Possible long-term downsides of antibodies caused by the COVID-19 vaccine

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There is no conflict of interest

Academic researchers, government agencies and pharmaceutical companies have made unprecedented efforts to rapidly develop the COVID-19 vaccine, and have managed to squeeze a process that actually required at least a few years to a few months. As a result, multiple COVID-19 vaccines have now entered the race for widespread application. Most of the preliminary trial results show a strong antibody response and an acceptable adverse effect profile. However, the news of death following the vaccination, though limited, necessitate to examine the question of whether these vaccine-induced antibodies are friend or foe.

One of the most important features of SARS-CoV-2 is the presence of several arginine residues at the S1/S2 cleavage site of the spike protein (S). This unique multibasic furin-like cleavage site may provide a gain-of-function, making SARS-CoV-2 easily enter into the host cell, thus efficiently spreading throughout the human population compared to other betacoronaviruses [1]. Similar to MERS-CoV, the S protein of SARS-CoV-2 may undergo furin-dependent proteolytic processing as it transits through the trans-Golgi network during viral biogenesis. Thus, spike protein is cleaved into S1 and S2 subunits that function in receptor binding and membrane fusion, respectively. S1/S2-cleaved SARS-CoV-2 is further cleaved at S2' domain by target cell protease, TMPRSS2, shortly after membrane receptor angiotensin-converting enzyme 2 (ACE2) binding [1][2]. Subsequently, proteolytic processing at the S1/S2 and S2' cleavage sites removes the covalent linkage between the two functional subunits. This allows shedding of the S1 unit and frees the S2 fusion peptide, which induces refolding of the fusion machinery for the cellular entry of virus [1].

In the light of this short SARS-CoV-2-related immunopathological data, let us consider the question of whether vaccine-induced antibodies can trigger paradoxical negativities? In fact, some studies suggest that these possibilities are not far at all. First, neutralizing antibodies can activate membrane fusion by recapitulating the action of the receptor via a competitive mechanism with the receptor ACE2, leading to the increase cellular entry of the virus even in cells, which do not express ACE2 [3]. Second, post-fusion shedded S1 could act as a decoy fragments that bind and sterically inactivate antiviral antibodies, which may augment viral pathologies [4]. Third, more importantly, a recent study demonstrated that SARS-CoV-2 neutralizing antibody titers in patients recovered from COVID-19 were positively correlated with the severity of lung injury [5]. Finally, although antibodies are fundamentally important components of protective immunity against all pathogens, antibody-dependent enhancement of SARS-CoV-2 entry in immune effector cells appears to be another concern awaiting vaccine [6]. Taken together, we have to reconsider group preferences in vaccination programs and begin to prepare people for the fact that vaccines may not always be as perfect as expected.

References

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