COVID-19 IgM/IgG false-positivity in a rheumatoid arthritis patient negative for RF and ACPA: exist of other serological interference?

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To the editor:

The outbreak of coronavirus disease 2019 (COVID-19) which rapidly spread throughout the world is still threatening the global health safety. Diagnostic tests for COVID-19 divided into two main categories: detection of viral RNA and serological detection of anti-SARS-CoV-2 immunoglobulins including specific IgM and  $IgG^{[1]}$ .

Recently, we came up with an 89-year-old RA patient. She was diagnosed of rheumatoid arthritis for interphalangeal joint pain and rheumatic factor (RF) positive over 15 years ago and had been taking prednisone 5mg per day. Since the spread of COVID-19, we gave her the test of SARS-Cov-2 IgM/IgG and nucleic acid routinely. The confusing results showed IgM and IgG positive and nucleic acid negative. This old woman had no epidemiological history due to poor lung function. To further clarify the diagnosis, we retest SARS-Cov-2 nucleic acid from throat, nasopharyngeal and anal swab specimen and got negative results again. Diagnosis of COVID-19 was eliminated. 6 months later, this lady was readmitted with persistent positive result of specific IgM and IgG and negative result of nucleic acid. Serological test of RF and anti-cyclic citrullinated peptide antibody (ACPA) showed negative.

According current reports, serum IgM arrived peak need 16-30 days and rapid decayed, while IgG remained relatively stable up to 105 days post-symptoms onset<sup>[2,3]</sup>. In our reported case, the IgM and IgG had persisted for more than 6 months.

Recent study reported that no cross-reactivity was observed between autoantibodies in autoimmune disease and SARS-CoV-2 antibodies<sup>[4]</sup>. Controversially, the false-positivity of anti-SARS-CoV-2 IgM was reported in RF IgM-positive serum<sup>[5]</sup>. Considering this case, some unknown factors besides RF IgM and ACPA may exist in serum of RA patients which cause persist false positivity of anti-SARS-CoV-2 immunoglobulin.

In conclusion, medical history combined with nucleic acid tests still played the key role in diagnosis of COVID-19 when come with positive result of SARS-Cov-2 IgM and IgG. The false positivity could involve either IgM or IgG which may be caused by other cross-reactive factors besides RF antibody and ACPA. The potential mechanism remained further explored.

## Reference

[1] Yuce M, Filiztekin E, Ozkaya KG. COVID-19 diagnosis - A review of current methods. Biosens Bioelectron, 2021, 172: 112752.

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- [2] Isho B, Abe KT, Zuo M, et al. Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients. Sci Immunol, 2020, 5(52).
- [3] Liu X, Wang J, Xu X, et al. Patterns of IgG and IgM antibody response in COVID-19 patients. Emerg Microbes Infect, 2020, 9(1): 1269-1274.
- [4] Teng J, Dai J, Su Y, et al. Detection of IgM and IgG antibodies against SARS-CoV-2 in patients with autoimmune diseases. Lancet Rheumatol, 2020, 2(7): e384-e385.
- [5] Vojdani A, Kharrazian D. Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. Clin Immunol, 2020, 217: 108480.