has reminded us of the importance of educating our patients with AI about the imperativeness of stress dosing. Since the majority of the COVID-19 patients

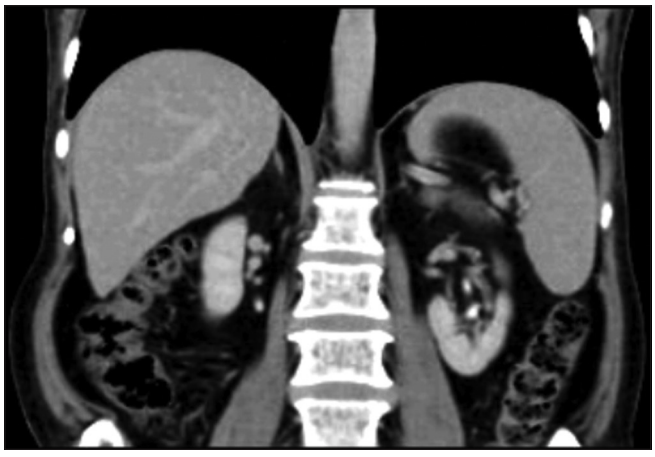

Figure 1: Coronal view CECT abdomen showing bilateral atrophied adrenals

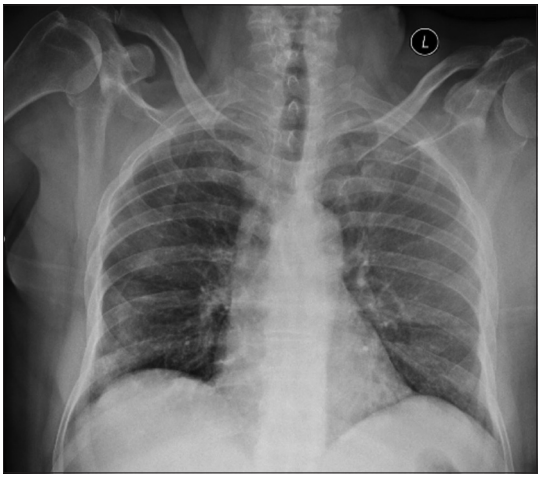

Figure 2: Chest X-ray during admission with COVID-19

are mildly symptomatic, we should suspect COVID-19 illness in patients with AI on supplementation who present with crisis despite compliance with therapy. A structured education programme is needed to improve the health education of patients with AI.

All authors have read and approved the final version of the manuscript. The requirements for authorship have been met. Each author believes that the manuscript represents honest work.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Somasundaram NP, Ranathunga I, Ratnasamy V, Wijewickrama PSA, Dissanayake HA, Yogendranathan N, *et al.* The impact of SARS-Cov-2 virus infection on the endocrine system. J Endocr Soc 2020;4:1-22.
2. Bornstein SR, Allolio B, Arlt W, Barthel A, Don-wauchope A, Hammer GD, *et al.* Diagnosis and treatment of primary adrenal insufficiency : An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2016;101:364-89.
3. Castinetti F, Amodru V, Brue T. Adrenal crisis may occur even in patients with asymptomatic COVID-19. Endocr Pract 2020;26:929-30.
4. Alzahrani AS, Mukhtar N, Aljomaiah A, Aljamei H, Bakhsh A, Alsudani N, *et al.* The impact of COVID-19 viral infection on the hypothalamic-pituitary-adrenal axis. Endocr Pract 2021;27:83-9.
5. Tan T, Khoo B, Mills EG, Phylactou M, Patel B, Eng PC, *et al.* Association between high serum total cortisol concentrations and mortality from COVID-19. Lancet Diabetes Endocrinol 2020;8:659-60.
6. Ur A, Verma K. Cytokine storm in COVID19: A neural hypothesis. ACS Chem Neurosci 2020;11:1868-70.
7. Frankel M, Feldman I, Levine M, Frank Y, Bogot NR, Benjaminov O, *et al.* Bilateral adrenal hemorrhage in Coronavirus disease 2019 patient: A case report. J Clin Endocrinol Metab 2020;105:3745-9.
8. Isidori AM, Arnaldi G, Boscaro M, Falorni A, Giordano C, Giordano R, *et al.* COVID-19 infection and glucocorticoids: Update from the Italian society of endocrinology expert opinion on steroid replacement in adrenal insufficiency. J Endocrinol Invest 2020;43:1141-7.
9. Arlt W, Baldeweg SE, Pearce SHS, Simpson HL. Endocrinology in the time of COVID-19: Management of adrenal insufficiency. Eur J Endocrinol 2020;183:G25-32.
10. Kienitz T, Hahner S, Burger-Stritt S, Quinkler M. Therapeutic patient education for adrenal insufficiency under COVID-19 pandemic conditions. Exp Clin Endocrinol Diabetes 2021;129:241-9.
11. Burger-Stritt S, Eff A, Quinkler M, Kienitz T, Stamm B, Willenberg HS, *et al.* Standardised patient education in adrenal insufficiency: A prospective multi-centreevaluation. Eur J Endocrinol 2020;183:119-27.