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Defense Mechanism of the Immune System Against Hepatitis C Infection

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***Keywords*— Genetic, Hepatitis C, Immune system.**

***Abstract*—** *Hepatitis C is an inflammatory process caused by a virus of the genus Hepacivirus. It can be triggered acutely or chronically, the latter being predominant. Chronic hepatitis C (CHC) has a worldwide prevalence in about 1% of the population. Hepatitis C virus infection (HCV) has a diverse genetic variety, which makes its elimination difficult.The present work emerges as a need to understand the mechanisms of defense action against HCV in the human body. The study was based on a literature review, based on research in articles from the SciELO and PubMed platforms, using the descriptors hepatitis C, genetics and immune system associated through the Boolean operators OR and AND. In the end, 15 articles were selected that guided the research of the work. In research, it was found that the virus infection can present in the acute phase or in the chronic phase, in which most cases tend to progress from an acute infection barely detectable by the immune system to a persistent chronic infection. In addition, it was observed that T cells during the chronic phase have their ability to resolve reduced, because, in the acute phase, because of the virus, a large variability does not allow T cells to create neutralizing antibodies or memory cells, therefore, when they present the chronic stage, it causes these defense cells to collapse. Much progress has been made in understanding the immune mechanisms that HCV stimulates, however there are still many gaps that need to be closed.*

I. INTRODUCTION

Hepatitis C is an inflammatory process caused by a virus of the Hepacivirus genus, of the Flaviviridae family. Its morphological structure is based on a single-stranded RNA with positive polarity, being enveloped and measuring approximately 50 to 70 nm in diameter [1]. In this sense, hepatitis C can be triggered acutely or

chronically, the latter being predominant. “Chronic hepatitis C (HCC) has a worldwide prevalence in about 1% of the population (~71 million infected). It is considered one of the biggest causes of liver disease and the seventh most frequent cause of death in the world” [2].

From this perspective, it is known that this pathology has a silent character, affecting the liver through an inflammatory process [3]. The transmission takes place through the sharing of objects, such as syringes contaminated with the infected person's blood, in the use of injecting drugs [4]. It also occurs through failures of health professionals, when reusing materials that can promote the spread of contamination, in addition to the absence of sterilization of manicure materials in salons, corroborate the transmissibility [5]. Furthermore, despite being less common and frequent compared to hepatitis B, unprotected sexual contact can be a way of contamination with HCV, however, the spread of the virus is inefficient in this form of exposure [1].

Parallel to this, the human organism, with its physiological processes, seeks to eliminate foreign bodies that infect them [6]. However, the HCV virus (Hepatitis C virus) has a diverse genetic variety. It has six genotypes and several subtypes. Due to this great viral diversity, the production of the vaccine has not yet been made possible, which ends up triggering the persistence of the virus in the human body. In Brazil, the predominant Hepatitis C virus is genotype 1 [3].

Regarding the defense mechanisms of the immune response, it is known that the pathogen receptors, after the virus enters the body, seek and recognize the viral products, resulting in the production of pro-inflammatory cytokines, such as the Tumor Necrosis Factor (TNF) and Interleukin 6 (IL-6), as well as type I interferons [2]. From this, there is the initiation of the immune response with the induction of antiviral products and the participation of NK Cells and T Lymphocytes, whose goal is to defend the organism in response to the attack of these pathogens [7].

Therefore, the present work arises as a need to understand the mechanisms of defense action against the Hepatitis C virus in the human body, given the various means that the pathogen develops to continue replicating, thus presenting the objective of this research.

II. METHOD

The study was based on a literature review, based on research in articles from the SciELO and PubMed platforms. To develop the work, some steps were followed, the first being the delimitation of the theme, then conducting research with specific descriptors, choosing inclusion and exclusion criteria, analyzing the articles and developing the writing.

The following article had the theme delimited in defense mechanism of the immune system, hepatitis C clinic and infection treatment.Thus, to carry out the search for the matter, the descriptors hepatitis C, revision, virus and immune system associated were used through the Boolean operators OR and AND. With the use of these descriptors, 152 references were initially found, with these 2 studies from scielo and 149 studies from pubmed, including scientific articles and scientific summaries of analyzes and systematic reviews. Thus, studies written and made available in Portuguese, Spanish and English were sought. Having as inclusion criteria used in the research, analysis and systematic review articles published from the year 2016, addressing the content of the given topic and excluding all articles that were not of the cited type, other than between the years of 2016 and 2021 and which does not refer to the subject outlined.

Finally, it was necessary to analyze each of the studies in order to select those that were related to the problem of the proposed theme and that corresponded with the determined inclusion criteria. In the end, 15 articles were selected that guided the research of the work.

III. RESULTS

According to the data obtained from reading the 15 selected articles, it was possible to verify that HCV has some interactions with the host organism that are not fully understood at the moment [8]. Besides the wide genotypic variability and interference on the immune system function, the viral infection can present in acute or chronic phase, which most cases tend to progress from an barely detectable acute infection by the immune system, to an persistent chronic infection [9].

The life cycle of HCV is directly associated with hepatic lipid metabolism and contributes for the viral persistence, in addition to interfering with the host's homeostasis of lipids, lipoproteins and cholesterol, which can cause, for example, hepatic steatosis, for example, an histological characteristic of the liver of patients infected with HCV [5].

Throughout this study, it was observed that there are component cells of the immune system that act as a line of defense related to the infection of the virus existing in the human organism, but these responses likely to vary according to the stage in which the disease is found on the host [3]. Among the immune system cells that act in response to viral infection, we can mention: interferons type I (IFNα and IFNβ), type II (IFNγ) and type III (IFNλ),

Natural Killers cells (NK), Neutralizing antibodies and TCD4 + and TCD8 + cells [4].

Another correlation that the texts refer to, is that NK cells and IFNγ. NK cells during the acute phase release the production of IFNγ, an important viral control factor that allows most precise elimination of viral load, through the inhibition of HCV replication [10]. However, in the chronic phase this cell decreases its capacity of liberate IFNγ and increases the production of cytotoxicity that takes to liver damage [3].

Furthermore, based on the encountered studies, identified that the high rate of virus replication when progressing to chronicity causes a low production of T CD4 + cells, leading to a low efficacy of T CD8 + cells and, therefore, targeting these TCD cells into a collapse stage, and consequently an faulty immune defense [11].

IV. DISCUSSION

In view of the studies read and proposed, it is understood that hepatitis C is a pathology which tends to chronicity in most cases, as the acute phase is mostly diagnosed as subclinical [5]. Thus, HCV is a highly complex pathogen. When analyzing its chronic phase, the attitude of the virus to decompensate the immune system causes an immunological failure in the elimination of the HCV infection [12]. So, the inefficiency of the immune system leads to persistent inflammation in the liver, cirrhosis, liver failure or the development of hepatocellular carcinoma [7].

Its replicative capacity together with countless genetic errors end up causing its high genetic variability, a fact that contributes to the exhaustion of T cells when trying to identify and kill the HCV virus.Furthermore, this pathogen has an escape mechanism which is still not fully understood, making its permanence in the host for a longer time causing its chronic phase of the disease [13].

HCV needs to be in hepatocytes to carry out its replication process [6]. Some studies indicate that the virus binds to very low-density lipoproteins (VLDL), allowing it to “camouflage” during this period and thus making it difficult for defense cells to identify [7]. In addition, there is an interference in lipid homeostasis that leads to disorders such as hepatic steatosis, which is a diagnosis present in patients with HCV infection [8].

Another important aspect is the NK cells that act during the acute and chronic phases, but have different effects in each of these stages.During the acute phase, NK cells produce the IFNγ that are sorely needed for the elimination of HCV infection.However, when chronicity persists, there is a decrease in IFNγ and an increase in cytotoxicity leading to serious liver damage [14]. Although interferon is highly resolving, it has a deleterious effect as the sustained production of type I IFNs can hamper the induction of virus-specific T cell responses [4].

It is also worth noting that T cells during the chronic phase have their resolving capacity reduced since, in the acute phase, because of the virus, a wide variability does not allow T cells to create neutralizing antibodies or memory cells, thus, when they have the chronic stage causes these defense cells to colapse [15]. By mechanisms not yet understood, CD4 + T cells that are seen in the acute phase lose their effectiveness in the persistence of the infection [10]. In addition to, it causes CD8 + T cells to lose their effectiveness against HCV and causes the exhaustion of CD8 + T cells, which occurs through a multi-step process in which antigen-specific cells progressively lose their effector functions and reduce their expression of cytokine receptors necessary for homeostatic proliferation of memory CD8 + T cells [11].

V. CONCLUSION

Much progress has been made in recent years in the knowledge of the immune mechanisms that HCV stimulates, however there are still many gaps that need to be closed. However, as far as is known, the diagnosis in the acute phase is still very underreported due to nonspecific signs and symptoms, having a better parameter when it has reached chronicity and organ damage. The tendency to chronicity and genetic variability of the virus causes the depletion of the immune system and the immune failure to eliminate the pathogen, in addition to preventing it from having an effective vaccine for the pathology. For these patients to have a better prognosis, further studies are needed to close these gaps, especially in the mechanisms that lead to reduced T cell efficacy in the acute phase.

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