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COVID-19 infection in a patient with Cushing's disease on osilodrostat treatment

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The clinical presentation of coronavirus disease 2019 (COVID-19) ranges from asymptomatic illness to severe respiratory failure requiring admission to the intensive care unit. The rate of morbidity and mortality is higher among patients with obesity, cardiometabolic disease, and immunodeficiency [1–3]. These conditions are very common among patients with Cushing's Syndrome (CS) [1, 2], making COVID-19 infection especially dangerous. Thus COVID-19 infection among patients with CS is a state of special emergency worth further consideration. Little is known about the risk and management of patients with CS and COVID-19 infection [4, 5].

We present the complex care of a 35-year-old woman with active Cushing's disease (CD) and COVID-19 infection.

She presented at the age of 28 years with clinical and biochemical signs of hypercortisolaemia due to a corticotroph pituitary neuroendocrine tumour (PiTNET). Subsequently, non-radical transsphenoidal surgery (2014) and CyberKnife radiotherapy (2018) were performed.

Despite combined treatment, the patient presented many complications of long-lasting hypercortisolaemia: heart failure (ejection fraction 45%), hypertension, mental disturbances, severe hepatic impairment, poorly controlled diabetes mellitus, proximal muscle wasting, morbid central obesity (body mass index 58 kg/m^2), and hypercholesterolaemia. The challenges in this case were aggravated due to very poor compliance. The patient refused treatment with Metopirone due to malaise. Eventually, treatment with osilodrostat was implemented in 2020 (4 mg daily) with good response and tolerability.

After one month of treatment, the patient presented with severe weakness, malaise, sweating, hypotension, diarrhoea, and vomiting. Biochemically, hyperkalaemia (6.06 mmol/L), hyponatraemia (129 mmol/L), exacerbation of renal parameters [estimated glomerular filtration rate (eGFR) 33 mL/min/1.73 m^2], and severe increase [100× upper limit of normal (ULN)] of liver function (alanine aminotransferase [ALT] 386 U/I, 584 U/I), and C-reactive protein (CRP) 11.2 mg/L (normal range [NR] < 5 mg/L) without leukocytosis were noted. Chest X-ray showed no signs of pneumonia. Adrenal insufficiency was suspected in the course of viral infection. Laboratory testing confirmed COVID-19 despite lack of respiratory symptoms. The patient did not consent to hospitalisation. We instructed the patient to start taking hydrocortisone at a dose of 20–50 mg/daily, discontinue osilodrostat, and adequately hydrate. Additionally, low-molecular-weight heparin (LMWH) as a prophylactic anticoagulative (40 mg enoxaparin daily) was implemented. Retrospective analysis of biochemical results did not confirm adrenal insufficiency (morning cortisol level 32.2 μg/dL — data from the time of infection; and free cortisol excretion in the urine [UFC] 121 μg/24 h, NR < 100 μg/24 h — data from just before the infection). After a few days her symptoms resolved and she restarted taking osilodrostat.

At the dose of 2 × 2 mg daily, clinical improvement, normalisation of UFC (20.1 μg/24 h), and morning cortisol concentration (17.1 μg/dL) were observed with a decrease of glycated haemoglobin (HbA_{1c}) (8.5%) and improvement of liver function [ALT, aspartate transferase (AST) in NR]. Currently the patient is in good general condition.

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Management of COVID-19 infection can be challenging, especially in patients with endogenous hypercortisolaemia due to impaired immune system and several comorbidities. Among patients with CS treated with steroidogenesis inhibitors, who develop COVID-19 infection, temporary discontinuation of medication and hydrocortisone supplementation (titration/halt) is suggested as a first-line management [3–5]. However, a block and replace regimen could be another option in patients with severe hypercortisolaemia. In our case, delayed cortisol results indicated that block and replace therapy could be the correct choice in patients with possible active disease and unknown biochemical results [4, 5]. Close monitoring of electrolytes, magnesium, cortisol, and electrocardiography is recommended [5] as well as close monitoring of interactions between drugs used in COVID-19 and in CS. Keeping in mind that CS itself and COVID-19 increase the risk of venothromboembolism, LMWH implementation is recommended [3, 4]. Hospitalized patients with CS having COVID-19 may require a treatment dosage of LMWH [4]. To summarize: 1. optimization of treatment of comorbidities that accompany CS may decrease the complications of COVID-19; 2. Titration/halt strategy with glucocorticosteroid supplementation or block and replace regimen should be implemented in patients with CS and COVID-19 – the choice should be individualized; 3. LMWH is recommended for patients with CS and COVID-19 – the dosage needs to be individualized; 4. Further observation of patients with CS and COVID-19 is needed to prepare clear recommendations on short- and long-term management of patients.

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Consents

Patient consent for publication: obtained.

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