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Mini-Review

Effect of COVID-19 on Immune System

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Introduction

During December 2019, there were many reports of pneumonia type incidences caused by some unidentified viral strain outbroke in Wuhan, China. The disease clinically resembled some new type of viral pneumonia and Flu. After the isolation of the virus and several analyses of its genomic sequence, a novel strain of coronavirus was identified which was designated as 'Severe Acute Respiratory Syndrome-Related Coronavirus-2' or SARS-CoV-2. The respiratory diseases were caused by this newly discovered 'SARS-CoV-2' which was later declared as 'Coronavirus disease 2019' (COVID-19) by World Health Organization.

COVID-19 virus is a member of a large group of viruses called corona viruses. These viruses are enveloped having single strand RNA. They called corona virus due to their crown-like morphology. They infect most of mammals and birds causing respiratory, enteric, hepatic, and neurologic diseases [1]. So far, seven species of corona viruses are known to cause human infection. Most of these human corona viruses have zoonotic origin. The four human corona viruses: HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 are endemic and prevalent [2]. Middle East respiratory syndrome corona virus (MERS-CoV) and newly identified sever acute respiratory syndrome corona virus (SARS-CoV2) are highly transmissible and pathogenic for human [3]. SARS-CoV2 has been identified as cause of corona virus disease 19 which is responsible for recent pandemic which occurred in 2019, hence the disease called COVID-19. Human corona disease (COVID-19) was first reported in Wuhan, China and rapidly spread all over the world infecting millions of people in every country of the world. SARS-CoV2 is member of the β-coronavirus

family which has extensive genetic similarities with bat coronavirus suggesting that bats are the natural host of this virus [4].

When COVID-19 virus enters body via respiratory airway binds to the angiotensin converting enzyme 2(ACE2) through spike (S) of the virus that covers surface of virus [5]. Once virus bind to its receptor which is present on the cell, it penetrates into the cell and start replication process then newly developed virus exit the infect cells by budding outward then released for doing more invasion. ACE 2 is present on various organs cells like: heart, kidney, testis, and respiratory epithelial cells [6]. When a host cell that has ACE 2 on its surface meet the COVID-19 virus would get infected then following release of new virus from infected cell, the spike of COVID-19 virus appears on its surface (during the budding out of the new virus); thus, this cell also would be the target of immune response alike the free virus itself [7].

The pathogenesis of COVID-19 is as result of an abnormal host immune response due to local production of large number of inflammatory cytokines, chemokines and free radicals that can damage to lungs or other organs that have receptor for the virus [8]. COVID-19 infection induces pneumonia which is characterized by fever, cough, dyspnea, and bilateral infiltrates [9]. Edema and inflammatory clusters with fibrinoid material and multinucleated giant cells have also been reported in lungs of COVID-19 infected patients [10].

Immune response against COVID-19 start after virus invades host and bind to its receptor. Following viral penetrating cell and replication within cell, the virus is released where it is met by host's innate immune system. T lymphocytes and dendritic cells are activated through pattern recognition receptors (PRRs) including C-type lectin-like receptors, Toll-like receptor (TLR), NOD-like receptor (NLR), and RIG-l-like receptor (RLR). The virus induces the expression of numerous inflammatory factors, maturation of dendritic cells and synthesis of type 1 interferons (IFNs) which limits the viral spread and accelerates macrophage phagocytosis of viral antigens resulting in clinical recovery. However, the nucleus protein (N) od SARS-CoV2 can help the virus escape from the immune responses and overreaction of the immune response generates high levels of inflammatory mediators and free radicals. These processes induce sever local damage to lungs and other organs causing multi-organ failure and even death. The adaptive immune response also has major role in fighting against virus. T lymphocytes including CD4+ and CD8+ T cells play an important role in this defense. CD4+ T cells stimulate B cells to produce virus-specific antibodies IgM and IgG which can kill virus infected cells by antibody dependent cytotoxicity, but CD8+ T cells are able to directly kill virus infected cells [11]. CD4+ helper T cells also produce pro-inflammatory cytokines to help defending cells. In spite of all these host's defense mechanisms, SARS-CoV2 can inhibit T cells functions by inducing programmed cell death (apoptosis) [12]. Cytotoxic lymphocytes (CTLs) and natural killer cells (NKs) are also important for control of viral infection; thus, decreased number of these cells may increase severity of diseases. In patients with COVID-19 the total number of NK and CTL are decreased in line with upregulation of NK inhibitory receptor CD94 [13]. Decreased number of CD4+ and CD8+ T cells in peripheral blood of COVID-19 infected patients increase proportion of HLA-DR (CD4+ 3.4%) and CD38 (CD8+ 39.4%) double-positive cells indicating highly activated cells [14]. In addition, it has been reported that activation of CD4+ and CD8+ are impaired which is evidenced by appearance of CD25, CD28, and CD69 expression on these T cell subsets [15]. These factors may account for the delay development of adaptive immune response and prolonged virus clearance in patients with sever cases of COVID-19 infection [16].

The cytokine storm syndrome is another manifestation id some of COVID-19 patients which is result of a hyperactivity of the immune system. In this condition the regulation of immune cells is often defective, resulting in the increased production and release of inflammatory mediators in blood stream by immune effector cells. These mediators are: INF-α, INF-δ, IL-1β, IL-6, IL-12, IL-18, IL-33, TNF-α, and TGF-β as well as certain chemokines such as CCL2, CCL3, CCL5, CXCL8, CXCL19 and CXCL10 [17]. Clinical symptom of cytokine storm is fever and confusion and laboratory tests show hyperferritinemia, lymphopenia, prolonged prothrombin time, elevated lactate dehydrogenase, elevated IL-6, elevated C-reactive protein, and elevated soluble CD25 [18].

Discussion

Since December 2019 that SARS-CoV2 was identified in several hospitalized patient in Wuhan, Hubei Province in China, until now several thousand research articles have been published describing many aspects of this highly transmissible and infectious virus that caused the viral pandemic of the current century. All research aims were focused on mechanisms of viral spread, infectivity, diagnosis host defense, treatment, and best strategy for vaccine development controlling the viral pandemic. In order to achieve most of these goals, studying mechanism(s) of host defense has been very crucial. Today, scientist unveil a lot of important information about immune response against COVID-19. Now we know that immune response to SARS-Cov2 begin with innate immune response get activated by free virus or infected cells and followed by activation of humoral and cellular immune response in order to kill virus and/or infected cells of the various organs that have ACE2 which act as COVID-19 virus receptor. The process of killing infected cell cause damage of organ which is the cause of certain clinical symptoms like sever respiratory syndrome, heart failure or kidney failure seen in many patients. Even though in patients with COVID-19 the white blood cell count may vary between leukopenia, leukocytosis, and lymphopenia, it seems that white blood cell counts in COVID-19 infected patients is very important indicator for prognosis of disease in patient [19]. It has been shown that lower lymphocyte counts indicated a poor prognosis. However, we do not know why some people get infected but that do not show any clinical symptoms or many patients suffer from mild infection the others very sever one. In addition, the reason for the resistance of children to COVID-19 is also unknown. Even though many vaccines have been developed and we know both humoral and cellular immune response are responsible for host defense but we do not know what titer of antibody provide sufficient immunity against re-infection or even if cellular immunity provide long term immunity. **In my opinion the cell mediated immunity has crucial role in immunity against COVID-19 infection and for monitoring immunity against reinfection we should test cellular immunity parameters such as absolute number of DC3+, CD4+, CD8+, CD19+, CD16+, and CD46+ as well as COVID-19 specific cytotoxic T cells instead of humoral immunity parameter such as anti IgG titer**. For treatment protocols or drug developments gap is even much further and serious research needs are felt.

Bibliography

1. Farashi-Bonab, F., Sarrafnejad, F. & Khansari, N. (2020). Corona virus disease 19 the large-scale corona pandemic. *CPQ Microbiology, 4,* 1-3.

2. Corman, V. M., Muth, D., Niemeyer, D., *et al.* (2018). Hosts and sources of endemic human coronaviruses. *Advances in Virus Research, 100,* 163-188.

3. Assiri, A., McGeer, A., Perl, T. M., *et al.* (2013). Hospital outbreak of Middle East respiratory syndrome coronavirus. *N. Engl. J. Med., 369*(5), 407-416.

4. Huang, C., Wang, Y., Li, X., *et al.* (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet, 395*(10223), 497-506.

5. Xu, X., Chen, P., Wang, J., *et al.* (2020). Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Life Sci., 63*(3), 457-460.

6. Tikellis, C. & Thomas, M. C. (2012). Angiotensin-converting enzyme 2 (ACE2) is a key modulator of renin angiotensin system in health and disease. *Int. J. Pep., 2012,* 256-294.

7. Imai, Y., Kuba, K., Rao, S., *et al.* (2005). Angiotensin-converting enzyme2 products from sever acute lung failure. *Nature, 436*(7047), 112-116.

8. Channappanavar, R. & Perlman, S. (2017). Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Semin. Immunopathol., 39*(5), 529-539.

9. Wang, D., Hu, B., Hu, C., *et al.* (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA., 323*(11), 1061-1069.

10. Tian, S., Hu, W., Niu, L., *et al.* (2020). Pulmonary pathology of early-phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. *J. Thorac. Oncol., 15*(5), 700-704.

11. Mortaz, E., Tabarsi, P., Varaham, M., Folkerts, G. & Adcock, I. A. (2020). The immune response and immunopathology of COVID-19. *Frontiers in Immunology, 11,* 2037-2045.

12. Ruoan, Q., Yang, K., Wang, W., Jiang, I. & Song, J. (2020). Clinical prediction of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med., 46,* 846-848.

13. Norbury, C. C., Malide, D., Gibbs, J. S., Bennink, J. R. & Yewdell, J. W. (2002). Visualizing priming of virus-specific CD8+ T cells *in vivo. Nat. Immunol., 3*(3), 265-271.

14. Xu, Z., Shi, I., Wang, Y., *et al.* (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Resp. Med., 8*(4), 420-422.

15. Cai, C., Zeng, X., Ou, A. H., Huang, Y. & Zhang, X. (2004). Study on T cell subsets and their activated molecules from the convalescent SARS patients during two follow-up surveys. *Chinese J cell. Med. Immunol., 20*(3), 322-324.

16. Cameron, M. J., Bermejo-Martin, J. F., *et al.* (2008). Human immunopathogenesis of sever acute respiratory syndrome (SARS). *Virus Res., 133*(1), 13-19.

17. Williams, A. E. & Chamber, R. C. (2014). The mercurial of neutrophils still an enigma. *J. Physiol. Lung Cell Mol. Physiol., 306*(3), 1217-1230.

18. Lei, C., Huigo, I., Liu, I., Liu, K., *et al.* (2020). Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Chin. J. Tuberc. Respir. Dis., 43,* E005.

19. Yang, S., Yu, Y., Xu, J., *et al.* (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir. Med., 8*(5), 475-481.