Immune Response and Immunobiology COVID-19 (Coronavirus Disease 2019)

Rachmat Hidayat¹#, Patricia Wulandari²

¹Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
²Cattleya Mental Health Center, Palembang, Indonesia

*Corresponding author:
Rachmat Hidayat
Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
Email: dr.rachmat.hidayat@gmail.com

ABSTRACT

SARS-CoV-2 not only activates an antiviral immune response but can also cause an uncontrolled inflammatory response characterized by the marked release of proinflammatory cytokines in patients with severe COVID-19, leading to lymphopenia lymphocyte dysfunction, and granulocyte and monocyte abnormalities. The immune pattern of COVID-19 includes lymphopenia, lymphocyte activation and dysfunction, granulocyte and monocyte abnormalities, increased cytokine production, and increased antibodies.

Keywords: COVID-19, SARS-CoV2, immunobiology
Introduction

The main principle of the immune system against microbes is divided into two types, namely, the innate immune system and the adaptive immune system. The innate immune response to microbes is rapid and non-specific, whereas the adaptive immune response is specific to microbes and has memory cells used when microbes re-infect. In general, the innate and adaptive immune systems play a direct role in eradicating viruses. Studies on the immune response of patients with SARS-CoV-2 infection found a lower lymphocyte count, as well as a lower percentage of monocytes, eosinophils, and basophils in severe cases of COVID-19.\(^1\)

SARS-CoV-2 not only activates the antiviral immune response but can also induce an uncontrolled inflammatory response characterized by the marked release of proinflammatory cytokines in patients with severe COVID-19, leading to lymphopenia, lymphocyte dysfunction, and granulocyte and monocyte abnormalities. The immune pattern of COVID-19 includes lymphopenia, lymphocyte activation, and dysfunction, granulocyte and monocyte abnormalities, increased cytokine production, and increased antibodies. Lymphopenia is a major feature of patients with COVID-19, especially in severe cases. CD69, CD38, and CD44 were highly expressed on the patient's CD4+ and CD8+ T cells, and virus-specific T cells from severe cases displayed a central memory phenotype with high levels of IFN-γ, TNF-α, and IL-2. However, lymphocyte dysfunction exhibits an exhaustion phenotype with programmed cell death protein-1 (PD1), T cell immunoglobulin domain and mucin domain-3 (TIM3), and an increase in the killer cell lectin-like receptor subfamily C member 2 (NKG2A) subfamily. Neutrophil levels were significantly higher in severe patients, while the percentages of eosinophils, basophils, and monocytes were reduced. Increased production of cytokines, particularly IL-1β, IL-6, and IL-10, is another major characteristic of severe COVID-19. The number of IgG cells also increased, and there was a higher total antibody titer in COVID-19 patients.\(^2,3\)

Humoral immune response

The humoral immune response is an antibody-mediated immune response. T cell helper helps B cells differentiate into plasma cells, which in turn produce antibodies (Abs) that are specific for viral antigens (Ag). In order to limit the infection, antibodies neutralize and completely block the virus from entering the host cells and therefore play a very strong protective role in the later stages of infection and also prevent the recurrence of infection in the future. In the case of SARS-CoV, to enhance the humoral immune response, both B and T cell
epitopes are being studied extensively and mapped for their structural and envelope proteins (S, N, M, E).4,5

During the study of SARS-CoV-2 infection, it was discovered that ACE2 (angiotensin-converting enzyme 2) is a receptor present in host cells. When the SARS-CoV-2 virus invades a host, it is first recognized by the angiotensin-converting enzyme (ACE) 2 receptor present on respiratory epithelial cells that allows virus entry. After viral replication inside the cell, the virus is released, where it meets the host's innate immune system. T lymphocytes and dendritic cells are activated via pattern recognition receptors (PRR), including the C-type lectin-like receptor, Toll-like receptor (TLR), NOD-like receptor (NLR), and RIG-I-like receptor (RLR). The virus induces the expression of various inflammatory factors, the synthesis of type I Interferon (IFN), which limits the spread of the virus and accelerates macrophages' phagocytosis of the virus, which results in clinical recovery and stimulates dendritic cell maturation. SARS CoV-2 attacks pneumocytes (both types I and II) and alveolar macrophages. After infection to the host cell, the virus will carry the antigen presented to the antigen-presenting cells (APC). Antigen presentation further stimulates the body's humoral and cellular immune responses mediated by virus-specific T and B cells. The adaptive immune response joins the fight against the virus. The emergence of adaptive humoral immunity in response to SARS-CoV-2 occurs within the first 7 to 10 days of infection. Strong B-cell memory and plasmablast expansion were detected early in infection with the secretion of serum IgM and IgA antibodies on days 5 to 7 and IgG on days 7 to 10 from the onset of symptoms. In general, serum IgM and IgA titers decreased after 28 days, and IgG titers peaked at day 49. Humoral immunity, including complement factors such as C3a and C5a and 11 specific B-cell-derived antibodies, is also important in combating SARS-CoV-2 infection.6,7

These mature dendritic cells have the ability to activate naive T cells and initiate T-cell responses. When the virus enters the cell, the viral antigen will be presented to the antigen-presenting cells (APC). Then via MHC class II, viral antigens are carried to naive T cells and initiate T cell responses. Helper T cells also play a role in isotype switching, and in the case of SARS-CoV, the antibody profile of this virus produces IgM and IgG, and in a later phase, seroconversion has been observed mediated by helper T cells. IgM disappears by the end of the 12th week, whereas IgG has been found to persist longer, suggesting the possibility of IgG being a strong Ab protector during infection. The current evidence strongly suggests that this type of Th1 response is key to successful control of SARS-CoV and mer-CoV and may be true for SARS-CoV-2 as well.8
Cellular immune response

Cellular immune response is a mechanism of adaptive immunity. Cellular immunity differs from the humoral immune response seen in infected cells, which is mediated by T-lymphocytes. T cells consist of CD4+, CD8+, and NK cells. Mature T cells that leave the thymus but have not been exposed to antigens are called Naive T cells. When naive T cells are exposed to MHC-bound antigens that are presented by APCs or are said to stimulate specific cytokines, they develop into subsets of CD4+ and CD8+ T cells with different effector functions. Helper T cells direct the overall adaptive immune response, while cytotoxic T cells play an important role in the clearance and killing of virus-infected cells. T lymphocytes, including CD4+ and CD8+ T cells, play an important role in this defense.\(^9,^{10}\)

Cluster differentiation is a cell surface molecule that is expressed on various types of immune system cells, indicated by numbering. CD4 is a glycoprotein expressed on the surface of helper T cells, regulatory T cells, monocytes, macrophages, and dendritic cells. Antigen captured, processed, and presented by macrophages in the context of Major Histocompatibility Complex II (MHC II) to CD4 cells. The CD4 count is reported as the number of cells in cubic
millimeters of blood. In healthy people, the CD4 count ranges from 500 to 1500 cells per cubic millimeter. CD4 cell counts were considered to have good predictive value within no more than 6 months of examination. Like CD4, CD8 is a transmembrane glycoprotein. However, CD8 is predominantly expressed on the surface of cytotoxic T cells but can also be found on Natural Killer (NK) cells, thymus cortical, and dendritic cells. These CD8 T-cells recognize the MHC-1 antigen complex presented by the Antigen Presenting Cell (APC). The CD8 count in healthy people is between 150 and 1000 cells per millimeter cubic

CD4+ T cells stimulate B cells to produce virus-specific antibodies while CD8+ T cells stimulate B cells to produce virus-specific antibodies while CD8+ T cells are able to directly kill virus-infected cells. T Helper produces proinflammatory cytokines to help defense cells. However, SARS CoV-2 can inhibit T cells by inducing programmed cell death (apoptosis).  

Referring to cases of infection caused by severe acute respiratory syndrome coronavirus and middle east respiratory syndrome coronavirus, it was reported that CD4+ memory T cells (TNFα, IL-2, and IFN) and CD8+ (TNFα, IFNγ) could survive in SARS-CoV patients. recovered for 4 years and were able to function by multiplying T cells, producing IFN-gamma, and by responding to DTH. When investigating 14 of 23 patients who recovered from SARS after 6 years of infection, it was reported that different memory T cells responded to the SARS-CoV S peptide. Hence, this information can also be useful in the case of SARS-CoV-2. However, in the case of SARS-CoV-2, recent reports have shown that peripheral blood mononuclear cells (PBMCs) from SARS-CoV-2-infected persons have shown an efficient reduction in the number of CD8+ and CD4+ cells, which may result in the generation of memory T cells disturbed and persistence in SARS-CoV-2 survived.

Simultaneously with the emergence of adaptive humoral immunity, SARS-CoV-2 activates T cells in adaptive cellular immunity in the first week of infection, and virus-specific memory CD4+ cells and CD8+ T cells were reported to peak in the second week but were still detectable in numbers. Lower cells for 100 days or more (Figure 2).
Conclusion

SARS-CoV-2 not only activates the antiviral immune response but can also induce an uncontrolled inflammatory response characterized by the marked release of proinflammatory cytokines in patients with severe COVID-19, leading to lymphopenia, lymphocyte dysfunction, and abnormalities in granulocytes and monocytes.

References


