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LETTER TO THE EDITOR

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Clinical value of anti-SARS-COV-2 serum IgA titration in patients with COVID-19

To the Editor,

Immunoglobulins A (IgA) represents the major antibody class that offers humoral protection against microbial pathogens at surface of respiratory, genitourinary, and gastrointestinal mucosae.[1] Although a comprehensive description of IgA biology shall be omitted here for space constrains, it seems important to mention that two major monomeric subclasses of this immunoglobulin can be synthesized, known as IgA1 and IgA2, which mostly differ for the structure of the hinge region and tissue distribution (e.g., IgA1 is more abundant and can be found on all mucosal surfaces, whilst IgA2 is synthesized at the lower extent and is prevalently found in the colon).[2]

Beside specific molecular characterization, IgA can also be arranged throughout a vast array of combinations, the most frequent of which encompass monomeric and dimeric forms. The former structure characterizes internal body fluids (e.g., blood and cerebrospinal fluid), whilst the dimeric form (also known as "secretory IgA" [sIgA]), encompassing the association of two single monomeric IgA linked through a joining (J) chain, is more typically found in external fluids and secretions, where these antibodies play a critical role in mucosal immunity and protection against pathogens which colonize and/or invade mucosal surfaces.[2]

Owing to the essential role in protecting the organism against respiratory pathogens, several lines of evidence hint that IgA-mediated defense may be also an essential part of immune protection against severe acute respiratory syndrome coronavirus disease (SARS-CoV-2), the virus causing the ongoing coronavirus disease 2019 (COVID-19) pandemic.[3]

In a recent article published in this journal, Xue et al.[4] demonstrated that anti-SARS-CoV-2 IgA titer was significantly correlated with respiratory and oxygenation indices of alveolar blood in patients with SARS-CoV-2 infection, concluding that anti-SARS-CoV-2 IgA assessment may help identifying COVID-19 patients at higher risk of developing severe pulmonary lesions. Some other published studies have addressed the role of anti-SARS-CoV-2 IgA in prognostication of COVID-19, such as that of Huang et al.,[5] who highlighted that anti-SARS-CoV-2 serum IgA may appear before anti-SARS-CoV-2 IgG, and that IgA titer appears higher in patients with severe or critical disease compared to those with milder illness.

Important evidence that human IgA may be strongly protective against SARS-CoV-2 infection has been provided in recent studies. For example, Ejemel et al.[6] showed that some human anti-SARS-CoV-2 monoclonal sIgA efficiently bind to the spike protein of SARS-CoV-2, competitively blocking receptor binding and thus being capable to neutralize the virus at mucosal surfaces. A highly significant correlation between anti-SARS-CoV-2 IgA serum titer and that of neutralizing antibodies has also been demonstrated in the study of Varnaitė et al.[7] Almost identical results have been published by Tang et al.[8] by demonstrating good correlation coefficients (i.e., 0.54–0.69) between three commercial anti-SARS-CoV-2 serum IgA immunoassays and neutralizing antibodies, thus strengthening the concept that the appearance of this class of secretory immunoglobulins may be accompanied with effective viral neutralization at the mucosal surface of the respiratory system.

Beside the putative role in disease prognostication and mucosal immunity, serum IgA titration may also offer important support for diagnosing acute SARS-CoV-2 infections. In a recent study, Infantino et al.[9] showed that anti-SARS-CoV-2 IgA titer was over twofold higher than that of anti-SARS-CoV-2 IgG 9 days after symptoms onset, but also that the early seropositivity rate of anti-SARS-CoV-2 IgA was double that of anti-SARS-CoV-2 IgG in anti-SARS-CoV-2 IgM-negative patients. In another interesting study, Sterlin et al.[10] showed that the overall seropositivity rate of anti-SARS-CoV-2 IgA targeting receptor binding domain and viral nucleocapsid protein was comparable to that of anti-SARS-CoV-2 IgG, and consistently higher than that of anti-SARS-CoV-2 IgM. This evidence pinpoints that early humoral neutralizing immunity against SARS-CoV-2 may be predominated by anti-SARS-CoV-2 IgA.

Reliable evidence that the anti-SARS-CoV-2 IgA serum titer would accurately reflect that of anti-SARS-CoV-2 sIgA has been provided in the study of Randad et al.,[11] who showed very high correlations (i.e., up to 0.85) between the concentration of serum and saliva SARS-CoV-2 antigen-specific IgA. This would essentially suggest that assessment of serum anti-SARS-CoV-2 IgA may yield reliable information on the status of anti-SARS-CoV-2 mucosal immunity.

In conclusion, recent data are seemingly converging to confirm the many important clinical aspects mirrored by measuring anti-SARS-CoV-2 serum IgA in patients with COVID-19, so that their titration would be effective for improving the accuracy of diagnosing SARS-CoV-2 infection in patients with negative or undetermined results of molecular testing, for enhancing the accuracy of anti-SARS-CoV-2 serological assessment, for reflecting the development of mucosal humoral immunity and, finally, may help predicting disease severity and progression (Table 1).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

TABLE 1 Evidence supporting the clinical importance of routine assessment of anti-severe acute respiratory coronavirus disease 2 (SARS-CoV-2) serum immunoglobulin A (IgA) titer in patients with suspected or confirmed coronavirus disease 2019 (COVID-19)

1. Contribute to diagnosing acute SARS-CoV-2 infection in patients with negative or undetermined molecular biology
2. Enhance accuracy of anti-SARS-CoV-2 serological assessment
3. Mirror development of mucosal humoral immunity
4. Predict disease progression and severity

KEYWORDS
antibodies, coronavirus, COVID-19, immunoglobulin A

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