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Studies on cytokine storm

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Abstract

The term cytokine storm or cytokine cascade was first used in an article published in 1993 and is still a term used for uncontrollable inflammatory responses, but it still cannot be fully explained today. Cytokine storm can occur in many diseases of the central nervous system, either infectious or non-infectious. In most of the patients, the release levels of proinflammatory cytokines such as interferons, tumor necrosis factor, interleukins and chemokines are significantly high. The molecular mechanism of the cytokine storm has not been clearly elucidated and most cases result in death. Since clinical treatments and immunomodulatory treatment methods in this area are insufficient, this issue should be discussed and investigated in more detail. In our current proceeding we are briefly discussing the cytokine storm.

Introduction

Cytokines are low weight molecules, about 8-40 kD, in the form of glycoproteins or peptides. Cytokines are also known as signaling proteins and intercellular communication providers that play an important role in protection against dangerous invaders, wound repair, and inflammation. They are produced by many cells and are named according to these cell types (monokine, interleukin, etc.). Cytokines are basically divided into two sections, proinflammatory cytokines aggravate the condition while anti-inflammatory cytokines work in opposite directions to repair and alleviate. Most commonly known proinflammatory cytokines can be listed as; TNF-a, IFN-y, IL-1, IL-6, IL-8, IL-12, and anti-inflammatory cytokines can be listed as; transforming growth factor (TGF-B), IL-10, is secreted as IL-4 [1 ,2]. Two well-known cytokines, TNF and IL-6, have important roles in the cytokine cascade by releasing large number of cytokines. IL-6 is involved in B cell transformation, immunoglobulin secretion, and suppression of inflammation and inflammation, supporting host defense against tissue damage and autoimmune diseases [3]. Too much secretion of this cytokine causes a cytokine storm, resulting in a systemic inflammatory response. TNF-α is a cytokine secreted by most of the immune system cells, plays a role in damage caused by the inflammation, and it is the first cytokine produced in the immune response. It can trigger inflammation, has functions in tumor necrosis [4]. When the uncontrolled production of these cytokines increases, symptoms of fever, swelling, hypotension occur and can cause tissue or organ damage and death [5, 6].

Results

The immune system creates an immune response against invading pathogens and eliminates these pathogens. As a result of this reaction, the tissue or organ environment returns to equilibrium, but if this balance cannot be achieved, the cytokines produced by the immune cells can increase uncontrollably and generally cause different disorders such as liver damage, heart muscle diseases, kidney failure, and cholestasis in patients [7]. Some studies have been done to prevent the cytokine storm. Understanding the exact mechanism is very important. In one study,

it was tried to prevent the cytokine storm by targeting the response of the immune system cells, but the result was not effective [8]. Immunoglobulin receptors are excitatory and inhibitory receptors known as Fc receptors. Immunoglobulins' Fc receptors are present on the surface of some immune system cells (macrophages, dendritic, NK and B cells). These Fc receptors are important to regulate the inflammatory response of different immune system cells. Positive results have been obtained in literature studies by blocking the Fc receptors [8,9]. In the literature, there are studies showing that the application of COX-2 inhibitors in therapeutic treatments modulates the immune response [5]. Inhibition of COX-2 can also be an efficient way of suppressing the cytokine storm. Various treatment modalities have been investigated, but most are not effective, so treatment strategies in this area need to be developed.

Conclusion

There are many studies focusing on the treatment of the cytokine cascade, but currently there are treatments that can only act on the upstream mechanisms, that is to reduce production levels of the peptides. Apart from this, although many methods have been investigated, they have not been effective. There are studies in the literature suggesting that immunomodulatory treatment can be applied to prevent the cytokine storm of severe influenza [10,11]. It is very important to maintain the balance in the main proinflammatory cytokines (TNF-α and IL-6, etc.) in the cytokine storm [5]. In general, since the agents applied in for the immunomodulatory targeting of the intracellular signaling pathways seem more potent, the development of this method will probably be more efficient. Targeting the signaling pathways will shut the downstream mechanisms to suppress the cytokine storm. Future studies will clarify this subject matter in more details.

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