Theory of autoimmunity and COVID-19 Mortality

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The COVID-19 pandemic has become a challenge for health services across the world. Treatment options are limited because the high mortality associated with this disease is not well understood. Understanding is critical to effective management and treatment strategies, and this paper presents a possible explanation for the current struggle to define a solution.

This disease is unusual in that the initial presentation of cough and fever predates the other respiratory and gastrointestinal symptoms by approximately a week. This suggests that the viral infection is not the primary driver of symptoms.

Research has demonstrated that COVID-19 binds to a specific ACE2 receptor that is related to blood pressure regulation and inflammatory responses (balance between ATR1 and ATR2 receptor). This specific target for the coronavirus is located primarily in the lungs and is also present in elevated levels in the serum of patients who have heart failure (Epelman 2008). This soluble form of the receptor in the blood may be the critical link to explain the increased mortality in certain groups of patients.

The combination of the coronavirus and soluble ACE2 receptor would appear antigenic to the immune system and trigger immune responses to multiple proteins that exist within this protein complex. It is likely therefore that antibodies are being produced not only against the coronavirus, but also against specific parts of the ACE2 receptor in an infected person. It has been shown that autoantibodies can be produced against this ACE2 receptor in the case of pulmonary hypertension in systemic sclerosis (Takahashi 2010). In the context of the coronavirus, this immune response appears to be highly likely rather than a mere possibility.

The major cause of mortality with COVID-19 is associated specifically with inflammation secondary to the cytokine storm in the lungs. This inflammatory response presents clinically as Adult Respiratory Distress Syndrome (ARDS) with a high mortality. It is unresponsive to antiviral medication and very difficult to treat. In terms of the timeline, inflammation generally occurs almost two weeks after the infection was contracted, suggesting that the inflammatory component is likely to be the more significant cause of the respiratory symptoms.

The overriding theory for mortality in COVID-19, is that certain individuals may produce antibodies against the virus and their own ACE2 receptors. This causes inflammation in the lungs which can lead to an irreversible response in the form of ARDS. Based on an improved understanding of the disease, it appears that targeting immunity is a path to saving lives.

References

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