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Catatonic syndrome during COVID-19 – a case study

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Summary

Catatonia is a neuropsychiatric condition involving qualitative psychomotor and volitional disorders. As a nosological unit, it is included in the international classifications of diseases – ICD-10 and DSM-5, but diagnostic criteria vary greatly between these classifications. COVID-19 is an infectious disease that primarily affects the respiratory system, sometimes other organs as well. There are individual reports of COVID-19 coexisting with catatonia in the literature. This case involves a young man who has been hospitalized with symptoms of acute psychotic disorder. During diagnosis, SARS-CoV-2 was diagnosed and full-symptomatic catatonia developed. The etiology of these disorders remains unclear to this day. The treatment, however, was highly complicated due to the need to administer benzodiazepines in large doses, which act depressingly on the respiratory system and thus may worsen the process of COVID-19. This case gives rise to a discourse on the classification of catatonic syndrome, the possible causes of its occurrence in this patient and the correct and safe treatment.

Key words: COVID-19, catatonia

Introduction

Catatonia is defined as a neuropsychiatric condition comprising qualitative psychomotor and volitional disorders, which include stereotypies, mannerisms, automatic obedience, echopraxis, negativism, impulsive actions, automatisms. [1, 2]. In psychopathology, the term *catatonic syndrome* is used much more frequently, as it reflects the number of symptoms that can occur in the course of catatonia. Catatonic syndrome consists of all of the above-mentioned symptoms, in addition to stupor (in a hypokinetic form) or motor excitation (in a hyperkinetic form). Delusions (mainly of an oneiric nature) and hallucinations with different content also occur frequently. Importantly, in this state, the facial expression and pantomimicry can express different emotions as an expression of the events the patients experience [3]. So far, the mechanisms that

are responsible for this state of affairs have not been fully understood [4], and the incidence of catatonia depends to a large extent on chosen criteria [5].

Catatonia has been included in international classifications of diseases – ICD-10, DSM-5 [6, 7]. An analysis of the current classification in Poland – ICD-10 – indicates the presence of catatonia in two diagnoses – organic catatonic disorder and catatonic schizophrenia [6]. This approach refers to the traditional characteristics of catatonia from the nineteenth century, when its symptoms were described by Kahlbaum, according to which catatonia could only be diagnosed as a subtype of schizophrenia. [8]. Much more broadly, the concept of catatonia is defined in DSM-5, where catatonic syndrome can be diagnosed in many other clinical situations [7, 9]. According to Tandon et al. [9], the correct diagnosis of catatonia together with its cause is extremely important in the subsequent treatment of patients. The authors of this article also point out that catatonia is a certain condition that may accompany a wider nosological unit, but does not have to be present all the time [9]. Among the diagnostic criteria for catatonic disorders, one can find common elements in both classifications. It is worth emphasizing, however, that in ICD-10 there are no important symptoms such as echophenomena, mannerisms, stereotypies, or grimaces [5–7].

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. So far, more than 260 million people have contracted the disease worldwide and more than 5.2 million have died [10]. In addition to the typical symptoms of COVID-19 infection such as fever, cough, loss of smell and taste, other symptoms can be found in the literature. These include arrhythmias, diarrhea and nausea, conjunctivitis, and various skin lesions. Among neurological symptoms, anosmia and ageusia dominate [11]. There are isolated reports of co-occurrence of catatonic syndrome with SARS-CoV-2 infection [12–23]. This is the case described by the authors. Its careful analysis indicates potential causes of catatonic syndrome and therapeutic options.

Case study

Data of the described person have been anonymized, details not relevant to the presentation of the case and which may allow identification of the patient have been omitted.

A 22-year-old psychiatric-naïve patient with no somatic disorders (he did not take any medications on a permanent basis) was brought to the hospital by the Medical Emergency Team because of agitation, active aggression towards family, disorganized thinking and behavior. In the conditions of the Hospital Emergency Department, he showed aggressive behavior towards medical personnel. Due to a sudden deterioration in mental health, a CT scan of the head was performed which did not show abnormalities. In chest CT, a number of lesions have been found which are likely to correspond to a viral infection. A urine drug screening test was also performed on-site, but all tested substances were negative. RealTime PCR test for SARS-CoV-2 infection was positive.

Due to the presented symptoms and positive test result, the patient was transferred to the department of psychiatry for patients with COVID-19.

At the time of admission to the ward, contact with the patient was difficult, he did not answer any questions, distractions of thinking were observed. He had an extremely labile mood – from crying to ecstasy, considerable psychomotor arousal and an unadjusted, stiff affect. He presented bizarre and disorganized behavior and was actively psychotic. Spontaneously, he uttered delusions of religious and grandiose content, behaving aggressively towards medical personnel.

During hospitalization, ambivalence, ambitendency, increased psychomotor drive, mannerisms, inadequate, bizarre utterances (including unarticulated sounds), and pale affect were observed. Due to the significant excitation and rapid destruction of the surrounding objects, the use of direct coercion (use of restraining belts) in accordance to Article 18 of the Polish Mental Health Protection Act was required [24]. 1 ampoule (50 mg) of zuclopenthixol acetate was administered resulting in relative sedation. From the beginning of the hospitalization, there were periods of remission in which a reasonably consistent contact could be made with the patient, but this was accompanied by numerous thought slides. Olanzapine was used as an antipsychotic treatment. Due to the unfolding symptoms of COVID-19 infection, the benzodiazepine group has been discontinued. During this period, passive oxygen therapy, treatment of lower respiratory tract infections in the form of antibiotic and steroid therapy, was introduced.

In the following days, a fundamental change in the patient's condition with developing elements of catatonic syndrome was observed, which included withdrawal, vision fixation at one point, mutism, waxy flexibility, periodic apparently pointless agitation with obtuse positions, airbag symptom, periodic complete lack of response to pain stimuli. During this time, the patient was assessed on the *Bush-Francis Catatonia Rating Scale* (BFCRS). It assesses 23 symptoms of catatonia, with the first 14 being the *Bush-Francis Catatonia Screening Instrument* (BFCSI). The form is completely filled out by the doctor, evaluating each symptom for which he can assign from 0 to 3 points, where 0 is the absence of a given symptom and 3 is the highest level of pathology in the tested range [25, 26]. The patient scored 53 points in the BFCRS and 36 in the BFCSI, confirming the clinical diagnosis.

In the following days, gradual resolution of symptoms of COVID-19 was observed. The treatment of catatonic syndrome in the form of 10 mg lorazepam intramuscularly in divided doses was implemented, obtaining a decrease in muscle spasticity and gradual increase in activity. Due to the persistent psychosis, aripiprazole has been introduced into the pharmacotherapy. Symptom variability was observed in circadian rhythms, with alternating periods of total non-contact with marked increases in muscle tone, and echolalia, coprolalia, active aggression against others, risky behaviors such as attempts of jumping from bed on the head, or of suffocation by a nylon bag. In the psychological examination, the patient was disoriented about time and place, self-orientation was incomplete, affect was stiff, mimic scant, mood was labile, inadequate to the situation.

He claimed that he had schizophrenia because he had long suspected it in himself, but was unable to substantiate his belief.

According to the patient's wishes, he was discharged in the 20th day of hospitalization to continue treatment in a psychiatric hospital of his and his family's choice. In connection with the preparation of this case report, as well as out of scientific cognitive curiosity, the center provided by the family was twice requested to provide information on the patient's further fate. Unfortunately, the authors did not receive any answer on this matter.

Objective anamnesis

The patient's mother contacted the psychiatric ward doctors by phone. In the first interview, she revealed that the patient had been fever-stricken four days before hospitalization, but the day before, his behavior was disturbing – he walked naked around the apartment claiming to be a parish priest and to carry out a mission related to the black race. During the night, he did not sleep, he did not recognize family members, and he was aggressive. The mother categorically ruled out the patient taking any psychoactive drugs, as he was not to leave the house for several days. The patient's grandmother had schizophrenia.

A week later, the mother reported that the patient had been recently (unable to give an exact date) "at a party" where he "consumed alcohol like everyone else, maybe some marijuana". She stated that he had returned home with a fever and was therefore using paracetamol. An empty box of this medicine has been found on his desk, but it is not known how much he took of the medicine.

Somatic state

On the day of admission to the psychiatric ward, the basic laboratory tests were performed, which revealed significant deviations from the standards for alanine aminotransferase (ALAT), aspartate aminotransferase (ASPAT), C-reactive protein (CRP), as summarized in Table 1. On the same day, in the evening, the patient had a fever of up to 41°C, arterial blood saturation (SpO₂) dropped to 92% – it was decided to implement appropriate treatment, passive oxygen therapy and cold compresses, obtaining a balance of parameters.

On the 7th day of hospitalization, the patient's fever was up to 40°C, and increased levels of ALAT and ASPAT were observed in laboratory tests (Tab. 1). It was decided to carry out imaging tests. No major pathologies were seen in the head CT scan, abdominal and pelvic CT scans showed features of generalized hepatic steatosis and no pathology. In the chest CT scan, ground-glass changes and perihilar inflammatory densities of consolidation type were observed – suspicion of aspiration pneumonia was raised and, after internist consultation, the antibiotic therapy used so far was modified.

On the 13th day of hospitalization, a significant increase in the monitored parameters was observed in laboratory tests – among others ALAT, ASPAT, creatine kinase (CK) (Tab.1). It was therefore decided, after consultation with a specialist in infectious diseases, that further tests should be carried out to rule out hepatitis A, B, C and Wilson's disease, but their results were within the normal range.

Parameter	Day of hospitalization						
	Day 1	Day 5	Day 7	Day 8	Day 13	Day 15	Day 18
ALAT [U/L]	200	716	836	700	2004	2067	1907
ASPAT [U/L]	233	307	304	177	620	420	439
GGTP [U/L]	61	145	168	167	205	239	-
CK [U/L]	965	553	408	827	1058	407	1104
CRP [mg/L]	51.3	9.30	3.30	2.30	3.20	2.10	2.10

Table 1. Presentation of selected patient laboratory test results during hospitalization

 $ALAT-alanine\ aminotransferase;\ ASPAT-aspartate\ aminotransferase;\ GGTP-gamma-glutamyl\ transpeptidase;\ CK-creatine\ kinase;\ CRP-C-reactive\ protein.$

Discussion

In this case, several reasons may be identified that have contributed to the patient's health status.

In the first place, we should consider COVID-19. The literature managed to find 12 items describing the co-occurrence of infection with SARS-CoV-2 virus and catatonic syndrome [12–23]. Nevertheless, most describe people over 40 years of age [12, 13, 15–19, 21–23] with a history of psychiatric hospitalizations, most often with a previously diagnosed mental illness or intellectual disability [13, 17–19, 21, 22]. One paper was found describing two cases of teenagers in Asia who experienced symptoms of catatonic syndrome with positive COVID-19 test results. The first case concerns a 12-year-old boy who was born with a perinatal encephalopathy diagnosis and was treated psychiatrically and neurologically mainly because of its consequences. However, the coexistence of COVID-19 catatonia in this case should be questioned, as the child presented only positive IgG COVID-19 antibodies without any symptoms of infection. The second case concerned a 17-year-old man without any disease. Positive symptoms had been developing since May 2020, and the patient was admitted to the hospital in January 2021 year. Symptoms of catatonic syndrome developed during this hospitalization. The authors, however, disregard the need to treat the patient with benzodiazepine drugs and have not evaluated the symptoms at any scale that would confirm catatonia [20].

The first described case concerns a 43-year-old psychiatric-naïve man who was first diagnosed with COVID-19 infection by a polymerase chain reaction test (PCR)

and developed symptoms of catatonic syndrome with associated auditory hallucinations on day 3 of hospital stay. Patients had low inflammatory and transaminase parameters at admission. However, these results were not repeated later and the patient recovered from catatonia with 4 mg lorazepam daily [12]. Analysis of this and other cases [12–19, 21–23] suggests that the catatonic condition may have been caused by SARS-CoV-2 infection.

It is worth considering other potential causes. Undoubtedly, such a young age of the patient could indicate the first episode of catatonic schizophrenia, and the symptoms fit into the diagnostic criteria of this unit in ICD-10 [6]. The health deterioration and high fever may have been due to neuroleptic malignant syndrome after the administration of zuclopenthixol. Due to the lack of data on the fate of the patient, it is difficult for the authors to take a final position on the correct diagnosis.

When considering the potential causes of these symptoms, it is also necessary to analyze objective anamnesis, which has proven to be inconclusive. It was only known that an empty paracetamol box was found on the patient's desk, which may indicate that the patient's well-being had been impaired before he went to the hospital. Isolated cases of catatonic syndrome have been reported in the literature from the use of a wide range of substances including acetaminophen overdose [27, 28]. The available publications on the toxicity of paracetamol focus primarily on liver damage. Biochemical parameters (ALAT, ASPAT) that may indicate actual liver damage increased significantly only on the fifth (ALAT) and thirteenth (ASPAT) day of hospitalization, which, in the light of the available literature, reduces the probability of actual acetaminophen poisoning, because the highest concentration of the tested parameters should occur between 72 and 96 hours from the consumption of a toxic dose, while up to a maximum of 14 days from that moment it should normalize, which was not the case in the described patient (Tab. 1) [29]. It should be noted here that the deviations from the norms in laboratory tests are generally not specific to any of the discussed causes of symptoms in the patient. Due to the above and the negative result of the urine screening test for psychoactive substances, it was reasonable to exclude catatonia as a complication after taking them.

The presented case also prompts reflection on the coexistence of catatonia and delirium. There is a lot of inconsistent information on this subject in the literature, and the DSM-5 classification does not fully solve this problem. In this context, this classification allows for the diagnosis of catatonia as "Catatonia associated with another mental disorder" and "Undefined catatonia" in co-occurring delirium, while excluding the possibility of "Catatonic disorder due to another medical condition" along with delirium [7, 30].

The course of the disease should also be considered. It is puzzling what could have caused such dynamic changes in the patient – differentiating between catatonic schizophrenia, COVID-19 and potential paracetamol poisoning and/or other psychoactive substances. Of course, the coexistence of these entities must be taken into account. In most of the described similar cases, most of the laboratory test data were omitted [13–15, 18–21, 23], while the ones that were made do not deviate from the normal

range as in the described patient [12, 16]. High levels of transaminases in peripheral blood may be attempted to explain by potential paracetamol poisoning, which, however, is relatively unlikely as shown above. When considering the influence of drugs on the patient's somatic state, it should be noted that he was not undergoing chronic treatment prior to hospitalization. However, during the stay in the Psychiatric Ward, apart from the aforementioned psychotropic treatment, ceftriaxone, amoxicillin with clavulanic acid, metronidazole, dexamethasone, enoxaparin, pantoprazole, timonacic, metamizole, probiotics, and fluid therapy were used in accordance with the recommendations of other specialists. However, taking into account that the patient's condition gradually improved during hospitalization, it is reasonable to assume that these drugs neither worsened nor caused catatonic syndrome. It cannot be ruled out that the entire course of the disease was caused by COVID-19 infection, because patients infected with SARS-CoV-2 are characterized by high levels of biochemical parameters such as ALAT, ASPAT, lactate dehydrogenase (LDH), CK, CRP, creatinine, or troponins [31–33]. According to a study analyzing individual cases of COVID-19 patients, the above parameters may reach values much higher than those of the described patient [34].

The last important aspect is the treatment of a patient with COVID-19 and catatonic syndrome. The latter unit is usually treated with high doses of benzodiazepines such as lorazepam daily up to 16 mg, another effective method is electroconvulsive therapy [35], which could not be used in this case due to its limited availability. A safety study of the benzodiazepine class of medicines in patients with various lung diseases has shown that low doses of these medicines do not put their lives at risk. However, the use of high doses of benzodiazepines – that is, those used to treat catatonia – was completely different and resulted in a significant increase in mortality in the study group [36]. For this reason, a careful dosing of lorazepam under saturation control was required with constant respiratory assessment.

Recapitulation

The analysis of the presented case leads to consideration of the nature of catatonia and its proper placement in international classifications of diseases. It is worth mentioning that the current ICD-10 classification does not exhaust all aspects and symptoms of catatonia [6]. Its association with schizophrenia seems to be outdated, and failure to meet all the diagnostic criteria for catatonic schizophrenia precludes a diagnosis of catatonic syndrome with associated psychotic symptoms. In contrast, the diagnosis of organic catatonic disorders indicates their secondary nature to primary brain dysfunction or other somatic disorders. Taking into account the overall symptoms of the presented patient, it seems that undifferentiated schizophrenia is the most sensible diagnosis, which, however, does not solve the problem of the localization of catatonic syndrome in international classifications of diseases discussed in this article.

It is worth remembering that the course of COVID-19 infection can be varied. Although the disease is sparse in most populations, apart from respiratory failure it can

also cause a number of other symptoms – including catatonic syndrome and failure of many different organs, including the liver with very high transaminase levels.

In view of the ongoing COVID-19 pandemic, the treatment of COVID-19 patients with the coexisting catatonic syndrome is of great importance. In addition to standard COVID-19 therapy, benzodiazepine preparations should be considered under close monitoring of vital signs according to the available literature. It seems that the doses of the administered medicines should to be slightly lower than those used in catatonia without SARS-CoV-2 infection due to an increased risk of respiratory failure. Another way is electroconvulsive therapy, which seems to be a safer alternative to benzodiazepines. However, it is necessary to remember the limitations of this method – the safety of anesthesia in the presence of symptoms of COVID-19, which should be assessed by an anesthetist before the procedure, the availability of an electric shock apparatus, and finally the infectivity of the patient and the need for thorough disinfection of the apparatus and the room in which it is located after each procedure on the patient infected with SARS CoV-2 virus.

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