General aspects of the inflammatory reaction to COVID-19

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1 INTRODUCTION

We are currently facing one of the most contagious viral infections in history, the pandemic produced by the SARS-CoV-2 coronavirus, the etiological agent of the WHO Organization as COVID-19. Coming to the attention of many at the end of 2019, COVID-19, which already existed before that date, gained great prominence after promoting a pandemic that lasted the years 2020 and 2021 and claimed thousands of victims around the world. Because its pathogenesis and mechanism of attack were practically unknown and little studied so far, health organizations could do little in a short period of time, and several people from all over 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, cardiovascular diseases, among others. From there, it was realized that there are numerous clinical forms of COVID-19 and the need to carry out studies that elucidate how each one works by understanding the specific role of TCD4+ and TCD8+ lymphocytes in directing inflammation, in addition to understanding how the reaction happens and what "motivates" 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 bibliographic review.

3 METHODOLOGY

A retrospective study of the theme was carried out based on international literature found on the PubMed and SCIELO electronic platforms, using the keywords: COVID-19, inflammation and TCD4+ and TCD8+ lymphocytes. The scientific articles chosen were published between the years 2020 and 2023, not in the same period.

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 regulation of lymphocytes 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. It is often common to have an inflammatory exacerbation, 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 becomes infected (the higher it is, the worse the infection) (PACES et al., 2020). It all starts with TCD4+ lymphocytes, which in the face of a new infection release early pro-inflammatory cytokines into the circulation, such as TNF-alpha and INF-gamma, which activate 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, the release of cytokines can be exacerbated, causing the so-called "cytokine storm", which in addition to causing tissue damage in patients can lead to septic shock (SETTE, CROTTY, 2021). Cell 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 lipid metabolism of the human body 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 inside the host cell, aggravating its pathogenesis (MUNAVALLI et al., 2022). The virus probably regulates lipid metabolism and causes de novo synthesis and lipid remodeling to increase, raising the amount of droplets inside cells. The means by which the virus accomplishes this feat is still unknown. In addition, there is a close relationship between lipid droplets and the production of inflammatory mediators and innate immune

cell signaling, producing a more pronounced inflammatory response through the increased release of pro-inflammatory cytokines and chemokines in obese people and those with HIV. overweight (NADER, NADER, DELLALIBERA, DELLALIBERA-JOVILIANO, 2023; NADER et al, 2023). This explains why the population with these phenotypic characteristics suffers such lethal disease conditions. SARS-COV 2-infected monocytes have been shown 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 manufacture of IL-4, an anti-inflammatory cytokine. Diacylglycerol acyltransferase 1 (DGAT-1) can be utilized to inhibit lipid droplets, making the infection milder and increasing IL-4 amounts (DIAS et al., 2020; PACES et al., 2020; NADER et al., 2023). The exacerbated inflammation in COVID 19 may also be associated with the pro-inflammation 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, some individuals often develop the severe form of the disease, producing Il-6 at a high rate, 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). Moreover, IL-6 overexpression causes lymphocytopenia and a decrease in immunoglobulin production, which leads to additional impairment in opsonization. In order to inhibit IL-6 and decrease its damage, a therapy using anti-IL-6 serum was developed, which showed positive results in blocking the interleukin and seems not to be harmful to SARS-COV 2 immunity in the long term. The anti-IL-6 serum decreased inflammatory markers such as CRP and in addition, increased the rate of lymphocytes and antibodies, as well as their immune responses. The study showed that after one treatment with the serum, antibody levels remained high and much higher than in patients who did not undergo therapy, showing better INF-gamma responses and less propensity for infectivity (MASIÁ et al., 2022).

5 FINAL CONSIDERATIONS

Having seen the way in which cellular immunity and inflammation occur in COVID 19, certain cases of aggravation that total the disease are perceived and require treatments that help to improve clinical conditions and prevent sequelae and the chance of death. The analysis of monocytes from patients infected with the pathology showed that these cells present 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, as the droplets function as a "phenotype" for the disease. The use of DGAT-1 inhibits acyl-COA and disrupts lipid metabolism, thus avoiding the prognosis of patients using it. Similarly,

anti-IL-6 serum therapy prevents an inflammatory exacerbation by inhibiting IL-6 and its receptors, and is recommended for the treatment of patients with the severe form of the disease. Thus, it is concluded that knowledge of what occurs in the human body when it is infected by 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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