State of the Immunological Status of Patients with Post-Covid Pneumonia

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ABSTRACT

During this global pandemic of COVID-19 infection, it became well known that morbidity and mortality is especially high at the extreme of life. This is presumed due to low immunity associated with other comorbid conditions like diabetes, hypertension, cardiovascular disease, obesity and metabolic syndrome. But the information available on the immune status of COVID-19 patients is limited. Adaptive response of increased CD8+ levels in COVID-19 patients seems to be useful in mild cases where it causes deteriorating effects in progressed severe disease patients resulting in destruction of type 2 pneumocytes hence inability to regenerate the alveolar epithelium. A phenomenon called cytokine storm activates violent immunological reactions in the lung tissue resulting in ARDS followed by multiple organ system damages in COVID-19 patients. Immune response to novel coronavirus is complex, involves both innate and adaptive immunity, and is biphasic. Significant differences were observed when comparing severe and non-severe patients. Analysis of the reported results from clinical trials clearly show an involvement of specific cellular immunity (predominantly leucopenia, decreased counts of CD3+, CD4+, and CD8+ T lymphocytes, changes of T cell compartment) and the so-called cytokine storm, which is associated with worsening of symptoms and the promotion of lung damage. An interesting finding regarding eosinopenia that can have both diagnostic and prognostic value is reported by some authors. Examination of selected immune parameters could help to identify severe patients with the risk of unfavorable course of the disease, predict the prognosis and recognize improvement in the clinical status.

Keywords: Immune status, COVID-19, coronavirus, lymphocyte subsets, pneumonia.

Introduction.

In December 2019, the acute viral respiratory diseases named as Coronavirus Disease 2019 (COVID-19) was reported in Wuhan, China. COVID-19 is caused by a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) has listed the novel coronavirus pneumonia epidemic as a public health emergency of international concern. As of April 1, 2020, over 700,000 SARS-CoV-2 infection had been confirmed all over the world.

Due to the lack of specific antiviral drugs and vaccine, own immune status become one of the most crucial factors affecting disease progression and prognosis. The clinical laboratory data of patients revealed that most COVID-19 cases displayed significantly low circulating lymphocyte counts, especially severe patients admitted to ICU1. In pneumonia, the lungs become filled with fluid and inflamed, leading to breathing difficulties. For some

people, breathing problems can become severe enough to require treatment at the hospital with oxygen or even a ventilator. The pneumonia that COVID-19 causes tends to take hold in both lungs. Air sacs in the lungs fill with fluid, limiting their ability to take in oxygen and causing shortness of breath, cough and other symptoms. While most people recover from pneumonia without any lasting lung damage, the pneumonia associated with COVID-19 can be severe. Even after the disease has passed, lung injury may result in breathing difficulties that might take months to improve. The clinical features of COVID-19 are diverse and range from asymptomatic to critical illness and death. Severe and critical cases represented 14% and 5% of laboratory-confirmed COVID-19 patients, respectively. This posed a high burden to the healthcare system as it consumed most of its medical resources and contributed to the majority of deaths. A phenomenon called cytokine storm activates violent immunological reactions in the lung tissue resulting in ARDS followed by multiple organ system damages in COVID-19 patients.

Th1 type immune reaction is the main component of adaptive immunity to most viral infections including coronaviruses. IgM antibodies tailor out at the end of the 12th week of viral entry whereas IgG antibodies last longer (6). Preliminary test results in COVID-19 patients have shown peak IgM at day 9 followed by a shift to IgG by 2nd week (1). The latest reports show a reduced number of CD4+ and CD8+ lymphocytes in COVID-19 patients(7) Along with lower lymphocytes counts, sever cases have elevated leukocytes counts and neutrophil-lymphocyte-ratio (NLR) and also decreased number of monocytes, eosinophils, and basophils (8).

One of the main protective characteristics of humoral immunity is the production of neutralizing antibodies against pathogens, which boosts the defense and recovery process of the infected body. Neutralizing antibodies efficiently block the entry of viruses into the target cells and may lead to the clearance of virus-infected and antigen displaying cells via the involvement of other immune components such as phagocytes and natural killer cells [7].

The disease is show increase levels of inflammatory cytokines and lower numbers of lymphocytes, monocytes, eosinophils,
and basophils, and negatively correlated with higher leukocyte counts (including neutrophils). The most affected lymphocytes in COVID-19 patients were T cells including helper ($CD4^+$) T cells, cytotoxic or suppressor ($CD8^+$) T cells, regulatory T cells, and memory T cells [8]. Moreover, in the early stages of SARS-CoV-2 infection, not only the total number of natural killer (NK) and cytotoxic T cells was markedly decrease, also their function was significantly impaire [9].

Memory T cells are T cells that have previously encountered their antigen and may be either $CD4^+$ or $CD8^+$ cells. They can be further subdivided into stem memory, central memory, effector memory, or tissue-resident memory T cells and are characterized by their expression of CCR7 and L-selectin and whether they continue to circulate in the bloodstream (as with stem, central, and effector cells) or reside in peripheral tissues until activated (as with tissue-resident cells). These cells are defined by their ability to mobilize quickly into activated T cells to initiate a sufficient immune reaction in response to a previously encountered immune challenge.

Natural killer T (NKT) cells (separate and distinct from natural killer cells, which are part of the innate immune system) may be either $CD4^+$ or $CD8^+$ or they may be double negative, expressing neither CD4 nor CD8. They recognize and respond to glycolipid antigens such as CD1d rather than peptide antigens presented by MHC class I. Activation of NKT cells leads to the production of IFNγ, which polarizes Th1 cells, and IL-4, which polarizes Th2 cells. The rapid production of T helper cells enhances the response of the immune system to challenge by mobilizing DCs, cytotoxic T cells, B cells, and macrophages.

Conclusion.

Understanding of the immune status of COVID-19 patients must be attempted with all the available limited research data and known knowledge on other coronaviruses. We characterized the clinical course and its

correlated immune function of patients with COVID-19 pneumonia. The decrease of $CD3^+$, $CD4^+$ and $CD8^+$ T lymphocyte correlated with the course of patients with COVID-19 pneumonia, especially in severe cases. The level of T lymphocyte could be used as an indicator for prediction of severity and prognosis of patients with COVID-19 pneumonia. This understanding must be remembered while devising and formulating strategies for development of vaccines and therapies for COVID-19 infection to enhance the outcome.

Literature.

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