

Article Review: The Phenomenon of Cytokine Storm

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ABSTRACT

Cytokine storms are much more common these days because of the corona epidemic. Cytokine storm is a serious complication known as an infusion reaction seen in the presence of infection or drug side effects. The reason for this is the increase in the number of white blood cells to fight viral and bacterial infections, as a result of which more cytokines are secreted and the feedback provided by them causes a severe inflammatory reaction and death if the patient does not focus on it. This article describes the concept of the Cytokine storm, how to increase cytokine and create a Cytokine storm, types of Cytokine storms, factors involved in its creation, and methods of diagnosis and treatment.

Keywords- Cytokine Storm, Increase Cytokines, White Blood Cell, Autoimmune Diseases.

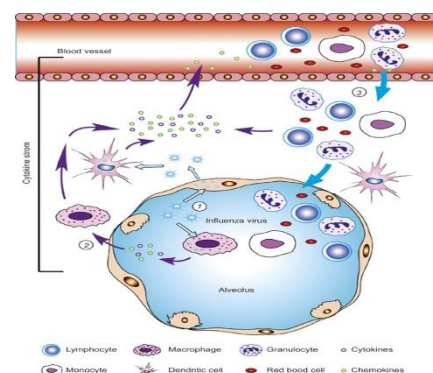
I. INTRODUCTION

When the body is exposed to infectious agents or a group of diseases, they secrete cytokines in large quantities. Cytokine is a hormone that is secreted in inflammatory diseases and increases the response to these diseases. Chronic secretion of cytokines and excessive inflammation lead to increased inflammation in the body, which in turn leads to diseases such as cancer and atherosclerosis. Cytokine storm does not occur alone and are not recognized as a disease alone, but are the result of the presence of infectious agents in the body. Cytokine storm has symptoms that assist the doctor in diagnosing and are effective in saving the patient's life. Fever, joint pain, anorexia, nausea, diarrhea and vomiting, high heart rate, seizures, and headaches are some of these symptoms. Cytokine storm is an infusion reaction that results from drug side effects, such as the use of drugs associated with lymphocyte T (Yiu, Graham, et al. 2012).

1.1. Cytokine storm:

Cytokine storm in its scientific and medical definition is when the body's immune system triggers an inflammatory response to a disease, also called cytokine release syndrome. I have also seen this condition when the patient uses monoclonal antibodies or treats for

lymphocytic T-related complications which are known as drug complications. It can be said that a cytokine storm occurs when cytokine release is severe. This phenomenon was first mentioned and named in patients who had a transplant. In these patients, the release of cytokines was seen in large quantities, and after a while, this title was also used for severe reactions to infectious diseases. In other words, when a group of diseases or a severe disease affects the immune system, the body produces frequent and numerous inflammatory signals that may lead to the death or failure of the patient's organs (Ye, Wang, et al. 2020).



1.2. Create a Cytokine storm.

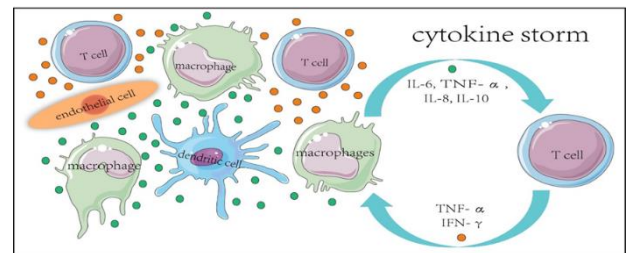
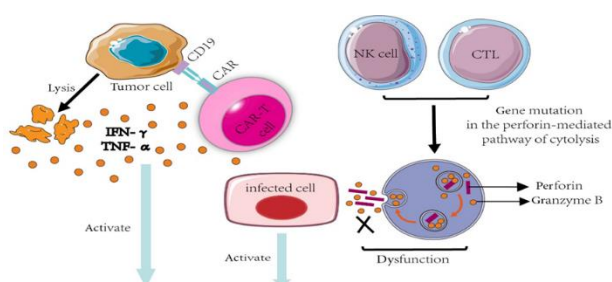
For a detailed study of the Cytokine storm, it is best to first describe the cytokine completely and conceptually. Different types of cytokines are known as signaling factors in inflammatory diseases, and each type of cytokine performs a specific function in the body, including the following:

- Cytokines that assist absorption in immune cells
- Cytokines involved in the production of antibodies
- Cytokines involved in the onset of symptoms

Cytokines normally perform important functions in the body, resulting in the coordination of the immune system against disease. Among the pathogens that lead to the activity of cytokines in the coordination of the immune system are infections and viruses. In cases where the amount of cytokine is produced more than normal due to abnormal reasons, problems and complications are seen as a result, which is known as autoimmune complications. It produced a more intense inflammatory response with additional cytokines. In this physical abnormality, a stronger immune system is a weakness that triggers a more severe inflammatory reaction, which is why in the recent pandemic, COVID-19, young people could die if they had severe coronary heart disease (Tisoncik, Korth, et al. 2012).

1.3. How to increase cytokines.

When white blood cells such as B lymphocytes, T lymphocytes, and NK cells are activated in large numbers and also monocytes and dendritic cells are activated, they release inflammatory cytokines to cause an inflammatory reaction. When inflammatory cytokines are released, more cells are released. And become more active, creating almost a positive feedback cycle. Infected cells lead to the activation of these cells, which eliminates necrosis in the body. Overgrowth of white blood cells against inflammation is a strong immune system error that leads to a weakened immune system and may lead to death (Iwasaki and Medzhitov 2011). In case of infection with viruses or other infections, the immune system tries to eliminate the pathogen normally. When the human immune system is fighting a pathogen, in some cases, cytokines malfunction and send abnormal signals to B and T macrophages and lymphocytes, leading to infection, which triggers immune cell function. It produces more cytokines and in a positive feedback process, a cytokine storm is created (Tang, Liu, et al. 2020).



1.4. Types of Cytokine storm.

Cytokine storm is a severe immune response to a pathogen that is not essential for the body and has devastating effects on the patient's body. Cytokine is a signaling factor that sends signals between different cells of the immune system. Disruption of this system causes many serious problems, the most severe of which is the Cytokine storm. Based on the intensity of the cytokine storm created during the immune system defense process, this phenomenon is divided into several categories with different intensities, which are from grade 1 to grade 5 (Sinha, Matthay, et al. 2020).

Grade 1: Due to the mild phenomenon of the Cytokine storm in these cases, there is no need to stop the drug infusion, and the patient can recover.

Grade 2: This is associated with a more severe cytokine storm than grade 1, which improves in the shortest possible time by discontinuing the drug infusion and establishing clinical patient measures. Taking care of the patient with nonsteroidal anti-inflammatory drugs (NSAIDs) is beneficial for the patient, and intravenous fluids and anti-inflammatory drugs increase the speed of recovery.

Grade 3: In this case, the cytokine storm is relatively severe and the patient will not respond immediately to healing drugs, and there may be serious risks for the patient not to go to the hospital, so in this case, hospitalization optimizes the recovery process. This is because, at this level of the cytokine storm, they indicate complications such as lung and kidney failure as symptoms (Suntharalingam, Perry, et al. 2006).

Grade 4: Cytokine storm in this degree leads to serious reactions of the body and leads to symptoms such as lung failure and consequently respiratory failure. Artificial respiration by specialists or special drugs such as antihypertensive drugs is useful for the patient's recovery and control of cytokine storm conditions.

Grade 5: The most acute reaction of Cytokine storm is in this category and the most severe type of reaction is in this stage, which leads to the loss of vital signs of the patient (Harrison 2010).

1.5. Causes of Cytokine storm.

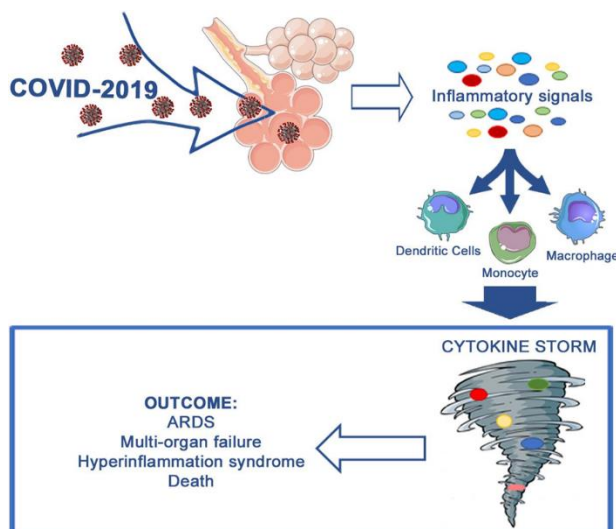
Cytokine storm and its types are fully described and the process of its formation in the body was thoroughly studied. But the causes that can predispose a person to such a complication fall into several distinct categories (Makhija and Kingsnorth 2002). Which we discuss below:

A. Genetic syndromes involved in Cytokine storm

Changes in genetic code are often the cause of a person's susceptibility to certain diseases and disorders. Specific genetic diseases may be involved in the development of the Cytokine storm. These diseases include hemophagocytic lymphohistiocytosis. This condition, called HLH for short, is a genetic defect in the cells of the immune system that is involved in causing a cytokine storm. Babies with this syndrome indicate signs of cytokine storm in the early months of life and are more vulnerable because the immune system is not sufficiently developed at this stage and the babies die. Genetic screening before pregnancy is important in these cases (Fajgenbaum and June 2020).

B. Infectious diseases and Cytokine storm

Infections As mentioned in the previous sections are one of the main causes of Cytokine storms. Infections are caused by bacteria, viruses, and other factors, one of which is influenza A, in which cases of Cytokine storm have been seen. There are other infectious diseases involved in the Cytokine storm, including the Ebola virus, avian influenza, graft-related diseases, sepsis, acute respiratory distress syndrome, covid-19, and coronary heart disease. Other important infectious viruses that cause cytokine storms are cytomegalovirus and Epstein-Barr virus. It should be noted that this complication is not seen in all infectious patients, but the simultaneous onset of several diseases and the involvement of several types of diseases can increase the risk of cytokine storms (Clark 2007).



C. The role of autoimmune diseases in the development of cytokine storm

Numerous autoimmune diseases can be involved in the development of cytokine storms, two of which are described below: lupus and idiopathic arthritis in young people. Lupus is an autoimmune disease, and as a result, it mostly affects the patient's skin and is associated with joint pain. There are two types of the disease, known as cutaneous and diffuse. The skin type, as its name implies,

affects the skin and spreads to other organs besides the skin. Idiopathic arthritis in young people, or JIA for short, is a disease of the tissues of the body that affects the patient's joints and causes inflammation and severe pain. Both of these conditions can increase a patient's risk of developing a cytokine storm (Chousterman, Swirski, et al. 2017).

D. Drugs and side effects of Cytokine storm

Treatments can have side effects, and we may see cytokine storms as a side effect during treatment. CAR-T treatment is a treatment for leukemia patients in which cells with chimeric antigen T lymphocyte receptor cells are used for treatment, one of the side effects of which is the Cytokine storm (Makhija and Kingsnorth 2002). Other treatments that can cause cytokine storms to include:

- Treatment The use of almethosumbe for patients with leukemia
- Some of the treatments adopted for MS patients
- Use of retoxicab treatment for patients with leukemia as well as autoimmune diseases
- Moromonab-CD3 is used in immunosuppression in organ transplantation as a method of organ acceptance

Specifically designed therapies with T lymphocytes that act as a treatment with the assistance of modified lymphocytes (Shimizu 2019).

1.6. Cytokine storm detection methods.

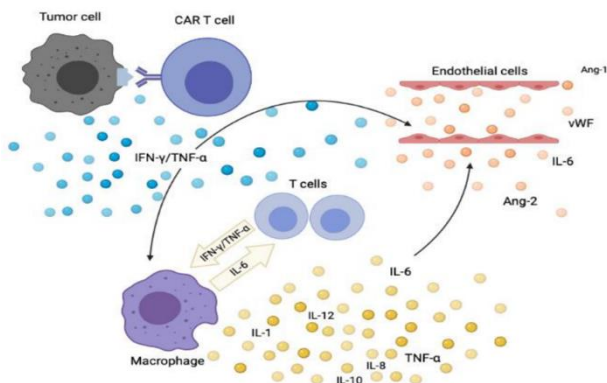
Examinations and clinical examinations are methods of diagnosing this problem, which first of all begins with clinical examinations. Knowing your heart rate and blood pressure, as well as your blood pumping rate, are the first steps used to identify a cytokine storm (Iwasaki and Medzhitov 2011). If these are difficult to diagnose, tests such as a chest x-ray and screening for inflammation can be helpful. Measurement of interleukin 6 is one of the cases that will determine the storm of cytokines. The use of interleukin-6 to diagnose Cytokine storm is reliable, and in addition, it can be used to measure the number of immune cells, increase liver and kidney markers, increase CRP, increase ferritin, and the presence of blood clot abnormalities to identify and diagnose Cytokine storm (Kelly, Klenerman, et al. 2011).

1.7. Cytokine storm treatment methods.

It should equip patients exposed to cytokine storms with respiratory equipment and their vital signs should be closely monitored. Medications and intravenous fluids can accelerate the patient's recovery, and the use of hemodialysis is promising for the patient. Treatment of this complication should not be done arbitrarily and recovery to a doctor is faster and more reliable. Corticosteroid drugs, aspirin in Cytokine storm grade 1, oxygenation of the patient through the respiratory tract, drugs affecting the immune system including cyclosporine, plasmapheresis therapy, statin drugs, and biological drugs that block the production of cytokinin are useful for these patients (Wang and Ma 2008).

II. CONCLUSION

The occurrence of cytokine storm is rare for no reason and generally, this complication is seen in the presence of several diseases at the same time its mild to moderate and even severe types are different from each other and the time of diagnosis, care, and treatment are different. The presence of this complication in patients necessitates their hospitalization until the risk of death is eliminated (Kansagra and Gallentine 2011). If the drug is taken arbitrarily, the patient's risk of death increases because the complication, although very easily controlled in the hospital, can be fatal if not referred to the hospital. The name of this complication is heard much more than before after the corona epidemic, and this is due to the presence of this complication in coronary patients, which poses a risk to their lives and necessitates the hospitalization of these patients (Suntharalingam, Perry, et al. 2006).



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