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Post-COVID-19 Complications: A Trigger for the Onset of Depression to Treatment-Resistant Depression: A Case Report

Shokouh Gheibi[1], Omid Rezaei[2], Morvarid Ahadi[2*]

1. Razi Educational and Therapeutic Psychiatric Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
2. Psychiatry Department, Psychosis Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) has been associated with both acute and long-term complications, spanning cardiorespiratory and neuropsychiatric domains. The neuropsychiatric sequelae may stem from immune system dysregulation, inflammatory cytokines, and psychosocial stressors, including threats to personal health, economic stability, and social standing. This case report presents a 55-year-old male with no prior psychiatric history who developed treatment-resistant depression following COVID-19 infection. The study emphasizes the psychological repercussions of the pandemic, particularly in individuals with fragile premorbid personality structures.

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, continues to be a global public health challenge [1, 2]. Affecting over 229 countries [3] and resulting in more than six million confirmed deaths worldwide [4], the pandemic has significantly impacted individuals' physical and mental well-being. Beyond its physical toll, COVID-19 has exacerbated psychological distress due to fears of infection and the social and economic upheavals imposed by quarantine measures [5]. Survivors often experience a decline in health-related quality of life (HRQoL), with many reporting persistent symptoms such as fatigue, dyspnea, and psychological disturbances [8]. These stressors have led to the emergence of new psychiatric conditions among individuals with and without a prior history of mental illness [6, 7].

From a biopsychosocial perspective, the interaction between biological, psychological, and social factors appears central to the development of post-COVID psychiatric syndromes. Biologically, SARS-CoV-2 infection can activate inflammatory cascades, increase cytokine production (e.g., IL-6, TNF-α, CRP), and disrupt monoaminergic neurotransmission, all

*** Corresponding Author:**
Morvarid Ahadi
Address: *Psychiatry Department, Psychosis Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.*
E-mail: *morvaridahadi1360@gmail.com*

of which may contribute to depressive symptoms [8]. Psychologically, prolonged fear of contagion, uncertainty, and loss of control have been linked to stress-related neuroendocrine dysregulation, including HPA axis hyperactivity [9]. Social isolation, economic instability, and reduced social support further exacerbate vulnerability to mood disorders [10]. While post-COVID depression has been increasingly recognized, cases presenting with treatment-resistant depression (TRD) remain rare and clinically challenging. The following report describes a previously healthy male who developed TRD after recovering from COVID-19 and enduring extended quarantine-related stressors. His presentation underscores the complex interplay of biological inflammation, psychological burden, and social adversity that distinguishes his case from typical post-COVID depressive episodes.

Case Presentation

A 55-year-old male presented with symptoms of depressed mood, lethargy, impaired concentration, and social withdrawal that had progressively worsened over the past four years, becoming refractory to treatment in the last 7–8 months.

The patient, an employee of the environmental department and the second of three siblings, had no significant medical, seizure, or psychiatric history. Despite three failed marriages—two of which occurred years prior without lasting emotional distress—his third marriage lasted 11 years and resulted in two children, aged 9 and 13, one of whom suffers from hepatoblastoma. During the COVID-19 pandemic, the patient contracted the virus three times, requiring hospitalization on one occasion. Despite receiving one dose of the COVID-19 vaccine, he developed persistent tinnitus, diagnosed by an ENT specialist as a complication of COVID-19. Subsequent symptoms included low energy, social withdrawal, anhedonia, and suicidal ideation, with a suicide attempt reported two years prior.

Despite ongoing psychiatric care and trials of various medications, based on NICE depression guidelines, the patient demonstrated no significant clinical improvement. His colleagues noted difficulties with focus and perceived neurotic behaviors, while his spouse described him as isolated. During divorce proceedings, he was diagnosed with borderline personality disorder.

On examination, the patient reported mood instability, apathy, suicidal ideation, and intermittent auditory disturbances. He also experienced significant weight loss (11 kg in 1.5 months). A comprehensive workup, including brain MRI, urinalysis, and blood tests, identified a 2-mm pituitary adenoma with elevated prolactin levels (PRL: 6000), successfully managed with cabergoline (PRL reduced to 17). Despite this, the psychiatrist concluded that the patient's symptoms were not attributable to the adenoma.

Given the lack of response to SSRIs and SNRIs, the patient underwent three sessions of electroconvulsive therapy (ECT), resulting in marked symptom improvement, stabilization of mood, and resolution of suicidal ideation. He was subsequently discharged on bupropion, aripiprazole, lorazepam, and fluvoxamine, with continued outpatient follow-up.

Discussion

The neuropsychiatric aftermath of COVID-19 reflects a complex interplay between biological, psychological, and social determinants. Mounting evidence indicates that SARS-CoV-2 infection triggers a sustained inflammatory response characterized by elevated levels of interleukin (IL)-6, IL-10, IL-18, and tumor necrosis factor-alpha [10]. These cytokines can cross the blood–brain barrier, inducing neuroinflammation, microglial activation, and disruption of monoaminergic neurotransmission, all of which are implicated in depressive pathophysiology [11]. Additionally, dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis, secondary to chronic stress and inflammatory signaling, may contribute to altered cortisol secretion and impaired stress adaptation [12].

From a psychosocial standpoint, prolonged isolation, uncertainty, and pandemic-related grief have exacerbated depressive symptoms, particularly in individuals exposed to quarantine or significant life disruption. Reduced social connectedness and loss of daily structure have been associated with increased vulnerability to mood disorders in the post-COVID era [13].

In this case, the emergence of treatment-resistant depression following COVID-19 infection and quarantine suggests that multiple pathways—biological inflammation, psychological stress, and social deprivation—may have converged to produce a severe and persistent affective syndrome. Although the patient's pituitary adenoma and resultant hyperprolactinemia were not considered primary causes of his mood disturbance, their presence may have served as secondary modulators through dopaminergic dysregulation, further complicating the clinical picture [14].

Compared to typical cases of post-COVID depression described in recent studies, this patient exhibited a more refractory course despite standard pharmacological and neurostimulation therapies, aligning with reports of persistent "long COVID"–related neuropsychiatric syndromes [15]. This highlights the need for integrated, multidisciplinary approaches to evaluation and management, encompassing biological, psychological, and social dimensions.

Conclusion

Clinically, this case emphasizes the importance of early screening for depressive symptoms among COVID-19 survivors, particularly those with comorbid endocrine abnormalities or prolonged psychosocial stress. Recognizing inflammatory and neuroendocrine contributions may guide more tailored interventions and improve outcomes in patients with post-COVID mood disorders.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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