

LETTER TO THE EDITOR

New IgM seroconversion and positive RT-PCR test after exposure to the virus in recovered COVID-19 patient

To the Editor,

To date, understanding whether acquired immunity and presence of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies protect against reinfection is one of the most important focus of the scientific community.^{1,2} Several studies suggest that acquired immunity may protect upon further exposure to SARS-CoV-2.³⁻⁶ Contrary to this picture, we describe a case of a patient recovered from COVID-19 pneumonia with positive serology, followed up by six negative nasopharyngeal swab polymerase chain reaction (PCR) tests performed along 1 month who later on, after exposure to the virus, presented another positive reverse transcriptase (RT)-PCR test and a second immunoglobulin M (IgM) seroconversion. This report opens up several possible interpretations.

A 69-year-old woman with type 2 diabetes mellitus and recently diagnosed urinary tract neoplasm arrived in the emergency room with mild fever and cough. Nasopharyngeal swab RNA test for SARS-CoV-2 resulted positive high-resolution computer tomography (HRCT) revealed bilateral parenchymal consolidations and ground-glass areas. Hydroxychloroquine and lopinavir/ritonavir were initiated. After symptoms resolution and two negative RT-PCR tests, the patient was discharged.

Twenty-three days later, the patient was again hospitalized for urinary tract infection. During hospitalization, four nasopharyngeal swab RNA tests for SARS-CoV-2 gave negative results, and serological analysis (chemiluminescence immunoassay) revealed the presence of SARS-CoV-2-specific IgG with no more evidence of specific IgM compatibly with remote recovered infection.

During recovery, the patient was accidentally in prolonged close contact with a misdiagnosed COVID-19 patient. Subsequent analysis revealed positive nasopharyngeal swab RNA test and IgM seroconversion (Figure 1). The patient was asymptomatic without leukocytes count or inflammatory indexes alterations. Another HRCT revealed resolution of the right parenchymal consolidation

and accentuation of the pre-existent left one. The immunological analysis was performed: lymphocyte typing revealed a reduction in the B and T8 lymphocyte population with a consequent increase in the T4/T8 ratio, but no alteration in humoral immunity was founded. Total serum levels of IgM, IgG, and IgA were normal, and quantitative assessment revealed a high concentration of COVID-19 specific-type IgG with 2.7 signal/cutoff (positive if >1.4). The patient is currently asymptomatic waiting for the fulfillment of discharge criteria.

To date, there is no evidence for cases of SARS-CoV-2 reinfections.¹

Some reports describe rare cases of postrecovery positive nasopharyngeal swab PCR tests performed during the quarantine period in asymptomatic or mildly symptomatic patients.

Lan et al⁷ describe four cases recovered COVID-19 patients with two negative RT-PCR that, after 5 to 13 days, developed positive RT-PCR tests, although no cohabitants were infected.

Consistently with our case, the patients from the above reports were asymptomatic or mildly symptomatic at the time of post-recovery positive RT-PCR results, and, when performed, radiological imaging found improving or stable pneumonia. Furthermore, only two negative tests were performed for meeting discharge criteria, and postrecovery positive test was performed less than 15 days after the last negative result.

Since high false-negative rates of the viral tests are described, it was suggested that these patients could have experienced a prolonged viral clearance rather than a recurrence or repositization.⁷ We consider our patient recovered because the probability of six consequent false-negative nasopharyngeal swab RNA test is 0.36^{6,8} that is, less than 0.08%. Moreover, in postrecovery positive PCR test reported in the literature, no evidence of specific Ig development is described, and their trends during the "re-infection" are never reported. In our case, new IgM seroconversion could derive from the

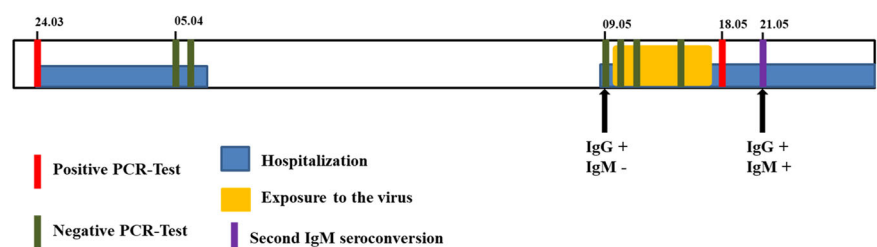


FIGURE 1 Timeline of severe acute respiratory syndrome coronavirus 2 infection. IgG, immunoglobulin G; PCR, polymerase chain reaction

expansion of IgM+ memory B cells. Postviral exposure positization of RT-PCR test and IgM seroconversion after more than 1 month from recovery can be difficult to explain with the current knowledge. Several studies indicate that acquired immunity guarantees protection after successive exposure to the virus,³⁻⁶ but to date, this question is one of the most important focus of the scientific community.

Nevertheless, our report seems to refute this hypothesis. Yet, the patient was asymptomatic at the time of postrecovery positive RT-PCR test, which could mean that, even if the antibodies do not protect from reinfection, they do protect against severe forms of the disease. It is also likely that a key role in protection against a second infection is played by cellular immunity. In fact, precedent studies performed on patient recovered from SARS-CoV1 during the 2003 outbreak demonstrated that T lymphocyte are fundamental for adaptive immunity against the virus. Specifically, it was found that CD8+ response predominates over CD4+⁹; so CD8 depletion may have played a role in our patient reinfection.

It is clear that there is still much to learn about acquired immunity against the SARS-COV-2 virus and the possibility of reinfection. It is possible that COVID-19 discharge criteria may have to be revised and the validity of the postrecovery positive PCR test re-evaluated.

CONFLICT OF INTERESTS


The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

EB participated in article preparation. All authors materially participated in the research and data collection, and have approved the final article.

ETHICS STATEMENT

Written informed consent was obtained by the patient for publication of this case report and accompanying images.

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