

Persistence of Anti-SARS-CoV-2 IgM Antibody up to 8 Months Post-COVID-19

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Abstract

Here, we present a longitudinal analysis of two patients who recovered from COVID-19 more than 8 months prior but showed persistent serological detection of anti-SARS-CoV-2 IgM. We still do not know the exact reason for this prolonged persistence of IgM in these patients. To our knowledge, these are the first reports of IgM persistence in the context of SARS-CoV-2 infection and point to the need for no longer using IgM as a diagnostic criterion for acute or recent COVID-19. One should opt for gold standard molecular methodologies due to their high sensitivity and specificity.

Keywords

COVID-19, SARS-CoV-2, Antibodies, IgM, Persistence

1. Introduction

Since November 2019, after the emergence of the novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) in Wuhan, China [1], numerous studies have been published in an attempt to understand: 1) the epidemiology of infection [2], 2) the immunological aspects involved in combating the virus and the immunopathogenesis [3], 3) immunological and viral diagnostic markers [4] [5], 4) treatment possibilities [6], interactions of environmental factors in the context of virus transmissibility [7], and more recently, 5) the efficacy of vaccines approved for use [8].

Despite the large number of publications on COVID-19 (coronavirus disease

2019) to date, many questions remain unanswered, and new information is generated every day, rendering the novel virus a continuous source of learning, especially in the context of the host immune response.

In recent study, Mallon *et al.* [9] reported that in subjects diagnosed with COVID-19, the IgM positivity was increased earlier, with the positivity peaking between days 32 and 38 post-onset of symptoms, but with a more rapid decline than the observed to IgG. Additionally, in a longitudinal study, Peghin *et al.* [10] observed IgM seroconversion in 90% of patients and its decline within 4 months. In our previous follow-up study, we reported a high frequency of loss of anti-SARS-CoV-2 IgG antibodies within 3 months after COVID-19 diagnosis in the Brazilian Amazon, but without information about IgM [11].

Here, we present laboratory results for two patients who recovered from COVID-19 more than 8 months prior with persistent serological detection of anti-SARS-CoV-2 IgM. This project was submitted to and approved by the Human Research Ethics Committee of the Institute of Health Sciences of the Federal University of Pará (CAAE: 31800720.1.0000.0018) in compliance with the guidelines and regulatory standards for research involving human beings. Both patients who agreed to participate in the study signed an informed consent form.

2. Case Report

2.1. Patient #1

The first patient, a 47-year-old female residing in Belém, capital of the state of Pará (Brazil), underwent her initial serological evaluation on 05/26/2020 and showed reactivity against IgM (6.0 AU/mL) and IgG (2.4 AU/mL) by chemiluminescent microparticle immunoassay (MCIA) in an Alinity i automated system (Abbott Laboratories, Chicago, IL, USA) following the manufacturer's protocol. Two more analyses were performed on 06/04/2020 and 12/28/2020, which showed IgM persistence at concentrations of 10.0 AU/mL and 5.3 AU/mL, respectively. In response to a clinical-epidemiological inquiry, the patient reported having the following COVID-19-related symptoms: headache, runny nose, dry cough, sore throat, body pain, diarrhea, loss of smell and taste, fatigue and alopecia. She reported symptoms for four or more weeks and was treated with the following drugs: hydroxychloroquine, ivermectin, anti-inflammatory agents, antipyretic agents and amoxicillin.

2.2. Patient #2

A second case of IgM persistence was monitored by our group to evaluate the clinical-epidemiological aspects. The patient, a 42-year-old male, had already undergone three serological evaluations by different methods (lateral immunochromatography and chemiluminescence). The first test was performed on 05/25/2020, showing seroreactivity against IgM and IgG by lateral immunochromatography (rapid test). The test was repeated on 12/15/2020, again by immunochromatography, and showed reactivity against IgM and nonreactivity

against IgG. After one week, on 12/23/2020, the patient underwent another test by chemiluminescence, and IgM persistence (2.53 AU/mL) and IgG absence were detected. In the last analysis, performed on 01/25/2021, the reactivity to IgM (2.79 AU/mL) was maintained.

3. Discussion

We still do not know the exact biological reason for this prolonged persistence of IgM in these patients. This phenomenon has been described following acute infection by hepatitis A virus (HAV) up to 60 days after patients recovered from the infection [12], in addition to other pathogens. Kapoor *et al.* [13] also reported the persistence of anti-West Nile virus IgM in cerebrospinal fluid samples from three patients at 110, 141 and 199 days after acute central nervous system infection.

The titers of IgM and IgG anti-SARS-CoV-2 antibodies specific for the spike-binding receptor domain (RBD) decrease significantly, while IgA is less affected during infection resolution [14]. According to Isho *et al.* [15] anti-SARS-CoV-2 antibody responses were readily detected in serum and saliva, with maximum IgG levels reached between 16 and 30 days after symptom onset. A longitudinal analysis of the patients revealed that the anti-SARS-CoV-2 IgA and IgM antibodies declined rapidly, while the IgG antibodies remained relatively stable up to 105 days in both biological fluids.

To our knowledge, the cases presented herein are the first reports of IgM persistence in the context of SARS-CoV-2 infection and point to the need for no longer use IgM as a diagnostic criterion for acute or recent COVID-19.

The role of serological tests for the diagnosis of SARS-CoV-2 infection has been sufficiently debated and discouraged for diagnostic purposes and remains today as a limited tool for epidemiological observation. Especially IgM, is a biomarker related to a high false positive rate. In turn, the persistence of IgM antibodies for months to years is now a phenomenon recognized as frequent and without clinical significance, given the high sensitivity of current serological techniques; thus one should opt for gold standard molecular methodologies due to their high sensitivity and specificity.

4. Conclusion

The IgM persistence, as observed in the cases presented herein, should not be a criterion for singling out those who fit this profile and preventing them from performing their usual activities, as has been observed, because such actions can have negative socioeconomic and professional impacts on these individuals.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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