



Case Report

## Manic Episode Associated with COVID-19 and Corticosteroids in a Patient with Prior Mild Cognitive Impairment

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### SUMMARY

**Background:** COVID-19 infection and its treatment with corticosteroids are associated with various neuropsychiatric complications. An increasing number of studies show that patients with COVID-19 may suffer from psychiatric disorders in acute and subacute phases of the disease. Post-COVID mania and mania associated with corticosteroids are two important complications, which clinicians should be aware. **Case:** We report a 69-year-old male patient who showed mild confusion and cognitive difficulties in the acute phase of COVID-19. With the addition of dexamethasone 8 mg in the treatment of COVID-19, the patient suffered from euphoria, grandiose delusions, reduced need for sleep and rapid and increased speech. The patient was admitted to the psychiatric inpatient clinic and diagnosed with medication-induced mania. The patient showed significant improvement with 15 mg olanzapine and 1000 mg valproate treatment in a week.

**Discussion:** Increasing number of studies focus on psychiatric complications of COVID-19. Although mania and psychoses are relatively rare complications of COVID-19, they deserve special attention from clinicians. Corticosteroids in COVID-19 treatment increase the risk of such mental disorders. This case shows that patients with COVID-19 should be screened for psychiatric disorders, and the use of corticosteroids in patients with specific risk factors should be evaluated regarding psychiatric complications.

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## 1. Introduction

The use of corticosteroids is associated with a wide range of psychiatric side effects and complications. The most common psychiatric complications of corticosteroid use are mood disorders like depression and mania, delirium, aggressive and suicidal behavior, anxiety and various isolated cognitive impairments.<sup>1</sup> Among these complications, euphoria and hypomania/mania are mostly associated with short-term use and depression is the most common complication in long-term use of corticosteroids.<sup>2</sup> Studies show that mania constitutes almost half of the corticosteroid-induced neuropsychiatric disorders and psychotic symptoms are also very prevalent, up to 40%, in these patients.<sup>3</sup> Although various risk factors like age, previous psychiatric disorders, underlying disease or gender are not proven to be directly related to the manifestation of corticosteroid-induced mania (CIM), it seems that higher doses of corticosteroids are associated with more neuropsychiatric complications.<sup>3</sup>

Since December 2019, the world has witnessed a pandemic caused by a novel coronavirus named SARS-CoV-2. The clinical picture caused by the SARS-CoV-2 virus named Coronavirus Disease 19 (COVID-19) and neuropsychiatric manifestations are one of the most commonest symptom clusters associated with COVID-19.<sup>4</sup> Although some case reports reveal a possible connection between COVID-19 and mania,<sup>5</sup> most of the literature focuses on the possible risks of

corticosteroid use in patients with COVID-19.<sup>6</sup> Apart from mania, some studies show an association between COVID-19 and psychosis and suggest a potential role of inflammatory response in pathogenesis.<sup>7</sup>

In summary, the use of corticosteroids is highly associated with mania and psychosis and some preliminary case reports also show a potential connection between COVID-19 and mania with moderator role of inflammation. Therefore, the findings suggest that patients with COVID-19 using corticosteroids may have double risk factors in the manifestation of the manic symptoms.

## 2. Case

A 69-year-old male was admitted to a Psychiatry & Neurology Hospital in İstanbul on 16.04.2021 with symptoms of psychomotor agitation, elevated mood, grandiose thoughts and refusal of treatment. The patient was accompanied by his wife and children, who explicitly demanded hospital admission based on difficulties caused by the patient. Apart from diabetes mellitus, the patient was a healthy non-smoker with no history of drug or alcohol use. He was married and had three children, lived with his family and owned a business in the plastic industry. The patient was tested as PCR positive for SARS-CoV-2 on 16.03.2021 after being referred to the hospital with mild upper respiratory system symptoms. The patient was prescribed favipiravir 2 × 400 mg and paracetamol 2 × 500 mg on 18.03.2021. Three days after this initial treatment, the patient started to complain of mild confusion and cognitive impairments.

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After a worsening of respiratory symptoms, the patient started to have frequent coughs and a chest Computerized Tomography revealed typical COVID-19 pneumonia features. Due to this exacerbation of COVID-19 symptoms, the patient was prescribed dexamethasone 8 mg once daily on 25.03.2021. After the first five days of dexamethasone, the existing neurocognitive impairments became more prominent as the patient showed slowness in everyday activities become more confused and forgetful. Despite the worsening of neurocognitive symptoms, the patient took dexamethasone for 10 days and the respiratory symptoms diminished gradually. By the end of the dexamethasone therapy, the patient became euphoric and even ecstatic, started to mention his grandiose ideas, spent a significant amount of money -mostly for charity-, became unusually talkative and became more energetic despite significantly diminished sleep. In this period, he wanted to give 200.000 Turkish Liras to one of his acquaintances, started to tell people that the government would give every citizen a mansion, tried to acquire acres of land from local authorities without paying any money. His cognitive abilities deteriorated further, and he started to forget his prayers, rules of card games, simple mathematical calculations, and he left tap water running for hours. Lastly, he left home at midnight and tried to buy a pastry shop at that very hour. These symptoms made his family very concerned, and they convinced the patient to be examined by a neurosurgeon on 05.04.2021. After an initial examination and cranial MRI investigation, the patient was prescribed Gingko Biloba and cobalamin due to mild cortical atrophy in MRI and existing neurocognitive symptoms. After this evaluation, the patient was referred to a psychiatrist. The patient's first contact with a psychiatrist occurred on 09.04.2021 and haloperidol 1 mg daily and quetiapine 25 mg on-demand were prescribed. Despite this treatment, the symptoms, disorganized behaviors, in particular, became worse and quetiapine 25 mg was rearranged to be once daily. As the clinical picture deteriorated despite the low dose of quetiapine and haloperidol treatment, his family decided to seek help from the psychiatry inpatient clinic.

By admission, the patient refused treatment, showed no insight and was explicitly agitated. He also rejected medication; therefore, he was treated in the de-escalation room with 10 mg haloperidol twice daily for 24 hours. His blood tests, including serum electrolytes, thyroid function tests and hemogram, as well as electrocardiography, revealed no remarkable abnormalities. After the first 24 hours, the patient was transferred to regular service, and the treatment was switched to olanzapine 15 mg and valproate 1000 mg. The first psychiatric evaluation revealed a euphoric mood and prominently grandiose delusions without significant cognitive impairments. The patient was fully oriented throughout the day. Therefore, the primary diagnosis was formulated as medication-induced mania rather than delirium. With the combination of antipsychotic and mood regulator medications, his agitation diminished significantly. The psychotic symptoms also gradually declined in a week, and the patient gained a complete insight into his condition.

Psychiatric anamneses revealed no prior history of psychiatric treatment or disorders. Although his relatives observed that the patient gradually became more inattentive, forgetful and emotional in the last five years, he showed no signs of functional impairment. Family history revealed Alzheimer's dementia and alcohol use disorder in the father, who was admitted to psychiatry clinic twice. His premorbid personality was described as a productive and enthusiastic man who is very charitable and altruistic. Two incidents were regarded as a psychosocial stressor; the death of his sister four months ago his brother's cancer diagnosis eight months ago. Besides these, the patient had a hectic schedule recently with many reorganizations

in home and workplace.

A neuropsychological assessment, including Wechsler Memory Scale, Stroop Test, Trail Making Test and Boston Naming Test, was also performed after 10 days of admission for differential diagnosis, and it showed that the patient had mild cognitive impairment with specific difficulties in executive functioning tasks and these impairments are mostly explained with anxiety and attention difficulties, possibly caused by underlying mild cognitive impairment.

The patient was discharged from the inpatient clinic with full remission and had no symptoms during the weekly follow-ups under olanzapine 15 mg treatment. Valproate was discontinued due to mildly elevated liver enzymes. As the current case was formulated as a secondary bipolar disorder due to organic causes, long-term treatment with a mood stabilizer was not considered a primary treatment option. The patient's written and oral consent was obtained for this case study.

### 3. Discussion

In this study, we report a 69-year-old male patient with manic symptoms associated with COVID-19 and corticosteroids, who probably suffered from mild cognitive impairment before this manic shift. The differential diagnosis of this case offers important insights into the potential association between COVID-19 and psychiatric complications. First of all, our patient suffered from mild cognitive impairments and confusion after COVID-19 and before dexamethasone treatment. This finding should be discussed with the other studies reporting various neuropsychiatric disorders associated with COVID-19.<sup>8</sup> Although mania and psychosis are relatively infrequent complications of COVID-19 infection, there are several case studies reporting such psychiatric disorders in patients with COVID-19.<sup>5,7</sup> Therefore, it may be suggested that COVID-19 may trigger some severe psychiatric conditions, especially in patients with specific risk factors. In this case, the preexisting mild cognitive impairment may be a risk factor for our patient. The second important insight from the current case is the risk of corticosteroid treatment, frequently used medications in moderate to severe COVID-19, due to neuropsychiatric complications. Several authors point out the theoretical risks of various psychiatric disorders associated with such treatments, but the current case shows that it is an actual risk, especially in specific patient groups.<sup>6</sup> The pattern of the manifestation of the mania after corticosteroid treatment, in this case, is also in line with the literature, as corticosteroids trigger manic symptoms in the acute phase and depressive symptoms in chronic use.<sup>2</sup> Another important insight from the current study is the treatment of mania associated with COVID-19 and corticosteroids. Although there are reports showing that subtherapeutic doses of olanzapine like 8.5 mg mean daily dose can also be therapeutic against corticosteroid-induced mania patients, our patient showed an adequate response only to therapeutic doses of antipsychotics and mood stabilizers, as subtherapeutic doses of haloperidol and quetiapine were ineffective in the first phases of treatment.<sup>9</sup> Therefore, we suggest using psychotropic medications in therapeutic dose ranges when an adequate response to subtherapeutic doses cannot be reached in such cases.

In summary, the current study shows a possible connection between the pathophysiology of COVID-19 and mania and the actual risks of using corticosteroids in the treatment of COVID-19 due to severe psychopathologic complications.

### 4. Learning points

- Various psychiatric symptoms, including mania and psychosis, are

frequently observed in patients with COVID-19.

- Several studies report that the use of corticosteroids in the treatment of COVID-19 is also associated with mania.
- The abovementioned case shows that COVID-19 and corticosteroids used in its treatment may cumulatively increase the risk of mania in specific patient groups.
- This case shows that clinicians should be aware of possible severe side effects of corticosteroids and a psychiatric evaluation of patients before such treatments may prevent these side effects.

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