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General Aspects of the Inflammatory Reaction in COVID-19

Aspectos Gerais da Reação Inflamatória na COVID-19

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ABSTRACT

Today, we are faced with one of the most contagious viral infections in history, the pandemic produced by the SARS-CoV-2 coronavirus, the etiologic agent of the WHO-appointed Organization as COVID-19. Coming to the attention of many in late 2019, COVID-19, which already existed prior to that date, gained great prominence after promoting a pandemic that lasted through the years 2020 and 2021 and claimed thousands of victims worldwide. Because its pathogenesis and mechanism of attack were practically unknown and little studied at the time, health organizations could do little in a short period of time, and many people from all parts of the world suffered the consequences of the disease, directly or indirectly. The side effects for each citizen were often different, ranging from the symptoms of a common cold to a severe acute respiratory syndrome, and becoming more lethal in patients with diabetes, hypertension, kidney failure, obesity, and cardiovascular disease, among others. From then on, the existence of numerous clinical forms in COVID-19 was realized and the need for studies to elucidate how each one works by understanding the specific role of TCD4+ and TCD8+ lymphocytes in directing inflammation, as well as understanding how the reaction happens and what "motivates" the lymphocytes to promote it (SURYASA et al., 2021; SETTE, CROTTY, 2021; GALVÃO, DELLALIBERA-JOVILIANO 2022).

Keywords: Inflammatory infections, Covid-19, Virus infections.

INTRODUCTION

Today, we are faced with one of the most contagious viral infections in history, the pandemic produced by the SARS-CoV-2 coronavirus, the etiologic agent of the WHO-appointed Organization as COVID-19. Coming to the attention of many in late 2019, COVID-19, which already existed prior to that date, gained great prominence after promoting a pandemic that lasted through the years 2020 and 2021 and claimed thousands of victims worldwide. Because its pathogenesis and mechanism of attack were practically unknown and little studied at the time, health organizations could do little in a short period of time, and many people from all parts of the world suffered the consequences of the disease, directly or indirectly. The side effects for each

citizen were often different, ranging from the symptoms of a common cold to a severe acute respiratory syndrome, and becoming more lethal in patients with diabetes, hypertension, kidney failure, obesity, and cardiovascular disease, among others. From then on, the existence of numerous clinical forms in COVID-19 was realized and the need for studies to elucidate how each one works by understanding the specific role of TCD4+ and TCD8+ lymphocytes in directing inflammation, as well as understanding how the reaction happens and what "motivates" the lymphocytes to promote it (SURYASA et al., 2021; SETTE, CROTTY, 2021; GALVÃO, DELLALIBERA-JOVILIANO 2022).

2 OBJECTIVE

To evaluate the role of TCD4 + and TCD8 + lymphocytes in promoting an inflammatory reaction in COVID19, studying the mechanism of action of these cells, their activation, effects on the body, and immunomodulation from a literature review.

3 METHODOLOGY

A retrospective study of the topic was conducted from international literature found on the electronic platforms PubMed and SCIELO, using the uniterms: COVID-19, inflammation, and TCD4+ and TCD8+ lymphocytes. The scientific articles chosen were published between the years 2020 and 2023, not and projects prior to 2020 were chosen. The prerequisites for the choice of articles were recent publication dates, subjects that cover the proposed theme, and that demonstrate lymphocyte regulation and pro-inflammatory markers. All information that did not embrace these previously selected were disregarded.

4 DEVELOPMENT

COVID 19 is a viral disease caused by the SARS-CoV-2 virus, presenting asymptomatic cases up to severe cases with risk of death. Many times it is common to have an inflammatory aggravation, occasionally excessive, related to the modifications that the virus leads to the leukocyte count, the elevation of C-reactive protein and the viral load with which the individual gets infected (the higher it is, the worse the infection is) (PACES et al., 2020). It all starts with the TCD4+ lymphocytes, which when faced with a new infection release early pro-inflammatory cytokines into the circulation, such as TNF-alpha and INF-gamma, which activate the cytotoxic TCD8+ lymphocytes, cells of the adaptive immune system, which promote cellular toxicity, destroying the infected cells and thus also the reservoir and the machinery that the virus uses to

replicate. Occasionally, cytokine release can be exacerbated, causing a so-called "cytokine storm," which in addition to causing tissue damage in patients can lead to septic shock (SETTE, CROTTY, 2021). Cellular toxicity caused by lymphocytes occurs through cell lysis. Cytotoxic TCD8+ lymphocytes have cytoplasmic granules in their cytoplasm that contain proteins such as perforins and granzymes. These proteins are transported to the infected cell through contact between the membranes of the lymphocyte and the target cell, exocytosis occurs, and the proteins pass through, inducing cytotoxicity to the host cell. For example, perforins produce pores on the surface of the plasma membrane, which leads to lysis (COSTA SILVA et al., 2022).

Relating obesity as a potential risk factor for death in COVID 19, recent studies have discovered a close relationship between the human body's lipid metabolism and the inflammatory reaction of the disease. This happens thanks to the existence of lipid droplets intracellularly, which apparently can facilitate and potentiate the viral replication of SARS-COV 2 within the host cell , aggravating its pathogenesis (MUNAVALLI et al., 2022). Probably the virus regulates lipid metabolism and causes de novo synthesis and lipid remodeling to increase, raising the amount of droplets inside the cells. The means by which the virus performs this feat is still unknown. Moreover, there is a close relationship between lipid droplets and the production of inflammatory mediators and innate signaling from immune cells, producing a more pronounced inflammatory response through the increased release of pro-inflammatory cytokines and chemokines in obese and overweight (NADER, NADER, DELLALIBERA, DELLALIBERA-JOVILIANO, 2023; NADER et al, 2023). This explains why the population with these phenotypic characteristics suffer such lethal pictures of the disease. It has been shown that monocytes infected with SARS-COV 2 began to synthesize more leukotrienes (LTB4), more chemokines such as IL-8 and CXCL 10, more inflammatory cytokines such as IL-6, TNF-alpha , IL-10 and IL-12, and decreased the manufacture of IL-4, an anti-inflammatory cytokine. Diacylglycerol acyltransferase 1(DGAT-1) can be used to inhibit lipid droplets , making the infection milder and increasing the amounts of IL-4 (DIAS et al., 2020; PACES et al., 2020; NADER et al., 2023). Exacerbated inflammation in COVID 19 may also be associated with the pro-inflammatory cytokine

IL-6, released during illness. This cytokine has numerous functions in the immune system, promoting the differentiation of B lymphocytes, cytotoxic T lymphocytes, and the functions of macrophages and monocytes. However, many times, some individuals develop the severe form of the disease, producing high Il-6, which starts to influence a deficient and negative viral immune response, impairing the functionality of TH1 cells and cytotoxic TCD8+ lymphocytes in promoting cell lysis (MUNAVALLI et al., 2022). Furthermore, IL-6 overexpression causes

lymphocytopenia and a drop in immunoglobulin production, which leads to further impairment in opsonization. In order to inhibit IL-6 and decrease its damage, a therapy using anti-IL-6 serum has been developed, which has shown positive results in blocking the interleukin and appears to be non-harmful to SARS-COV 2 immunity in the long term. The anti-IL-6 serum declined inflammatory markers such as CRP and furthermore increased the rate of lymphocytes and antibodies, as well as their immune responses. The study showed that after one of treatment with the serum, antibody levels remained high and much higher than in patients who did not receive therapy, showing better INF-gamma responses and less propensity for infectivity (MASIÁ et al., 2022).

5 CONCLUDING REMARKS

Having seen how cellular immunity and inflammation occur in COVID 19, it is possible to notice certain cases of aggravation that totalize the disease and require treatments that help to improve the clinical picture and prevent sequelae and the chance of death. The analysis of monocytes from patients infected with the pathology showed that these cells have an accumulation of lipid droplets, and the explanation is based on the summoning of transcription factors for lipogenesis after 24 hours of infection. This alteration in lipid metabolism may function as an important finding for the discovery of SARS-COV 2, because the droplets function as a "phenotype" for the disease. The use of DGAT-1 inhibits acyl-COA and disrupts lipid metabolism, preventing prognosis in patients using it. Similarly, anti-IL-6 serum therapy prevents against an inflammatory exacerbation by inhibiting IL-6 and its receptors, and is recommended for the treatment of patients with the severe form of disease. Thus, it is concluded that knowledge of what occurs in the human body when it is infected with the SARS-COV 2 virus is of utmost importance, as a good understanding of this process may be crucial for finding key treatments for the various clinical forms of COVID 19.

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