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CASE REPORT – OPEN ACCESS

Pituitary Insufficiency Diagnosed After Coronavirus Disease-19: A Case Report

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ABSTRACT

Background: Severe acute respiratory syndrome-coronavirus (SARS-CoV) and SARS-CoV-2 might affect the hypothalamic-pituitary-adrenal axis. This paper presents a rare case of pituitary insufficiency diagnosed after CoV disease (COVID)-19.

Case Report: On December 7, 2020, a 67-year-old male patient presented to the Endocrinology Department of Lokman Hekim University with weakness, weight loss, and abdominal pain lasting for 3 weeks. In his medical history, he had a positive real-time polymerase chain reaction test result for SARS-CoV-2 based on the nasopharyngeal swab analyzed on September 30. Central hypothyroidism, secondary adrenal insufficiency, hypogonadotropic hypogonadism, and a low dehydroepiandrosterone-sulfate level were detected in the laboratory examinations. Steroid therapy was initiated.

Conclusion: Non-specific adrenal insufficiency symptoms such as fatigue and weakness, and psychosomatic symptoms can be seen during the course of COVID-19 or the post-COVID-19 period. Physicians should be aware about the systemic effects of SARS-CoV-2 infection and follow-up patients with a history of COVID-19 accordingly.

Keywords: Coronavirus disease-19, endocrine system, hypothalamic-pituitary-adrenal axis, pituitary

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INTRODUCTION

Severe acute respiratory syndrome-coronavirus (SARS-CoV-2) primarily affects the lungs, entering the pneumocyte using the host angiotensin-converting enzyme 2 (ACE2) as a receptor (1). Hypothalamic and pituitary tissues can be targeted by the virus since they express ACE2 receptors. Hypophysitis, thyroiditis, and adrenalitis secondary to viral infection in general have been reported. Endocrine abnormalities occur commonly in CoV infections.

The biochemical evidence of hypothalamic-pituitary-adrenal (HPA) axis involvement in SARS was first reported by Leow et al. (2) in 2005. In that study, 61 survivors of the SARS outbreak were evaluated for hypocortisolism. Twenty-four (39.3%) patients were reported to have a low serum cortisol level, and it was noted that hypophysitis or direct hypothalamic damage might have led to hypothalamic-pituitary dysfunction. Another study investigating endocrine cells in adenohypophysis obtained from autopsies of five patients with SARS revealed that both the number of positive cells and the staining intensity of immunoreactivity for growth hormone, thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH) were remarkably decreased and the levels of prolactin, follicle-stimulating hormone, and luteinizing hormones were significantly increased in the patient group compared to the controls (3).

The literature contains limited studies showing that the HPA axis may be affected by SARS-CoV-2 infection. Herein, we present a rare case of pituitary insufficiency diagnosed after CoV disease (COVID)-19.

CASE REPORT

A 67-year-old male patient presented to our endocrinology clinic with the complaints of weight loss, hypotension, weakness, and abdominal pain. He was using a combination of sitagliptin and metformin, insulin glargine 20 IU for diabetes, and perindopril for hypertension. His symptoms had started 3 weeks before his admission.

In the history of the patient, there was a diagnosis of COVID-19 confirmed by a positive RT- polymerase chain reaction (PCR) test for SARS-CoV-2 2 months earlier (September 30, 2020). The patient described his symptoms at the time as headache, sweating, and smells and taste loss. He also had loss of appetite. After the COVID-19 diagnosis, he suffered from anosmia and ageusia for 3 weeks. The patient had received favipiravir and hydroxychloroquine treatment for COVID-19. Glucocorticoids were not given during that period. The patient had been isolated and treated at home due to the mild severity of the infection.

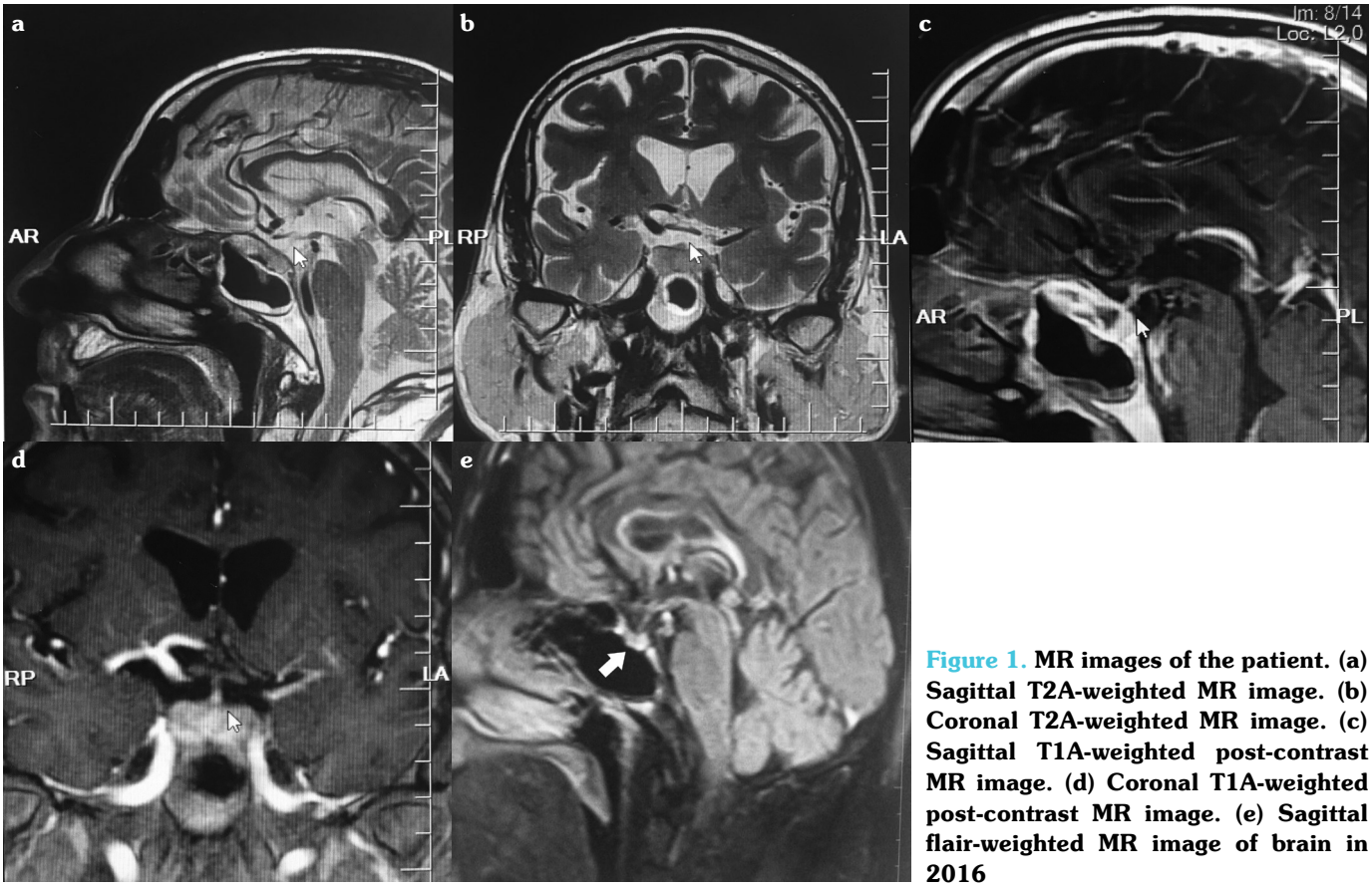

Figure 1. MR images of the patient. (a) Sagittal T2A-weighted MR image. (b) Coronal T2A-weighted MR image. (c) Sagittal T1A-weighted post-contrast MR image. (d) Coronal T1A-weighted post-contrast MR image. (e) Sagittal flair-weighted MR image of brain in 2016

On December 7, 2020, the patient was hospitalized for further investigations with symptoms including fatigue, nausea, vomiting, abdominal pain, and hypotension. There was no history of head trauma as a possible cause of partial empty sella and pituitary insufficiency. The hypophysis gland was markedly thinned and measured to be approximately 4.5 mm at its thickest point on the pituitary magnetic resonance image. The serum sodium and potassium values, urinary density, and prolactin were in normal ranges. Fasting blood glucose was 146 mg/dl and the HbA1c value was 7.2. He did not have polyuria or polydipsia. He also did not describe visual disturbance. The thyroid autoantibodies were negative. The PCR test was negative for SARS-CoV-2.

In his physical examination, blood pressure was 90/60 mmHg and pulse rate was 102 beats per minute. The thyroid function tests revealed low levels of free triiodothyronine (FT3), free thyroxine (FT4), and TSH. Other anterior pituitary hormones were examined, and pituitary magnetic resonance imaging (MRI) was performed after the diagnosis of central hypothyroidism. The serum cortisol level was 0.74 µg/dl, and the ACTH level was 6.15 ng/L. Secondary hypothyroidism, secondary adrenal insufficiency, hypogonadotropic hypogonadism, and a low dehydroepiandrosterone-sulfate level were detected in the patient's laboratory examinations.

For the treatment of suspected acute adrenal insufficiency, 20 mg parenteral methylprednisolone was administered, followed by 10 mg intravenous methylprednisolone 4 times a day for 2 days. Abdominal pain, nausea, and weakness markedly decreased. The patient's treatment continued with daily oral prednisolone at a dose of 5 mg and levothyroxine at a dose of 75 mcg.

The patient was followed up for his outcome. At the control examination undertaken in February 2021, it was observed that his general condition was good. The serum cortisol level, which was measured 36 h after the last prednisolone dose, was 1.5 µg/dl. The patient's hormone levels were still compatible with partial pituitary insufficiency. The laboratory data are shown in Table 1.

DISCUSSION

COVID-19 is a multisystemic disease which mostly affects the respiratory system; however, other organs such as endocrine glands may also be involved. The viral ribonucleic acid of SARS-CoV-2 has been detected in the plasma or serum of COVID-19 cases. Endocrine glands such as the pancreas, thyroid, testis, ovary, adrenals, and pituitary glands express the ACE2 receptor (4, 5). A report on the isolation of the virus from the adrenals and pituitary glands of four patients who died of SARS proposed that theoretically these organs could be target of the virus (6). Another study suggested the possibility of direct hypothalamic injury or reversible hypophysitis caused by SARS-CoV leading to hypothalamic-pituitary dysfunction (2). Alzahrani et al. (7) reported the impact of COVID-19 on the HPA axis. In that study, the morning plasma cortisol level was measured in 28 consecutive patients with COVID-19 and determined as <100 nmol/L in eight patients (28.6%), <200 nmol/L in 14 (50%), and <300 nmol/L in 18 (64.3%).

Table 1. Laboratory findings of the case at the time of diagnosis and 2nd-month follow-up

Laboratory test	First admission on December 7, 2020	Follow-up on February 9, 2021	Reference range
TSH Uu/ml	0.11	0.00	0.27–4.2
FT4 ng/dl	0.65	1.36	0.89–1.76
FT3 pg/ml	2.32	2.31	2.3–4.2
Cortisol µg/dl	0.74	1.5	7.0–29.0
ACTH ng/L	6.15	12.6	7.2–63.0
FSH mIU/mL	4.16	2.48	1.5–12.4
LH mIU/mL	0.42	0.71	1.5–9.3
Testosterone ng/mL	<0.025	<0.025	1.93–7.4
DHEAS µg/dL	3.21	11.53	33.6–249
Prolactin ng/mL	8	3.3	3.5–20.0
Somatomedin–C ng/mL	117	104	69–200
Growth hormone ng/mL	0.45	0.55	0.06–6.0
Serum sodium mmol/L	136	138	135–145
Serum potassium mmol/L	4.5	4	3.5–5.5
Serum calcium mg/dL	9.9	9.6	8.4–10.0
Urinary density	1030	1025	1005–1030
COVID-19 PCR	Negative		

TSH: Thyroid-stimulating hormone; FT4: Free thyroxine; FT3: Free triiodothyronine; ACTH: Adrenocorticotropic hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; DHEAS: Dehydroepiandrosterone sulfate; PCR: Polymerase chain reaction; COVID-19: Coronavirus disease-19

The patient had experienced a mild clinical form of COVID-19 and had no any symptoms of pituitary insufficiency during the acute period of the infection. At the time of admission to the hospital, the pituitary gland was markedly thin, measured to be approximately 4.5 mm at its thickest point in the pituitary MRI. The former radiological records of the patient taken for the differential diagnosis of essential tremor in 2016 and 2018 were reviewed again, and no sellar and parasellar pathologies were observed (Fig. 1).

It was considered that the patient had no previous hypothalamic-pituitary pathology since the previously examined thyroid functions were FT3 2.91 pg/mL, FT4 1.25 ng/dL, and TSH 0.83 uIU/ml during COVID-19. In addition, the patient lacked a hospitalization indication for COVID-19 due to mild infection.

The presence of secondary adrenal failure and secondary hypothyroidism imply that these axes were probably involved either directly by COVID-19 or indirectly due to hypophysitis triggered by the viral infection. Posterior pituitary functions were considered normal since the patient had normal urinary output and normal urinary density. Therefore, urinary osmolality was not evaluated. In addition, negative thyroid autoantibodies implicated SARS-CoV rather than autoimmunity as a pathogenetic mechanism.

CONCLUSION

Non-specific adrenal insufficiency symptoms such as fatigue and weakness and psychosomatic symptoms can be seen during the course of COVID-19 and the convalescence period. HPA axis disorders should be considered in the differential diagnosis. During the COVID-19 pandemic, physicians should be aware of the systemic effects of SARS-CoV-2 infection including those affecting the endocrine system during both the acute and post-COVID-19 periods.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Author Contributions: Concept – MGK; Design – MGK; Supervision – MG; Resource – CE; Materials – CE; Data Collection and/or Processing – MGK; Analysis and/or Interpretation – MG; Literature Search – MGK; Writing – MGK; Critical Reviews – MG.

Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal 2020; 10(2): 102–8.
2. Leow MK, Kwek DS, Ng AW, Ong KC, Kaw GJ, Lee LS. Hypocortisolism in survivors of severe acute respiratory syndrome (SARS). Clin Endocrinol (Oxf) 2005; 63(2): 197–202. [CrossRef]
3. Wei L, Sun S, Zhang J, Zhu H, Xu Y, Ma Q, et al. Endocrine cells of the adenohypophysis in severe acute respiratory syndrome (SARS). Biochem Cell Biol 2010; 88(4): 723–30. [CrossRef]
4. Pal R, Banerjee M. COVID-19 and the endocrine system: Exploring the unexplored. J Endocrinol Invest 2020; 43(7): 1027–31. [CrossRef]
5. Chang L, Yan Y, Wang L. Coronavirus disease 2019: Coronaviruses and blood safety. Transfus Med Rev 2020; 34(2): 75–80. [CrossRef]
6. Ding Y, He L, Zhang Q, Huang Z, Che X, Hou J, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: Implications for pathogenesis and virus transmission pathways. J Pathol 2004; 203(2): 622–30. [CrossRef]
7. 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(2): 83–9. [CrossRef]