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Clinical Aspects of Comorbidity of Coronovirus Infection and Paranoid Schizophrenia

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Abstract - On the example of 65 patients with paranoid schizophrenia, the effect of coronavirus infection on this group of patients was studied. It has been established that coronavirus infection can manifest itself in patients with paranoid schizophrenia in the form of transient psychoses, which are represented by schizophrenic symptoms, as well as clinical manifestations of confusion syndromes. An assumption was made about the possibility of coronavirus infection to influence different links of pathogenesis, during the formation of psychotic disorders in this group of patients.

Key words: coronavirus infection; schizophrenia; Covid-19; SARS-CoV-2; psychosis

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Introduction

Coronavirus infection is currently one of the most important global health problems. This pathology is characterized by clinical polymorphism, including due to the ability to influence the central nervous system [1-5]. Such manifestations go beyond the classical exogenous mental disorders described by K. Bonhoeffer and confirmed the results of long-term observations of this group of patients [6]. Traditionally, children, the elderly and those suffering from chronic diseases are at risk groups for infection and the development of clinical complications. The latter include patients with paranoid schizophrenia, who remain one of the most common nosological forms in psychiatry [7,8]. Such patients in themselves seem to be a difficult task in terms of diagnosis and treatment, and the addition of coronavirus infection naturally complicates the management of such patients, causing the relevance of this study. The purpose of this research was to study the clinical features of the course of coronavirus infection in patients with paranoid schizophrenia.

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Subjects and Methods

In total, for the period from April 2020 to January 2021, 65 patients with paranoid schizophrenia who fell ill with coronavirus infection and who were observed in the interdistrict center of medical rehabilitation (ICMR) and the multidisciplinary medical center "Profimed" in St. Petersburg were studied by a continuous method. The study was based on both cases personally observed by the author of the article, carried out within the framework of external counseling, and assessed retrospectively, according to the surveyed persons, their relatives, and a survey of medical workers, confirmed by medical documentation. Consent to participate in the study was confirmed either by the subjects themselves or by their legal representatives in writing also, consent was obtained to conduct this

study from the ethical committee of the outpatient-polyclinic association of St. Petersburg, the structural unit of which was the MCMR. All subjects were men and women aged 25 to 45 years. The average age of the subjects was 35.4 ± 4.3 years. The choice of the age period for the study was due to the desire to exclude age-related mental changes, which could complicate the assessment of comorbid relationships of schizophrenic and the infectious process. The average duration of a processual illness was 14.2 ± 3.6 years. The type of the course of the schizophrenic process is continuous-progressive. Inclusion criteria are: 1) compliance of the diagnosis of paranoid schizophrenia with the criteria of the ICD-10 revision (F20.0); 2) the state of medication remission of schizophrenia itself, with signs of an increasing procedural personality defect; 3) a positive laboratory test result for the presence of SARS-CoV-2 RNA by immunochromatographic analysis, regardless of clinical manifestations. The exclusion criteria were: 1) psychotic level of disorders prior to the moment of inclusion in the study; 2) clinical signs of coronavirus infection, not confirmed by laboratory and instrumental data. The article uses the terminology inherent in the domestic (Russian) school of psychiatry. By remission was meant "the weakening and mitigation of all symptoms, providing, to one degree or another, the social and labor adaptation of the patient, and embracing a wide range of conditions from those bordering on practical recovery to those in which the symptoms of a defect already clearly appear" [9].

Schizophrenic defect or, in the modern interpretation, neurocognitive procedural changes, was understood as "the consequences of a mental illness that occur in conditions of a complete stop of the process, lead to persistent (and not progressive) loss or dissociation of mental functions with personality changes and are accompanied by a decrease in its functioning" [9]. The definition of "non-suicidal autoaggressive actions,"included a variety of actions directed against one's health and accompanied by a violation of the integrity (functions) of organs or organ systems. At the same time, there was no demonstration of intent to commit suicide [10].

The main research method was clinical observation, the results of which were formulated in accordance with

the national recommendations adopted in the Russian Federation and the criteria set out in the international classification of diseases 10 revision.

Results

Clinical and diagnostic assessment of the coronavirus infection itself was carried out in accordance with the guidelines for the management of such patients operating on the territory of the Russian Federation [11]. The basic clinical characteristics of the schizophrenic defect corresponded to the concepts that were introduced into practical work by E. Kraepelin, and which were developed in scientific works of other authors [12]. It was about intellectual disabilities, designated by K. Conrad as a phenomenon of "decrease in energy potential", accompanied by changes in the personality structure and behavioral disorders [13].

Patients showed a decrease in the ability to purposeful stimulating activity, a decrease in tolerance to physical and mental stress; Narrowing of the range of interests, emotional coldness and unmotivated aggression, especially towards close relatives. Depletion of expressiveness in facial expressions and movements, silence, inactivity, slowness, refusal to observe the rules of hygiene, decrease in working capacity. Low adaptive abilities led to the implementation and subsequent consolidation of non-suicidal auto-aggressive behavior Self-harm was inflicted in the form of superficial cuts in the forearms, inner thigh, and lower leg. All subjects took antipsychotics (olanzapine, risperidone, haloperidol, paliperidone). Drug remission was extremely unstable, which led to a high frequency of hospitalizations in psychiatric hospitals, on average 1.8 ± 0.6 hospitalizations per person per year. There was a certain pattern in the development of a psychotic episode in the subjects we examined. At the very beginning of the exacerbation of the disease, all patients showed a gradual increase in anxiety, fluctuations in the mood of negativism towards others, and sleep disturbances. At these moments, the patients arbitrarily stopped treatment, conflicted with others. A decrease in criticism of one's condition and the level of social danger required involuntary hospitalization, on average, in 24 ± 1.2 of the examined persons. The average

duration of the subacute period was 27 ± 2.2 days. Assessment of the clinical manifestations of the psychotic period of the schizophrenic process itself made it possible to distinguish three groups of patients. Of these, 45 patients developed Kandinsky-Clerambo syndrome, or hallucinatory-delusional syndrome. The ideas of persecution, influence, a feeling of openness of thoughts to others, inability to control their body dominated. Among the perceptual deceptions, auditory perceptual deceptions dominated, which patients described as «voices sounding inside the head.» Moreover, the imperative nature of the voices ordering to kill, to commit suicide at the height of the disease was noted in 32 patients. In another 9 patients, at the height of the hallucinatory-delusional syndrome manifestations, signs of mutism were noted, but without the symptoms inherent in catatonic stupor in the form of wax flexibility, pillow, staircase symptom, and episodes of catatonic excitement were also absent.

Finally, in 4 patients in the structure of the hallucinatory-delusional syndrome, a high proportion was occupied by paraphrenic delusional ideas of greatness and wealth, but without signs of dulling of consciousness. The average duration of the acute period was 36.1 ± 1.3 days. The reverse reduction of psychotic symptoms also had a number of patterns. At first, hallucinatory-delusional experiences lost their relevance, their affective charge diminished, patients began to speak about them in a neutral tone. Feelings of anxiety, negativism decreased, sleep improved. Further, such patients were discharged for outpatient treatment with the transition to supportive therapy. Criticism to their condition in patients was absent or was formal. In another group of patients (10 people), during the period of exacerbation, signs of acute paranoid dominated. Such patients expressed ideas of the relationship, often changed their place of residence, fleeing from "persecutors". There were separate phenomena of an influx of thoughts, an increase in the fragmentation of thinking, sporadic unstable ideas of influence. The average duration of the acute period was 42.1 ± 2.1 days. The reverse reduction of psychotic symptoms proceeded in the form of a decrease in psychomotor agitation, the severity of aggressive and autoaggressive tendencies. At the same time, the patients remained delusional for a long time, formally, but briefly agreeing with a critical assessment of their behavior, in the future they continued to "look for" signs of surveillance or persecution (the so-called "overvalued ideas syndrome").

Finally, in the third group (10 people), pronounced mood swings dominated in the subacute period, from hypomanic to sub-depressive. As the transition to the acute period progressed, the clinical picture was defined as affective-delusional, with ideas of self-abasement, auditory hallucinations of an imperative nature, and suicidal tendencies. The average duration of the acute period was 33.1 ± 1.9 days. As psychotic experiences subsided, suicidal tendencies, ideas of self-accusation and self-abasement initially weakened. The longest remained affective vibrations that did not reach the psychotic level, supplemented by episodes of protopathic anxiety, fatigue, mentism from the existing somatic pathology - hypertension stage 1-2 in 7 patients (I 11.9 according to ICD-10). In 3 patients, an insulin-independent form of diabetes mellitus in the compensation stage (E11 according to ICD-10) was found. The following manifestations of acute respiratory viral disease were common to all examined persons: increased body temperature; dry cough or cough with a little mucus secretion; shortness of breath, physical weakness, sleep disturbances; perspiration in the oropharynx; a feeling of congestion in the chest. In 55 subjects, a moderate course of coronavirus infection was observed, which included the following criteria: body temperature up to 38° C; respiratory rate > 22 per minute, shortness of breath on exertion; Changes in computed tomography of the lungs were typical for a viral lesion; SpO2 < 95%; Serum C-reactive protein > 10 mg/l. systolic blood pressure over 90 mm Hg or diastolic blood pressure of at least 60 mm Hg; diuresis of at least 20 ml/

hour. In 10 subjects, a severe course of the infectious process was noted, which met the following criteria: body temperature > 3 °C; Respiratory rate > 30/min; SpO2 ≤ 93%; systolic blood pressure less than 90 mm Hg or diastolic blood pressure less than 60 mm Hg; diuresis less than 20 ml/hour.

Treatment regimens for an infectious disease included the following prescriptions: favipiravir, 2000 mg 2 r/day on day 1 and then 800 mg 2 r/day on days 2-10 (15 patients). Hydroxychloroquine 400 mg on the 1st day (200 mg 2 r/day), then 200 mg per day (100 mg 2 r/day), for 6-8 days; dexamethasone 20 mg/intravenous in two injections for at least 3 days, followed by a gradual dose reduction; oral administration of azithromycin at a dose of 150 mg per day for five days; Oxygen therapy; Aminophylline 150 mg 3 times a day. Depending on the nature of psychotic experiences during the course of the coronavirus infection, two groups of patients were identified. The first group (42 people) included patients with schizophrenic psychotic manifestations. Of these, 38 patients had a course of moderate coronavirus infection, and 4 patients had a severe degree. The second group of patients (23 people) included patients with various clinical variants of confusion. Of these, 17 patients had a course of moderate coronavirus infection, and 6 patients had a severe degree. At the same time, the general characteristic of the examined persons, regardless of the revealed features of the course of the infectious process, was the outcome in physical and mental weakness, emotional lability, decreased concentration of attention, deterioration of short-term memory without forming a critical attitude to their condition. In the first group, as the severity of the infectious process subsides in the form of normalization body temperature and blood pressure, increased blood saturation in the subjects began to reveal unstable delusional ideas of influence, persecution, a sense of reading thoughts by people around, elements of mental automatism, auditory imperative deceptions of perception. The indicated schizophrenia-like symptomatology was of a reduced and unstable nature, in comparison with the symptomatology usual for patients during the period of exacerbation of schizophrenia itself. The duration of the course of psychotic experiences was, on average, 17.8 ± 1.3 days. The resolution of the disease was of a lytic nature, followed by asthenia. In turn, in this first group, three clinically outlined variants of the development of schizophrenic symptoms were identified. The first option provided for the gradual subsiding of schizophrenic-like symptoms with an immediate outcome in asthenic syndrome (27 patients). In the second variant, there was a so-called "intermediate stage" in the form of attenuation of psychotic symptoms, in which the schizophrenic symptoms, but before the development of asthenic syndrome, were replaced by symptoms characteristic of exogenous infectious diseases (9 patients). As a clinical example, the development of visual hallucinosis during this period (2 patients) can serve. Or twilight clouding of consciousness, accompanied by pronounced psychomotor agitation with aggressive and auto-aggressive tendencies (9 patients). In the third variant, the schizophrenic symptomatology was supplemented by psychopathological phenomena that were not previously characteristic of the subjects, but which also could not be verified as truly exogenous (6 patients). For example, in four patients, while maintaining the elements of mental automatism, a modification of the clinical picture occurred due to the addition of Capgras syndrome. The patients began to complain that their relatives were replaced by strangers; admitted that they were ill-wishers capable of harming them. There were also cases of «recognition» in strangers of their relatives(delirium of a positive double). Two more subjects showed clinical signs of catatonic stupor (immobilization of the patient, a symptom of an "air cushion." In the second group of patients (25 patients), the realization of a psychotic episode occurred at the height of infectious manifestations, initially revealing clinical symptoms characteristic of an exogenous infectious process. temperature reac-

tion in 21 patients, manifestations of delirious stupefaction were observed. Such patients had protopathic anxiety, agitation, especially in the evening; visual deceptions of perception with elements of aggressive behavior. At the same time, the patients retained their orientation in their own personality and place of stay, confused only in the current dates. Three more patients showed signs of twilight clouding of consciousness with chaotic arousal, silent aggression and autoaggression.

Finally, in one subject, amentive confusion of consciousness with the affect of bewilderment, lack of contact with others, disorientation in time, self-identity and place of residence was observed. The duration of the psychotic exogenous episode averaged 9.6 ± 0.6 days, the recovery from it was critical, with a sharp break in psychotic symptoms through drug sleep. Discussion. In the process of studying comorbid relationships between coronavirus infection and paranoid schizophrenia, a pronounced polymorphism of clinical manifestations of the psychotic register was found in the examined patients. At the same time, it became necessary to consider a number of practical issues that were not included in the stated purpose of the study, but could potentially affect its results. Considering that coronavirus infection is a source of high social stress, one might assume that it played the role of a kind of psychological trigger in the development of psychotic symptoms in the examined patients. However, the development of psychotic symptoms solely against the background of the course of the infectious process, polymorphism of clinical symptoms, which is more characteristic of an exogenous process, makes this assumption untenable in relation to the individuals we examined. It seems likely that a more severe course of coronavirus infection is in patients with paranoid schizophrenia due to the latter's predisposition to pathology of the respiratory system, and to infectious diseases in particular. This can be facilitated by long-term use of antipsychotics by the examined individuals, which can worsen the functions of the pulmonary system against the background of impaired functions of the immune system. The latter is manifested by a tendency to increased synthesis of cytokines, activation of the enzyme indoleamine-2,3-dioxygenase, violations of T-cell immunity and the work of the main histocompatibility complex. This, in turn, affects the activity of the serotonergic, dopaminergic and glutamatergic mediator systems [14-19]. An obstacle to a more complete analysis of the effect of coronavirus infection on the course of the schizophrenic process was the absence of a control group that would include patients with paranoid schizophrenia, but without an infectious disease. A small representative sample did not allow for a comparative correlation analysis between the severity of the infectious process and individual clinical manifestations. However, clinical observations did not allow forming a belief about the influence of the severity of the infectious process on the nature of psychotic experiences. This phenomenon seems somewhat strange from the point of view of the doctrine of infectious, somatogenic psychoses, formulated in his time by K. Bonhoeffer, and indicating the relationship between the intensity of somatogeny and the severity of mental disorders, and requires further clarification. The possibility of the appearance of psychotic symptoms as a result of side effects of anti-infective drugs cannot be ruled out [20]. Or as a result of their ability to alter the metabolism of neuroleptic drugs proper by influencing the cytochrome p-450 system. Finally, the onset of psychotic symptoms could be due to the possible impact of inflammatory processes associated with COVID-19 on the metabolism of antipsychotics. The results of this study do not allow unambiguous answers to these questions, which require further study. The main issue of differential diagnosis required to distinguish exacerbations of schizophrenic disorder proper, on the one hand, from exogenous transient psychoses, on the other. In the case of the schizophrenic-like disorders we observed, there was no typical patient model of exocerbation of the disease. There was no tendency

to expand the plot of hallucinatory-delusional experiences, even with the presence of previously uncharacteristic psychotic elements in the form of Capgras syndrome, visual hallucinosis and vice versa, there was symptomatology characteristic of exogenous disorders within the framework of various syndromes of confusion. The duration of the psychotic period was significantly shorter than the usual figures with exacerbation of the underlying disease, taking about 2-2.5 weeks.

Finally, the outcome in physical and mental weakness, emotional lability, decreased concentration of attention, impairment of short-term memory, a shortened duration of the psychotic period itself, compared with a typical exacerbation, also testifies in favor of the introduced character of psychosis [21].

The identified cases of psychotic symptoms in patients with paranoid schizophrenia with identified concomitant coronavirus infection were of a transient exogenous nature. Clinical manifestations of psychotic experiences found their formulation in the framework of schizophrenia-like disorders and confusion syndromes. At the same time, the ability of coronavirus infection to cause psychotic disorders, apparently, is realized due to various pathogenetic mechanisms, including pharmacogenic, metabotropic, psychogenic, etc. This phenomenon, in turn, requires further study to increase the effectiveness of therapeutic and diagnostic measures in this group sick.

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Conflict of interest

None to declare.

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Klinički aspekti komorbiditeta infekcije koronovirusom i paranoidne shizofrenije

Sažetak - Na uzorku od 65 bolesnika s paranoidnom shizofrenijom istraživan je učinak infekcije koronavirusom. Utvrđeno je da se infekcija koronavirusom u bolesnika s paranoidnom shizofrenijom može manifestirati u obliku prolaznih psihoza, koje odgovaraju simptomima shizofrenije, te se također manifestira konfuznim stanjem. Postavljena je pretpostavka o tome kako infekcija koronavirusom može utjecati na različite procese u patogenezi, tijekom formiranja psihotičnih poremećaja u ovoj skupini pacijenata.

Ključne riječi: infekcija koronavirusom; shizofrenija; Covid-19; SARS-CoV-2; psihoza