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First-episode psychosis requiring electroconvulsive therapy following SARS-CoV-2 infection – description of two cases

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Summary

COVID-19 is a systemic disease. Since the beginning of the pandemic, there have been increasing reports of neuropsychiatric complications of the infection. The excessive inflammatory response during the infection induces changes in neurotransmission, which can result in nonspecific manifestations of affective and psychotic disorders, among other symptoms.

We present descriptions of two cases involving previously untreated psychiatric patients, in whom the first-episode psychosis occurred immediately after SARS-CoV-2 infection. The commonality between both cases, besides the preceding SARS-CoV-2 infection, was the nonspecific and highly variable course of the psychotic disorder episode. This led to numerous diagnostic challenges and the necessity to change the diagnosis during treatment for both patients. In the case of a 58-year-old woman, persistent delusional disorders were initially diagnosed, followed by organic affective disorders. However, the evolution of symptoms ultimately led to the diagnosis of severe psychotic depression. In the case of a 68-year-old man, initially diagnosed psychotic depression turned out to be a first-episode of late-onset schizophrenia. Due to significant symptom exacerbation and evident treatment resistance, electroconvulsive therapy was implemented, resulting in complete symptomatic and functional remission.

The first-episode psychosis post-COVID-19 is a newly emerging complication of infection, increasingly reported but still poorly defined and described in the literature. It appears to exhibit significant differences from previously encountered disease entities. The described cases underscore the ongoing need to consider a history of SARS-CoV-2 infection as a precipitating factor for first-episode psychoses, as it can impact both the course of the illness and diagnostic and therapeutic decisions.

Key words: psychosis, electroconvulsive therapy, COVID-19

Introduction

The SARS-CoV-2 coronavirus emerged in the city of Wuhan, Hubei province, China, in December 2019, with the first fatal case recorded on January 11, 2020 [1]. On February 11, 2020, the World Health Organisation (WHO) designated the new coronavirus disease as COVID-19, and a month later, on March 11, when the epidemic had spread to about 114 countries, WHO declared COVID-19 a pandemic [2].

Neuropsychiatric consequences of COVID-19 infection have been observed since the early days of the pandemic [3]. The severe inflammatory response induced by SARS-CoV-2 infection is considered one of the possible mechanisms leading to affective and psychotic symptoms [4]. Infection and stress caused by SARS-CoV-2 contribute to the development of excessive inflammation, which can result in changes in neurotransmission in various areas of the brain, including the ventral striatum, hippocampus, amygdala, raphe nuclei, and locus coeruleus. This contributes to the development of psychotic, mood and anxiety disorders or exacerbates pre-existing conditions [5]. Studies suggest that immune responses, such as direct viral invasion, dysregulation of cytokine networks, and migration of peripheral immune cells, may be potential causes of neuropsychiatric complications [6].

Reports on neuropsychiatric complications during COVID-19 infection surfaced early in 2020, indicating the frequent occurrence of headaches during infection [3]. A comprehensive analysis of data conducted by Nalleballe et al. [7] on a group of 40,469 individuals showed neuropsychiatric complications in 22.5% of them. Neuropsychiatric consequences associated with COVID-19 have also been described in recovering patients. The study by Qi et al. [8] found that the most commonly reported neuropsychiatric symptoms included chronic fatigue (53.6%), anxiety and depressive symptoms (26.8%) and PTSD symptoms (12.2%).

We present two cases of patients without a psychiatric or family history, in whom psychotic disorders developed following SARS-CoV-2 infection, requiring intensive treatment with electroconvulsive therapy (ECT). Patients gave their consent for the publication of case reports. All sensitive patient data were anonymised.

Patient 1

Mrs J, a 58-year-old patient, was hospitalised three times in the local Psychiatry Department from March to November 2021. Mrs J comes from a full family and resides in a small town. At the age of 14, she moved out of her family home to study at a vocational school. She met her current husband in school. Although she briefly worked in her trained profession, she later found employment elsewhere and she has held this position for twenty years. Her current husband was her first partner and they make a good couple. They have three children and a few grandchildren. Before hospitalisation, she denied any previous episodes of depressive, hypomanic or manic episodes, denied family problems, did not abuse alcohol, and had no history of psychiatric disorders in her family.

The onset of Mrs J's symptoms was linked to a SARS-CoV-2 infection she had in November 2020, which resulted in a loss of smell. According to her daughter, the

infection was associated with a significantly elevated body temperature that persisted despite symptomatic treatment with anti-inflammatory drugs. Since then, the patient began experiencing digestive issues, believing that her constipation problems were related to the dysfunction of abdominal organs. Additionally, since December 2020, she experienced olfactory hallucinations in the form of smelling a musty odour, and a month later, she started complaining of a mood decline and reduced appetite, she decreased her daily activity and lost all interest. Caring for her grandchildren, which had previously brought her immense joy became a burden.

In March 2021, she was admitted to our department. At that time, the patient presented with delusions of reference, persecutory, catastrophic and nihilistic delusions, experiencing persistent olfactory hallucinations. Interview collected from the family confirmed the appearance of a mood decline, abulia, anhedonia, sleep disturbances, loss of appetite and weight loss secondary to productive symptoms. The course of the illness suggested COVID infection as the likely precipitating factor. During her stay, the previously prescribed outpatient pharmacotherapy was modified. Olanzapine (10 mg per day) and mirtazapine (45 mg per day) were discontinued, and risperidone was introduced up to 6 mg per day. The diagnosis of persistent delusional disorders was established. Due to the severity of symptoms and the patient's lack of cooperation in fluid and food intake due to delusional motivations, qualification for ECT was initiated, to which she consented. Six ECT sessions were performed with a bitemporal electrode arrangement using the ultrabrief pulse width technique with a maximum charge of 276 mC (pulse-width – 0.25 ms; duration – 7.8–8.0s; frequency – 80–100 Hz; current – 0.9 A). Just after the second session, mood began to stabilise; after the fourth, circadian rhythms normalised, and anxiety, apathy, abulia, and anhedonia started to subside. Delusions of reference, persecution and nihilism only diminished after mood stabilisation. Mrs J was discharged in a stabilised mental state.

After 2 months, Mrs J. was readmitted to the ward. Upon admission, she reported experiencing olfactory hallucinations, nihilistic delusions involving the belief in the disappearance of her own organs and the poisoning of the entire world, as well as delusions of guilt and punishment that recurred about 2 weeks after her discharge from the hospital, accompanied by anhedonia, abulia, anergia, and a lowered mood. Initially, she was distrustful, tense, maintained the presence of productive symptoms, and responded perfunctorily to questions. She expressed anxiety related to her health, was uncritical of the experienced productive symptoms, reported a lowered mood, alogia and reduced complex activity.

Due to the lack of effectiveness of previous antipsychotic treatment (risperidone 6 mg per day), perazine (250 mg per day) was introduced, leading to a gradual reduction of productive and affective symptoms, with complete resolution within 24 days of hospitalisation. Psychological diagnostics were deepened with MMPI-2 and SCID-II tests, revealing the presence of personality disorders, specifically an avoidant personality with dominant defence mechanisms of repression and somatisation. At that time, in our assessment, psychotic and affective symptoms were deemed secondary to defence mechanisms associated with personality disorders.

Three months after the last hospitalisation, Mrs J. was admitted to the ward for the third time. The patient admitted to dissimulating symptoms due to delusional motives. Features of endogeneity of a depressive episode emerged with intensified psychotic symptoms, pseudo-olfactory hallucinations (the perception of an unpleasant smell emanating from the body with delusional interpretation), nihilistic delusions (of the disappearance of her own organs, poisoning of the entire world), and delusions of guilt and punishment. Ultimately, a diagnosis of severe depressive episode with psychotic symptoms was established. Pharmacotherapy was modified by discontinuing perazine (600 mg per day, modified in outpatient settings) and introducing venlafaxine up to 300 mg per day, mirtazapine up to 45 mg per day, and sulpiride up to 400 mg per day. Due to the significant exacerbation of psychotic and depressive symptoms, the patient was qualified for electroconvulsive therapy (ECT) and underwent a basic series of 9 sessions with a maximum charge of 201 mC (pulse-width – 0.25 ms; duration – 6.7–7.2 s; frequency – 50–70 Hz; current – 0.9 A). The applied treatment resulted in complete symptomatic and functional remission, mood stabilisation, the return of spontaneity, hedonic capacity, complete cessation of productive activity, and normalisation of circadian rhythms. Mrs J. actively participated in sociotherapeutic activities in the ward, establishing proper relationships with other patients. Deep psychoeducation on psychopharmacotherapy and mood disorders was conducted, resulting in a complete understanding of intrapsychic processes and a high motivation to maintain the therapeutic alliance. Due to short remission periods, the patient was qualified for maintenance ECT at a rate of 1 session every 4 weeks. Metabolic changes were not observed in either physical or laboratory examinations during the entire pharmacotherapy period, and cardiovascular risk was stable. Mrs J. was discharged with a diagnosis of recurrent depressive disorder. The patient has returned to normal functioning and has been in full symptomatic and functional remission for a year and a half.

Patient 2

Mr J, a 68-year-old retired miner, was transferred to our clinic from the Surgical Department after attempting suicide by inflicting stab wounds on himself with a knife. Prior to hospitalisation, he had never received psychiatric treatment, did not abuse alcohol, and there were no known mental illnesses in his family. He lived with his wife, remained professionally active for a long time, and had always been an active person. In late 2020, he contracted COVID-19. The infection manifested with a significantly elevated body temperature, reaching 40 °C, with relatively mild shortness of breath. The general practitioner, during two home visits, did not find indications for hospitalisation as the patient maintained respiratory efficiency and oxygen saturation at 93–95%. Apart from symptomatic treatment with anti-inflammatory and antipyretic drugs, no other interventions were required. This condition persisted for 14 days, but in the second week of the illness, his behaviour gradually began to change, initially attributed by his wife to exhaustion related to the prolonged infection.

Despite the end of home quarantine, Mr J. stopped leaving the house, limited daily activity to basic hygiene, and seemed to lose all interest. His wife repeatedly encour-

aged him to meet with their children, go for a walk, or even spend time tinkering in the garage, activities that had always brought him great satisfaction before the illness. However, every attempt proved ineffective. He became reticent, apathetic, periodically stared blankly at one point, did not respond to questions, ate less, and consequently lost a significant amount of weight in a short period. The family described him as a person who had lost all will and energy to live, immersed in constant sadness, apathy, focusing mainly on internal experiences that caused significant suffering. Initially, his wife, though concerned about her husband's condition, attributed it to the aftermath of the coronavirus infection, hoping it was a temporary deterioration that would likely soon subside. She was unable to persuade her husband to seek psychiatric help. One evening, Mr J. asked his wife to prepare dinner. As soon as she left the room, he calmly went to the kitchen, took out a 20-centimetre-long knife from the drawer, and, standing in front of the mirror, stabbed himself in the abdomen. He then delivered another blow to the chest, aiming for the heart.

He was transported to a multispecialty hospital and admitted to the Surgical Department, where an emergency exploratory laparotomy of the abdominal cavity was immediately performed to save his life. Due to extensive internal bleeding from multiple splenic injuries, a splenectomy was performed, incisions in the diaphragm were sutured, pleural effusion was drained, and suction drainage was placed in the pleural and pericardial cavities.

During the almost two-week hospitalisation in the Surgical Department, he was psychiatrically consulted twice. The first time was due to consciousness disorders during delirium in the course of a somatic illness, and the second time, the consulting psychiatrist diagnosed a severe depressive episode with psychotic symptoms. The patient then admitted to hearing a voice instructing him to commit suicide as a punishment for sins committed in life. After stabilising his somatic condition, the patient was transferred to the Department of Psychiatry and Psychotherapy for further diagnostics and treatment. In the first days of hospitalisation, he mainly exhibited profoundly reduced mood and drive, flattened affect, slowed thinking, and his statements were perfunctory, almost laconic, mainly focusing on a sense of meaninglessness and lack of hope for any improvement in his condition. He expressed delusions of guilt and punishment, although delusions of reference towards the staff were already noticeable. When asked about the reasons for attempting suicide, he adopted a dissimulating attitude, confirming that he heard a voice at that time but categorically refused to answer clarifying questions about the circumstances of the event. Due to the extremely high suicide potential and symptoms strongly indicative of a severe episode of psychotic depression, sertraline up to 100 mg per day and risperidone up to 6 mg per day were included in the treatment, and qualification for ECT procedures, to which he agreed, began. During the treatment, his condition improved slightly with each session, with his mood almost constantly deeply lowered.

An in-depth, objectifying interview with the patient's wife was conducted. She admitted that Mr J. had been claiming for some time that he was constantly being spied on by foreign intelligence services, the Internal Security Agency, and even his own wife, who he believed was an undercover agent. Feeling threatened, he covered

ventilation grates, power outlets and even windows with foil, convinced that electromagnetic forces were being sent to him through radar devices. Confronted with this new information, the patient reluctantly admitted that this was the reason he withdrew from social life and stopped communicating with others, unwilling to reveal any information about himself. Furthermore, a few days before the first hospitalisation, demonic figures began to appear to him in the form of shifting, frightening masks emerging from the walls and floor. He saw the ground beneath him splitting, and he himself falling into hell. Terrifying voices of several men whispering commands and instructions, commenting on his actions in a hallucinatory dialogue, also appeared. It was these voices that instructed him to make the first knife strike, and then the second when they realised there was too little blood.

The diagnosis was verified, recognising the first-ever late-onset episode of schizophrenia with COVID-19 infection as a probable precipitating factor. Sertraline and risperidone were discontinued, and olanzapine up to 20 mg per day was introduced. Due to the continued lack of effectiveness of olanzapine in treating psychosis, a gradual transition to clozapine treatment was initiated, reaching a maximum daily dose of 200 mg. During this time, 10 ECT sessions were performed with bilateral electrode placement using ultrabrief pulse-width technique and a maximum charge of 202 mC (pulse-width – 0.25 ms; duration – 7.2–8.0 s; frequency – 60–100 Hz, current – 0.9 A). Only with this intensified approach were the first satisfactory effects achieved, and after the eighth ECT session, complete remission of psychotic symptoms was achieved – liveliness of affect returned, mood stabilised, the patient became more talkative and he began to form friendly relationships in the ward.

Due to unacceptable drooling, the dose of clozapine was reduced to 150 mg, and it was effectively corrected with atropine drops. At discharge, there were no residual symptoms of schizophrenia, including the negative dimension. Metabolic changes were not observed in either physical or laboratory examinations during the entire pharmacotherapy period, and cardiovascular risk remained stable. Mr J. has remained in full remission for 20 months and is under constant psychiatric care. He has returned to normal functioning.

Discussion

COVID-19 is primarily a respiratory system disease, but SARS-CoV-2 can also penetrate the central nervous system in many patients. The first reports emerged of patients experiencing psychotic symptoms after SARS-CoV-2 infection [9]. Ferrando et al. [4] described three cases of psychotic symptoms in COVID-19 patients without any significant respiratory symptoms. Smith et al. [10] presented a case of brief psychotic disorder in a woman who had persecutory delusions, a lowered mood and sleep disturbances, with the onset of symptoms directly related to COVID-19 infection. Rentero et al. [11] reported a series of patients with psychosis and COVID-19 infection, but details regarding symptoms and treatment were not provided. Parra et al. [12] described 10 patients presenting psychotic symptoms such as persecutory delusions,

auditory and visual hallucinations directly related to SARS-CoV-2 infection. Similar to our cases, these patients had not received psychiatric treatment before falling ill. A research team led by Benedict Michael from the University of Liverpool presented an analysis of 125 out of 153 cases submitted to the CoroNerve.com platform [13]. All patients had recovered from COVID-19, but neurological or psychiatric disorders were also diagnosed. The patients' ages ranged from 23 to 94 years, with an average of 71 years. Neurological or psychiatric disorders were diagnosed in 39 patients (31%), including 16 with psychiatric disorders related to organic causes such as encephalopathy or encephalitis, and 23 meeting the criteria for mental illness. In 10 cases, new-onset psychosis was observed, 6 had dementia and 4 exhibited affective disorders.

It is increasingly evident that patients with SARS-CoV-2 show more pronounced symptoms of depression, anxiety and post-traumatic stress disorder compared to the healthy population [14]. In a recently published case report, it was suggested that affective symptoms may be a delayed response to CNS infection by SARS-CoV-2 in patients without a history of mental illness [15].

The above reports align with our experiences. Cases of mental illnesses (whether affective or psychotic) directly associated with coronavirus infection distinctly differ in course and symptomatic presentation from their classical endogenous counterparts. In the case of the first patient described by us, numerous diagnostic challenges and the atypicality of the entire clinical picture prevented a definitive diagnosis. The onset of psychotic symptoms, such as persecutory delusions, delusions of reference, olfactory hallucinations, preceding mood decline is not typical for an episode of psychotic depression. Therefore, we inclined to a diagnosis of delusional disorders, treating depressive symptoms as secondary to psychosis. It was only during the third hospitalisation that the disease picture evolved towards psychotic depression, with features of an endogenous depressive episode. The patient expressed a wide range of nihilistic delusions related to the state of her body and the surrounding world. This finally allowed for the correct diagnosis and the initiation of intensive antidepressant pharmacotherapy, which was significantly delayed due to the highly atypical course of the illness following SARS-CoV-2 infection.

In the second case we described, we faced reverse difficulties. The patient initially presented classic symptoms of psychotic depression, meaning during the symptomatic COVID-19 infection, there was a mood decline, sadness, reduced activity, social isolation, slowed thinking and speech, as well as depressive delusions of guilt and punishment. Only during therapy did he reveal an underlying delusional system typical of schizophrenic psychosis. Thus, in this case, we speculate that the coronavirus infection was the triggering factor for the first episode of late-onset paranoid schizophrenia, which is itself a rather rare phenomenon.

Psychotic disorders after COVID-19 infection are a new and increasingly diagnosed phenomenon. The described cases emphasise the need for high vigilance and precision in searching for the triggering factor in the emergence of mental disorders, as well as further research to understand the neuropsychiatric aetiology of psychosis after SARS-CoV-2 infection.

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