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REVIEW ARTICLE

CHALLENGES TO THE MANAGEMENT OF PSYCHIATRIC HOSPITALS CAUSED BY THE CONTINUED POSITIVE ANTIBODIES OF PATIENTS WITH SCHIZOPHRENIA AFTER COVID-19: TWO CASE REPORTS

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Abstract

In the context of the global pandemic of COVID-19, with the epidemic epicenter located in the Wuhan City, China, patients with severe mental illness have also been deeply affected by the epidemic. In this paper, two patients with schizophrenia who recovered from COVID-19 were reported. Because of the long-term positive results of the SARS-CoV-2 serum antibody IgM test, they had to undergo medical isolation and social restrictions for a long time. After the situation was effectively identified by the medical staff and they were eliminated as a potential virus carrier and released from the medical isolation center. Since psychiatrists often lack systematic knowledge of infectious diseases, the authors hope that this paper can provide a reference to avoid unnecessary wastage of medical resources and prevent placing serious mental burden on such patients in the future. ***ASEAN Journal of Psychiatry, Vol. 22(7), August 2021: 1-6.***

Keywords: SARS-CoV-2 Antibody, IgM, IgG, COVID-19, Schizophrenia

Introduction

As is known, coronavirus disease 2019 (COVID-19) was declared by the World Health Organization (WHO) as a global pandemic on March 11, 2020. According to reports, Wuhan City, Hubei Province, China was the first area to be affected by the disease, and patients with mental illnesses living in this area were also deeply affected by the epidemic [1-3]. Accordingly, the local government set up designated hospitals for the treatment of mental illnesses in patients infected with COVID-19 [4].

The detection of SARS-CoV-2 nucleic acid is the most sensitive and important basis for the diagnosis of COVID-19 [5], and it has become the gold standard for COVID-19 diagnosis. In addition, the virus serum antibody test is an important auxiliary method for the diagnosis of COVID-19 [6,7]. Based on this core concept, medical workers who participated in the fight against the epidemic in Wuhan also conducted medical treatment for confirmed and suspected patients with reference to the diagnosis and treatment regime of coronavirus disease-19 (7th Trial Edition) [8]. On April 22, 2020, the mental health institution of the author announced that all mental patients previously infected with COVID-19 and in their recovering period were released from isolation, but the 120 capacity isolation ward was reserved to deal with homeless convalescent patients manifesting infections and new sporadic infections. The reserved isolation ward included two special case patients. Although the SARS-CoV-2 nucleic acid test tested negative multiple times, the patient's serum antibody IgM remained positive for a long time, requiring restrict contact with others and live relatively loosely alone. Eventually they were lifted all activity restrictions on August 11, 2020.

Case 1: Persistent False Positive of SARS-CoV-2 Serum Antibody IgM

A 55-year-old homeless patient with schizophrenia was admitted to the Wuhan Mental Health Center on December 5, 2019 due to a strange behavior and refusal to eat. After admission, no

obvious abnormalities were detected in the routine blood tests, biochemical examinations, electrocardiogram, and chest CT. On January 24th, 2020 the patient began to develop fever. At that time, his Leukocyte Count was 3.85×10^9/L and his C-reactive protein was 12.8 mg/L and his chest CT revealed a patchy infection on both the lungs. On January 28th, his SARS-CoV-2 nucleic acid test came positive, and his diagnosis was COVID-19. The patient was transferred to the isolation ward on the same day. The 2nd chest CT scan revealed that both the lungs had patchy infections, which had progressed more than that on February 11th, and the first SARS-CoV-2 antibody test (IgM, IgG) was double positive (detection by the colloidal gold method) on February 14. On March 11, the patient's blood cell count (mainly WBC, neutrophil, and lymphocyte counts had returned to the normal range). The 7th SARS-CoV-2 nucleic acid tests on March 23 turned into negative. On May 1st, his 8th chest CT scan basically showed absorption of the lung infection.

After the initial detection of SARS-CoV-2 antibody (IgM positive and IgG positive) during February 14th, 2021 to July 28, 2021 he tested double positive for the antibody reexamination 18 times. On July 25, the tested Rheumatoid Factor (RF) value was 84 IU/ml; and the same to on July 29. On July 31, the detection method for SARS-CoV-2 antibody was improved to the urea dissociation method [9,10], the results of which showed SARS-CoV-2 antibodies (IgM, IgG) as negative and positive, respectively. On August 11, the same urea dissociation method revealed SARS-CoV-2 antibody (IgM, IgG) as negative and positive, respectively. Accordingly, the patient was immediately released from medical isolation. The evolution of patients with COVID-19 is depicted in Figure 1.

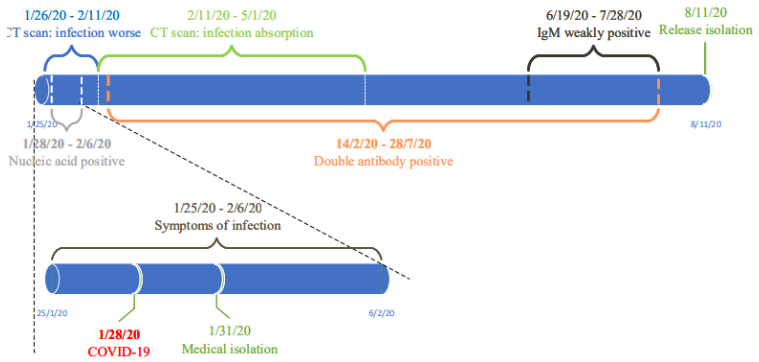

Figure 1. The Evolution of the Patient's Condition in Case-1

Case 2: Persistent Positive of SARS-CoV-2 Serum Antibody IgM

An unattended 49-year-old female patient with schizophrenia who has been hospitalized in Wuhan Mental Health Center for a long-term developed fever and dry cough on January 30, 2020. On the same day, the blood routine indicators were normal, and the C-reactive protein was 15.9 mg/L. Chest CT scan the next day showed: patchy infection in both lungs. He was immediately treated as a suspected COVID-19 case for medical isolation. From February 3rd to February 6th, 2 consecutive SARS-CoV-2 nucleic acid tests were all positive and confirmed as COVID-19. On February 12, 2020, the patient's first SARS-CoV-2 serum antibody test was double positive (IgM positive and IgG positive).

During the subsequent observation and testing, the patient's blood cell count was always not significantly abnormal, the clinical symptoms of infection disappeared completely on February 10 and the C-reactive protein level returned to the normal range (6.9 mg/L) on February 20. On March 19, a CT scan of the lungs indicated that the lung infection was basically absorbed. Although a total of 10 nucleic acid tests after the 7th SARS-CoV-2 nucleic acid test on February 26, 2020 were negative, the patient's serum antibody to SARS-CoV-2 was still double positive until the 34th test on April 16, 2021. From July 25 to August 11, 2020, we conducted a total of 6 tests on the patient's RF level, all of which were below 15I U/ml. At the same time, we also adopted a variety of methods (including

fluid gold method and urea dissociation method) to detect the SARS-CoV-2 serum antibody of patients, and the repeated test results were double positive. After multiple rounds of joint consultations, on August 11, 2020, the patient and the patient in Case 1 were removed from all activity restrictions. After multiple rounds of joint consultations, although we did not find the reason why the patient's antibody continued to be positive, on August 11, 2020, the patient and the patient in Case 1 were removed from all activity restrictions. The evolution of patients with COVID-19 is depicted in Figure 2.

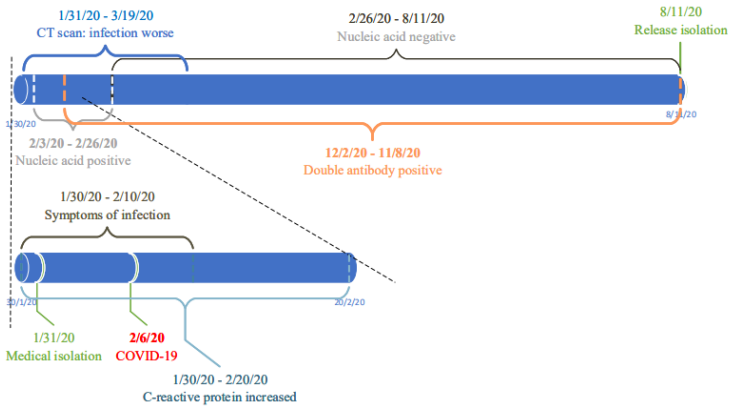

Figure 2. The Evolution of the Patient's Condition in Case 2

Discussion and Conclusion

SARS-CoV-2 antibody detection was performed as a supplement to viral nucleic acid detection, which together play an important role in the diagnosis of COVID-19 [11,12]. The latest version of Diagnosis and Treatment of Coronavirus Disease-19 (7th Trial Edition) released on March 11, 2020 also employs the SARS-CoV-2 antibody detection as one of the diagnostic criteria for COVID-19. According to a recent research report [13], the average time of serum conversion of IgM and IgG is 6 and 3 days, respectively; the antibody levels of IgM and IgG reaches the peak at approximately 18 and 23 days, respectively, after which the IgM value falls below the baseline level at around 36 days, while the IgG value remains at a relatively high level. On the premise that false-negative [14-16] nucleic acid test caused by low virus concentration or improper sampling method cannot be completely ignored, IgM-positive result represents that the patient is at the early stage of SARS-CoV-2 infection with a potential risk of virus transmission [17]. However, the duration of serum IgM and IgG double positive in the two patients lasted as long as several months, especially, as the positive duration of IgM was much higher than that of the vast majority of patients with known infection, and the test of patients infected at the same time had turned negative, which raised doubts about the clinical staff. In fact, the patient was worried that he was still in a newly infected state with the ability to spread the virus. In China, psychiatric hospitals are generally characterized by small spaces, poor equipment, and crowded living environments for patients. The physical fitness of mentally ill patients is also poor. These are all unfavorable factors preventing the spread of infectious diseases in hospitals. In addition, the local government also requires all medical institutions that undertake the treatment of COVID-19 patients to implement the main responsibility, in the spirit of medical humanitarianism, with a highly responsible attitude to patients and society, treat every infected patient and do their utmost to curb the spread of COVID-19 in the hospital. As the two patients are homeless or unattended, they cannot be separated from the environment of the mental hospital, it is necessary to be very careful when to remove the medical isolation. Since April 22, 2020, these two patients have become the only double antibody positive patients in our unit. We have to set aside a floor and equip corresponding medical staff to treat them to avoid any possibility of nosocomial transmission.

Considering that the two patients showed no symptoms and signs of infection related to COVID-19 for several months and tested negative on the nucleic acid test were together used as support factors to establish a professional consultation team on July 22, 2020 for discussing and analyzing the

possibility of "double antibody false-positive" report of the patient, which required investigation of the influencing factors that could have caused false-positive results by the colloidal gold method. Past studies have shown that rheumatoid patients, patients with other diseases, and even normal people often contain higher or different concentrations of RF [18]. Normally, the RF is IgM RF [19] with the characteristics of non-specific binding to denatured IgG. In immunoassays, it can lead to false positive IgM test results [20]. In summary, the medical staff tested the patient's RF level twice, and both the times, his levels were higher than the normal. Based on this observation, it can be inferred that SARS-CoV-2 serum antibody IgM result was false-positive in the patient of case 1. In order to verify this inference, the inspectors employed the urea dissociation method [9,10] to determine the patient's serum IgM antibodies twice, with all the results being negative. Unfortunately, we did not find a similar phenomenon in case 2. In order to rule out the patient's possibility of spreading COVID-19, we performed a total of 17 nucleic acid tests on the patient of case 2 to ensure that the nucleic acid test results are not false negative and there is no recurrence of positive. Finally, the patients were released from medical isolation on August 11, 2020.

In psychiatric hospitals, a vast majority of medical staff lack systematic knowledge of non-psychiatric diseases, as mentioned for the two cases. In the face of continuing severe pressure of epidemic prevention and control, the control of the risk of the spread of this epidemic in the hospital, on the premise that patients possess the ability to spread the virus, medical isolation and maintenance of social distancing remain important means to control the epidemic. The present report will provide a reference for other psychiatric hospitals all across the world. For special cases with positive SARS-CoV-2 serum antibody IgM result over a long period of time, we should actively organize social consultation to determine the causes and eliminate interference. This seems the only way to make a clear diagnosis, avoid unnecessary wastage of medical resources, and, more importantly, avoid the serious mental burden on patients caused by long-term medical isolation.

Ethics Statement

The participant involved in this case report were approved by the Ethics Clerk of Wuhan Mental Health Center. The participant provided informed consent to participate in this paper. Written informed consent was obtained from the individual for the publication of any potentially identifiable data included in this article.

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Conflict of interest

None.

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