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Review Article

A REVIEW: TOCILIZUMAB, A RAY OF HOPE IN COVID-19 PNEUMONIA

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ABSTRACT

With the increased number of cases of coronavirus disease 2019 (COVID-19) all over the world which was discovered in December 2019 in Wuhan city of China, there are more positive rates and deaths encountered during the second wave due to this dreadful infection mainly focusing on youngsters diagnosed with COVID-pneumonia. Amidst this devastating situation, there is ray of hope by the emerging clinical trials on Tocilizumab, a potent interleukin-6 (Il-6) inhibitor which likely reduces the mortality of those patients having severe COVID-19 pneumonia as a result of Cytokine Release Syndrome. This syndrome is triggered by burst of inflammatory markers secondary to COVID-19 which is characterized by decrease in T-cells and Natural Killer cells, an increase in IL-6, fever, organ and tissue dysfunction, and an abnormal coagulation function eventually leading to death.

Keywords: COVID-19, Cytokine release syndrome, Coronavirus disease 2019 pneumonia, Tocilizumab.

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INTRODUCTION

In December 2019, a new strain of coronavirus, severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2), was perceived to arise in Wuhan, China. Along with SARS-CoV and Middle-East respiratory syndrome–coronavirus, SARS-CoV-2 is the third coronavirus to cause extreme respiratory illness in humans, called coronavirus disease 2019 (COVID-19). This was declared as a pandemic by the World Health Organization in March 2020 and has had considerable economic and health impacts all over the world [1].

With its mutating strains, COVID-19 has caused more anguish in the second wave than the first. This time, many young people, including children, are also being infected, data from several resources have shown. However, there is expansion in death rates not only in geriatric, comorbid patients yet additionally in healthy youths due to multi-organ failure as a result of cytokine release syndrome (CRS) in COVID-19 pneumonia.

WHAT IS CRS?

CRS is a form of systemic inflammatory response syndrome which is triggered by different mechanisms related to certain drugs and infections. It was previously stated as influenza like syndrome which occurred after systemic infection such as sepsis and immunotherapies such as Coley's toxins [2]. It occurs when large numbers of white blood cells are activated and release inflammatory cytokines, which induce more white blood cells production. CRS is also an adverse effect of some monoclonal antibody medications and also adoptive T-cell therapies. This can produce some detrimental effects on various body functions [3].

CAUSES OF CRS

CRS occurs when excess amounts of white blood cells, including B-cells, T-cells, natural killer cells, macrophages, dendritic cells, and monocytes are activated and release inflammatory cytokines, which further activate more white blood cells in a positive feedback loop of pathogenic conditions [3]. This can occur when the immune system is battling pathogens, as cytokines produced by immune cells increases more effector immune cells such as T-cells and inflammatory monocytes (which differentiate into macrophages) to the site of inflammation or infection. Likewise, activation and stimulation of further cytokine production are the result of pro-inflammatory cytokines binding their associated receptor on immune cells. This process, when dysregulated, can be dangerous due to systemic hyperinflammation, hypotensive shock, and multi-organ failure [4].

Severe CRS or cytokine reactions not only occurs in adoptive T-cell therapies but also in a number of infectious and non-infectious diseases including graft-versus-host disease, COVID-19, acute respiratory distress syndrome (ARDS), sepsis, Ebola, avian influenza, smallpox, and systemic inflammatory response syndrome [5].

Although SARS-CoV-2 is adequately cleared by the early acute phase against viral response in most individuals, some advancement to a hyperinflammatory condition can be life-threatening due to pulmonary involvement. Thus, systemic hyperinflammation leads to inflammatory lymphocytic and monocytic infiltration of the lung and the heart, causing ARDS and cardiac failure [6].

Patients with severe COVID-19 and ARDS have traditional serum biomarkers of CRS including elevated C-reactive protein (CRP), lactate dehydrogenase, interleukin (IL)-6, and ferritin [7].

SYMPTOMS OF CRS

Clinical manifestations include fever, fatigue, loss of appetite, muscle and joint pain, nausea, vomiting, diarrhea, rashes, fast breathing, rapid heartbeat, low blood pressure, seizures, headache, confusion, delirium, hallucinations, tremor, and loss of coordination. Laboratory tests and clinical monitoring show low blood oxygen, widened pulse pressure, increased cardiac output (early), potentially diminished cardiac output in later stage, high levels of nitrogen substances in the blood, elevated D-dimer and transaminases, factor I deficiency and excessive bleeding, and elevated level of bilirubin [3].

PATHOPHYSIOLOGY OF CRS

CRS and sepsis share several symptoms in common, and patients with CRS are at increased risk of infections, not only for the immunosuppressive treatments but likely also for the CRS-related immune dysregulation and tissue damages, specifically at mucosal barrier. However, infections principally involve the respiratory tract in patients having CRS.

The exacerbated reaction as a result of infections or biological therapy is brought about by the quick recruitment of macrophages and