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Primary Immunodeficiency Diseases in COVID-19 Pandemic: A Predisposing or Protective Factor?

Dear Editor:

The novel coronavirus disease 19 (COVID-19) is an acute infectious respiratory disorder that emerged from Wuhan, China in the late 2019.[1,2] Due to its rapid distribution, the disease spread globally in a period of three months to the point that as of March 12, 2020 the World Health Organization (WHO) declared COVID-19 a pandemic. According to the latest data, up to mid-July 2020, the number of confirmed cases worldwide passed 13 million; of which about 600 thousand cases had died.[3] Clinical manifestations of affected individuals vary, ranging from asymptomatic to severe alveolar damage resulting in acute respiratory distress syndrome (ARDS).[4,5] Most critical cases are likely to be among elders and men; also, several comorbidities have been identified as risk factors for this viral infection such as diabetes, hypertension, chronic respiratory disease, cancer and cardiovascular disease.[6] These conditions render both the innate and adaptive immune system imperfect in the long-term, making it fail to mount proper immune responses against various pathogens.[7]

In the same context, increasing number of patients with primary immunodeficiency diseases (PIDs) who develop COVID-19 are expected to be seen. Since most PID cases have major defect in at least one component of humoral or cellular immunity, predisposition to viral and bacterial infections is expected.[8] Conversely, the number of reported COVID-19 cases with underlying PID is scarce. To date, only three separate studies have reported PID cases who developed COVID-19: One was a small case series from Italy describing clinical characteristics of 7 cases of primary antibody deficiency (PAD) with COVID-19, the other reported a boy with specific antibody deficiency (SAD) affected with COVID-19 infection; and the third reported 2 cases of X-linked agammaglobulinemia (XLA) who showed pneumonia as COVID-19 manifestations.[9-11] Interestingly, it seems that the severity of PAD negatively correlates with the severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. According to Quinti et al.,[10] patients with agammaglobulinemia who lack B lymphocytes showed milder course of disease and did not require intensive care or mechanical ventilation, as compared to patients with common variable immunodeficiency (CVID) who are characterized by dysfunctional B cells. Similarly, the two XLA cases reported by Soresina et al.[9] recovered from SARS-CoV-2 infection despite developing pneumonia in the setting of B cell deficiency.

These observations, along with other reports, either suggest that T cell response is probably more important in immunity against the virus or highlight the role of B cells in SARS-CoV-2-induced inflammation. Little is known about the exact pathogenesis of this virus; however, it is well-described that hyper-inflammation, as seen in cytokine storm, aggravates the clinical profile of individuals with COVID-19 and is associated with fatality of COVID-19.[7,12] Hence, in these PID cases the intrinsic lack of B cells is considered as an advantage by preventing the development of inflammation. As seen in children who appear to better contain disease due to their immature anti-inflammatory response,[13] it could be postulated that PID patients are surprisingly less likely to develop or experience severe phases of the infection as a result of immune system defect.

Some PID cases with antibody deficiency receive monthly immunoglobulin replacement therapy to compensate for the lack of proper antibody production.[14] Despite limited evidence of efficacy, infusion of polyclonal immunoglobulins that were derived from plasma of healthy donors is used as one of the treatment modalities in COVID-19 patients.[15] Speculation is that the pool of immunoglobulin might possess antibodies with the ability of cross-reacting with SARS-CoV-2 proteins as well as modulatory function on monocytes and macrophages that have a central role in the known cytokine storm.[9,16,17] Therefore, it could be suggested that PID subjects who receive routine immunoglobulin replacement therapy are provided with these antibodies prior to infection.

In the absence of larger and/or thorough data, it remains unclear whether PID is a predisposing or, paradoxically, a protective factor for SARS-CoV-2 infection. Therefore, broader surveys of patients with PID in national and international levels are required to draw more compelling clinical conclusions.

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