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Opinion

Role of Immunoglobulin A in Treating COVID-19

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DESCRIPTION

Immunoglobulin A (IgA) is the first line of defence in the resistance against infection, *via* inhibiting bacterial and viral adhesion to epithelial cells and by neutralization of bacterial toxins and virus, both extra-and intracellular. IgA also eliminates pathogens or antigens *via* an IgA- intermediated excretory pathway where binding to IgA is followed by poly immunoglobulin receptor- mediated transport of immune complexes. Secretory Immunoglobulin A (SIgA) has an important part in mediating the adaptive (antigen specific) humoral (antibody (Ab) - based) immune defence at mucosal exteriors (gastrointestinal, respiratory and urogenital tracts). Mucosal surfaces are the gate of entry of numerous pathogens. SIgA is produced exorbitantly at mucosal surfaces and is the predominant class of Ig found in human external secretions and in tears. IgA are glycoproteins and one of five classes of Ab. Ab classes are defined by the number of Y-like units (comprised of 4 polypeptides, 2 identical heavy chains and 2 identical light chains) and the type of heavy chain (in the case of IgA, ana- chain). IgA can be oligomeric, comprised of 2 – 4 IgA monomers.

SIgA is always oligomeric in structure, primarily dimeric, and the polymers are linked by additional polypeptide chains, including a 15KD joining chain (J chain) and a 70KD secretory component chain produced in epithelial cells and involved in the transcellular transport of SIgA. In humans, following antigen presentation to T helper cells (Th), and isolation of Th to Th2, the cytokines interleukin (IL)-10, IL-4 and transforming growth factor beta (TGF) – b are involved in causing the preferential development of B cells (B- cell Ab class- switching and isolation) into B cells that are committed to producing IgA. In humans there are two types of IgA, generally IgA, found in serum and derived in bone marrow, and IgA2, a secretory form of IgA.

Unless immunized, everyone is susceptible to SARS-CoV-2 infection. The variability of COVID-19 suggests that the individual vulnerable response to SARS-CoV-2 may play a critical part in determining the clinical course ranging from asymptomatic to mild upper respiratory tract illness, or moderate to severe complaint with respiratory torture and multi- organ failure requiring deep care and organ support. To pathogens for which there is no pre-existing immunity, our organism reacts by swiftly engaging the innate immune system with the intent of limiting the infection and giving time to adaptive immune response to generate the most specific and effective tools high- affinity antibodies and memory B and T cells. Extensive analysis of the antibody response, showed that SARS-CoV-2 induces virus-specific antibodies, mediated by all immunoglobulin iso types including IgM, IgG, and IgA; all IgG subclasses were produced by individualities with COVID-19, with IgG1 being the most dominant.

CONCLUSION

The kinetics of specific immunoglobulin production against spike-1 receptor- binding domain and nucleocapsid protein shows that the vast majority of patients produce detectable neutralizing IgG and IgA antibodies within 2-3 weeks from onset of symptoms. Also, neutralizing anti-RBD IgG and anti-NC titers increased and reached a plateau around the fourth week after symptom onset, while IgA decreased by day 28.

IgA is active against several pathogens, including rotavirus, poliovirus, influenza virus, and SARS-CoV-2, it modulates excessive immune responses in inflammatory disorders and it's further effective in engaging neutrophils for cell payoff. Peripheral expansion of IgA plasma blasts with mucosal-homing eventuality has been detected shortly after the onset of symptoms. The contagion-specific antibody responses are intermediated by all isotypes, but IgA contributes to contagion neutralization to a lesser extent compared with IgG and presumably associated with protection against reinfection. During the first six months after-SARS-CoV-2 memory B cell response evolves with accumulation of Ig physical mutations. Participating of VH sequences has been demonstrated between IgA and IgG, suggesting that the same B cells may induce a clone that undergoes progressive selection, specialization and class-switching. In convalescent cases, it has been demonstrated that duplicates of IgM-, IgG-,and IgA- producing B cells decide from common progenitor cells. In addition, dimeric IgA was more potent than IgA monomers and IgG against the same target.

Being a mucosal targeted contagion, SARS-CoV-2 secretory IgA plays an important role in the early defense and viral containment. As we specified over, IgA serum concentrations decreased one month after the onset of symptoms, while negativing IgA remained sensible in saliva for a longer time. A human monoclonal IgA antibody cross-reactive with SARS-CoV and SARS-CoV-2 spike proteins was able to neutralize SARS-Cov-2 infection *in vitro*

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when converted to sIgA. Secretory IgA in the gut and monomeric IgA in the serum are clonally related. sIgA specific for SARS-CoV-2 has been detected in the milk of SARS-CoV-2 infected mothers, thus demonstrating that sIgA is produced in response to the infection and it's passed to the neonate for protection. It has been suggested that also in grown-ups the measurement of SARS-CoV-2 sIgA might help to identify those individualities that, defended by sIgA, In conclusion, the strikingly different course of COVID-19 in cases affected with different antibody deficiencies, including the SIgAD reality, requires in- depth studies. PAD is rare conditions while Picky IgA Deficiency is the most frequent antibody insufficiency, frequently undiagnosed for the deficit of symptoms.

did not develop symptoms and disease.