

CASE REPORTS

PRIKAZI SLUČAJEVA

University of Novi Sad, Faculty of Medicine Novi Sad¹
Clinical Center of Vojvodina, Psychiatry Clinic, Novi Sad²
General Hospital Vrbas, Psychiatry Department, Vrbas³

Case report
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UNDERSTANDING THE STATE OF CONFUSION IN PATIENTS WITH PSYCHOSIS DURING COVID-2019 PANDEMIC – A REPORT OF TWO CASES

KAKO RAZUMETI KONFUZNO STANJE KOD PACIJENTA SA PSIHOZOM U VREME PANDEMIJE COVID-19 – PRIKAZ DVA SLUČAJA

Mina CVJETKOVIĆ BOŠNJAK^{1,2}, Željko BIBIĆ³, Aleksandra NEDIĆ^{1,2}, Olga ŽIVANOVIĆ^{1,2}, Vesna VASIĆ² and Dušan KUJANČIĆ²

Summary

Introduction. There is a lot of evidence that coronavirus disease 2019 has various manifestations. This paper presents a report of two cases with the aim to indicate the multifactorial etiology of confusional states in patients with mental disorders at the time coronavirus disease 2019 pandemic. The severe acute respiratory syndrome coronavirus-2 affects not only the respiratory and cardiovascular systems, but also the brain, kidneys and other organ systems. One of the first manifestations of this infection can be mental confusion. **Case Study.** The first patient, a woman diagnosed with schizoaffective psychosis, suddenly presented with confusion, followed by hypersedation which was at first attributed to overmedication. In another patient, with the diagnosis of bipolar affective disorder, sudden confusion (delirium) was initially recognized as an element of mental disorder deterioration. A more detailed observation revealed that the confused state in both patients was caused by severe acute respiratory syndrome coronavirus-2 infection. **Discussion.** It is common for the manifestations of severe acute respiratory syndrome coronavirus-2 infection to include respiratory and cardiovascular symptoms. However, symptoms related to other organs and organ systems, including changes in neurological and psychological status, should not be ignored. **Conclusion.** It was noticed that confusion and delirium-like states are quite common early symptoms of coronavirus disease 2019. In psychiatric patients, it is always necessary to rule out the organic etiology of the consciousness disorder and immediately proceed with the diagnostic procedures. One should certainly keep in mind that diagnostic errors are possible, not only due to various manifestations of the infection, but also due to the stigmatization of mental illness, which must be overcome in order to provide the best possible treatment effects.

Key words: Psychotic Disorders; Confusion; Delirium; COVID-19; Pandemics; Signs and Symptoms

Sažetak

Uvod. Postoji mnogo dokaza da infekcija virusom korona ima različite manifestacije. U radu su predstavljene studije dva slučaja kako bi se ukazalo na multifaktorsku etiologiju konfuznih stanja kod pacijenata sa mentalnim poremećajima u vreme infekcije. Virus SARS-CoV-2 utiče ne samo na respiratorni i kardiovaskularni sistem, već aficira i mozak, bubrege i druge organske sisteme. Jedna od prvih manifestacija ove infekcije može biti konfuzno stanje svesti. **Prikaz slučaja.** Prva pacijentkinja se lečila zbog shizoafektivne psihoze. Kod nje se iznenada ispoljila konfuznost, praćena hipersedacijom, što je u prvi mah delovalo kao intoksikacija psihofarmacima. Kod pacijenta sa dijagnozom bipolarnog afektivnog poremećaja, konfuzno-delirantna klinička slika je u prvi mah prepoznata kao element pogoršanja mentalnog poremećaja. Detaljnijom opservacijom utvrđeno je da je konfuzno stanje kod oba pacijenta uzrokovano infekcijom SARS-CoV-2. **Diskusija.** Uobičajeno je da manifestacije infekcije SARS-Cov-2 obuhvataju simptome respiratornih i kardiovaskularnih organa. Međutim, ne treba zanemariti simptome koji se odnose na druge organe i organske sisteme, između ostalih i promene u neurološkom i psihičkom statusu. **Zaključak.** Konfuzno-delirantna stanja svesti neretko su rani simptomi COVID-19. Kod psihijatrijskih pacijenata uvek je neophodno isključiti organsku etiologiju poremećaja svesti te odmah pristupiti potrebnim dijagnostičkim procedurama. Svakako treba imati u vidu da su dijagnostičke greške moguće, ne samo zbog različitih manifestacija infekcije, već i zbog stigmatizacije mentalnih bolesti, koju je neophodno prevazići radi najboljeg mogućeg efekta lečenja.

Glavne reči: psihoze; konfuzija; delirijum; COVID-19; pandemija; znaci i simptomi

Abbreviations

COVID-19	– coronavirus disease 2019
SARS-CoV-2	– severe acute respiratory syndrome coronavirus-2
PCR	– polymerase chain reaction
CT	– computed tomography

Introduction

Infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a major health problem for the World Health Organization nowadays. For nearly two years, the whole world has been fighting a battle against COVID-19 infection. Health workers in primary, secondary and tertiary health care institutions, have learned a lot about clinical features of COVID-19 and a lot of information has been published worldwide [1–3]. All the medical staff has become familiar with COVID-19 symptoms, diagnosis and treatment options [4–7]. However, it is interesting that one common symptom, mental confusion, is underestimated and sometimes hard to recognize, especially in psychiatric patients who were previously psychotic and then were infected with SARS-CoV-2 [7–13]. Although almost 30% of patients with moderate to severe SARS-CoV-2 infection develop psychiatric symptoms, including confusion, agitation, auditory hallucinations and speech dysfunction, there still persists the diagnostic problem of these symptoms in psychiatric patients [14–16]. Nevertheless, psychiatric patients with COVID-19 infection belong to a vulnerable category and there is a diagnostic dilemma about the etiology of confusion. Presently, there is limited source of literature discussing the possible pathophysiology and risk factors for developing confusion in COVID-19 [16–20]. In psychiatric patients, medical professionals need to identify if confusion is a manifestation of psychiatric exacerbation, a result of psychotropic overmedication, or it is a result of SARS-CoV-2 infection. Here, we present two patients with psychosis and SARS-CoV-2 infection. In both patients the leading symptom of COVID-19 infection was mental confusion.

Case 1

We present a 57-year-old female patient (N. M.), divorced, lives alone, has a 16-year-old daughter who lives with the patient's former husband. The patient has a long psychiatric history. Thirty years ago, her disorder started as a generalized anxiety disorder. Later on, depressive episodes appeared, followed by a few suicidal attempts by medication overdose.

Several years ago, the clinical picture deteriorated with psychotic elements and the patient was treated in a psychiatric hospital several times.

On admission, she was confused, presenting with auditory hallucinations, hypomanic and depressive symptoms. Due to such symptoms, the diagnosis was changed to schizoaffective disorder. The patient showed non-compliance and spent a few months in the hospital, whereas the symptoms gradually improved. Satisfying remission with a limited

functionality has been accomplished and the patient was discharged with a therapy including lithium, antipsychotics and benzodiazepine.

Several days later, the patient visited an emergency psychiatric clinic. She was pale, and presented with somnolence, weakness, bradypsychia, confusion, and dehydration. The rapid antigen test for SARS-CoV-2 was negative. An intoxication with psychiatric medications was suspected and the patient was admitted to the Psychiatry Clinic. A biochemistry test showed that lithium levels were within therapeutic range, but inflammatory markers were elevated, C-reactive protein was 79.9 mg/L, D-dimer was 10 mg/l, erythrocyte sedimentation rate was 102, while the white blood cells count was normal. The urine test result was normal. Ultrasound of the abdomen and urinary tract was unremarkable. Internal medicine specialist suggested a computed tomography (CT) of the abdomen. The abdominal CT showed ground glass opacity like changes in the basal pulmonary parts. Antibiotic therapy was initiated. Polymerase chain reaction (PCR) test for SARS-CoV-2 was done and the result showed that our patient had SARS-CoV-2 infection.

The patient was transferred to the Clinic for Infectious Diseases. Her general condition was good, oxygen saturation in room air was 98% all the time, she did not have fever, and soon after beginning the therapy with two antibiotics (ciprofloxacin and erythromycin) she was feeling well and inflammatory markers were not out of range. Ten days after the admission, the PCR was negative, and she was transferred back to the psychiatry unit. She became conscious, coherent, without psychotic symptoms, though she felt fatigue for some time. Lithium was started again, as part of her therapeutic regimen, as well as other psychopharmaceuticals and the patient was discharged in psychiatric remission.

Case 2

A 62-year-old male patient (M. M.), married, with bipolar affective disorder, received psychiatric treatment for more than 20 years. Over two years, he was in complete remission, taking psychiatric medications all the time (valproate 1000 mg/day, lithium carbonate 600 mg/day and clonazepam 0.5 mg/day). The patient presented with comorbidities, including hypertension and benign prostate hypertrophy under medical control.

The symptoms occurred suddenly, after several sleepless nights. One night the patient developed psychomotor agitation and confusion (he did not recognize his wife and his home), became incoherent, with optic and auditory hallucinations. He was taken to the hospital, where a brain CT was done, followed by wide spectrum of blood tests. The rapid antigen test for SARS-CoV-2 was negative, as well as the PCR test. There was a diagnostic dilemma, if this was a new psychotic episode, since in the past he presented with fully disorganized behavior symptoms. On the other hand, organic etiology could not be excluded. The patient was observed and his labo-

ratory test results showed very high levels of C-reactive protein - 335 mg/L, D-dimer of almost 8 mg/L, and leukopenia - $2,5 \times 10^9/l$. The PCR for COVID-19 was repeated and this time the PCR test was positive. The CT scan of thorax showed initial pneumonia in both basic segments of the lungs. Due to the protocol for treating COVID-19 infections, all necessary medications were initiated together with antipsychotics and benzodiazepins to treat his acute delirious state. Lithium was excluded and valproate dose was reduced. After three days of therapy, his mental confusion resolved, and in the following period the patient had no psychiatric symptoms. During hospitalization, the patient was in psychiatric remission. After three weeks, the patient was negative for SARS-CoV-2 on two PCR tests, and all blood parameters were normal. The pneumonia was in regression, and patient was discharged. In the next few weeks, he completely recovered, without symptoms of mental disorder.

Discussion

Confusion was the leading symptom of COVID-19 infection in the presented cases. During the first few days, other symptoms were mild or absent. The first SARS-CoV-2 rapid antigen SARS-CoV-2 tests were negative in both patients, but followed by positive PCR tests. Infection was suspected due to elevated inflammatory parameters and ground-glass opacity changes seen on thorax CT scans.

The very beginning of symptoms could have been attributed to psychotic relapse or overdose of psychiatric medications (which was not the first episode of these symptoms in neither of these patients). It has been noticed that both the confusion and delirium-like state are quite common early symptoms of COVID-19 disease [1, 2, 4–6]. In fact, these symptoms are among the six most common symptoms of SARS-CoV-2 infection [7–12, 17–20]. According to the present literature, the evidence of acute confusional state is found in about 15 - 35% during the acute phase of COVID-19 infection [8, 21–23]. Pathophysiology of such state is

usually multifactorial. Almost 30% of such patients have hypoxemia, [6, 8, 24], older patients frequently have various comorbidities, including dementia and psychiatric illness [4, 7, 14, 15]. Also, therapy with glucocorticoids, part of the therapy protocol for COVID-19 infection may also exacerbate inflammation-associated neural damage [8, 23, 24]. In patients who need sedation, confusion or fluctuating alertness, with delayed awakening after stopping sedation was described [6, 14, 17]. These two cases were presented in order to refresh the knowledge of medical professionals and to remind that confusion and delirious states, due to stigmatization and overgeneralization, can be easily attributed to psychiatric manifestations only. Medical professionals must keep in mind that COVID-19 has many clinical forms and manifestations [7–11]. Also, patients with comorbidities, including psychiatric illness, are at greater risk for confusion and delirious symptoms [8, 12–15]. It is very important to bear in mind that, when de novo confusion appears in psychiatric patients, physicians should consider COVID-19 as a possible cause of such symptoms as well as other possible medical causes [8, 9, 12, 13].

Conclusion

It is certain that misdiagnosed coronavirus disease 2019, presenting with delirium, may only cause failure to start adequate therapy in timely manner. Confusion, as a symptom of coronavirus disease 2019, affects usually older people, without fever and other symptoms of infection, but it can also happen to young people, particularly with comorbidities, including psychiatric disorders. In clinical practice, misdiagnosis of confusion as the main symptom of severe acute respiratory syndrome coronavirus-2 infection is a serious problem. This happens because the family members as well as medical staff do not recognize confusion as an important symptom, or attribute it to the psychiatric disease, which is, in many cases, due to the stigmatization of mental illness. Thus, in patients with mental problems, the focus should be on the physical etiology of these symptoms.

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