



(CASE REPORT)



Severe leukocytosis and cytokine storm in a patient with covid-19 pneumonia

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Abstract

Since the emergence of the first cases of COVID-19 that was first reported in Wuhan China, the virus has spread globally at a fast rate. It has carried a significant increase in the mortality rate. Most of these cases have been secondary to severe pneumonia as well as an increased incidence of thromboembolic complications leading to pulmonary embolism, myocardial infarctions, and strokes. It has been observed that many of these severe COVID-19 pneumonias have been associated with an increased levels of inflammatory markers including Cytokines and Interleukin 3 and 6 which can lead to an exaggerated humoral response with increased immunoglobulin production and tumor necrosis factors that can lead to lung tissue destruction. There is an overwhelming demand to find a mechanism to stop that vicious cycle and minimize tissue destruction. Thus, there is a need for more extensive studies regarding this medical dilemma in order to minimize the number of deaths around the world which so far has almost reached 2.5 million.

Keywords: Covid-19 Infection; Pneumonia; Cytokines; Interleukins; Tumor Necrosis Factor; Tocilizumab

1. Introduction

COVID-19 has been associated with severe mortality and morbidity leading to death. Pneumonia and hypoxia have been one of the major indicators of severe disease and carry poor prognostic signs. We herein report a case of a patient with chronic lymphocytic leukemia who developed severe pneumonia associated with cytokine storm leading to her demise.

2. Case report

A 64 years old African American lady with past medical history of type 2 diabetes mellitus non-insulin dependent, hypertension and stable asymptomatic chronic lymphocytic leukemia under observation by an oncologist, presented with an 8 days history of fatigue and intermittent fevers of 101 degrees Fahrenheit. She stayed at home hoping that her symptoms would resolve spontaneously. The morning prior to coming to the emergency room department, she woke up with inability to get out of bed, worsening dyspnea, and a fever of 100.6 degrees Fahrenheit. On arrival at the emergency room she had a fever of 103.5 and an oxygen saturation of 87% on room air. Blood pressure was 110/60 with a pulse rate of 110 beats per minute. Physical examination revealed extensive crackles in both lung fields. She was also using her accessory muscles of respiration and was breathing around 22 times per minute. Chest radiograph showed extensive bilateral pulmonary alveolar airspace infiltrations suggestive of extensive bilateral pneumonia.

The rapid PCR test for SARS CoV-2 Coronavirus test using nasopharyngeal swab was positive. Both blood and sputum cultures were negative. Initial CBC was significant for severe leukocytosis with WBC count of 186 E3/ uL (normal range 3.7-10.6 E3/uL). Due to her CLL, her baseline WBC on her last visit to the oncologist a month prior to her illness was 54 E3/uL. Hemoglobin was 10.4 g/dl with a platelet count of 109 E3/uL. Other blood tests showed a blood urea nitrogen of 32 mg/dl and a creatinine of 1.13 mg/dl. Patient had a potassium of 6.8 mmol/L (normal range 3.5-5.1 mmol/L).

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Plasma potassium level was 5.4 mmol/L. Picture was felt to be due to pseudohyperkalemia. C-reactive protein was 75 mg/L (normal range ≤ 10 mg/L). Ferritin level 777ng/ml (normal range 11.1-264 ng/ml). Interleukin6 (IL-6) level was 10 pg/mL (normal range < 1.8 pg/mL), Blood smear was consistent with significant leukocytosis with few atypical white blood cells compatible with the patient's history of CLL. The patient was admitted to the intensive care unit. Because of hypoxia, she required high-flow oxygen, placing her in a prone position. She received convalescent plasma, Actemra (Tocilizumab) as well as high dose steroids. WBC count peaked at $204 \times 10^3/\mu\text{L}$.

Despite above measures, the patient's condition continued to deteriorate with worsening hypoxia requiring intubation and mechanical ventilation. On the sixth day of admission, she developed cardiopulmonary arrest with unsuccessful resuscitation.

3. Discussion

COVID-19 has been associated with significant mortality and morbidity. According to the coronavirus resource center, as of end of February 2021, there were 2,528,535 total deaths worldwide, with cases of death exceeding half a million in the United States of America. One of the major causes of death has been attributed to severe lung injury and respiratory failure. The virus has been connected to its ability to molecularly trigger an acute inflammatory process through its molecular mimicry, triggering multi-organ damage [1]. One of the mechanisms of injury related to COVID-19 was felt to be due to activation of Cytokine storm [2, 3] This process has been observed with a number of conditions including sepsis [4], viral infections [5] Similar to many severe diseases, COVID-19 has been associated with an increased level of Interleukin 6. This is a polypeptide cytokine which is produced by T cells. This activates the production of humoral response B cells to produce the immunoglobulins IgG, IgM and IgA. It does work synergistically with Interleukin 3 (IL-3) [6]. In addition, Interleukin 1 (TNF tumor necrosis factor) also gets activated in this process. Such exaggerated responses to COVID -19 act as pleiotropic chemotactic to neutrophils, lymphocytes and macrophages that would attack the inflamed sites, which are usually the lung tissue leading to cell necrosis and cytolysis [7, 8]. One of the possible approaches to treat high level interleukin 6 Covid-19 pneumonia is utilizing Tocilizumab an Interleukin 6 inhibitor as a potential approach to cytokine storm [9]. However, several studies have been inconclusive with further studies needed to evaluate its efficacy.

In this case, we believe that the patient had a cytokine storm, causing leukemoid reaction in a patient with underlying chronic lymphocytic leukemia, with elevated inflammatory markers and clinical presentation supporting this diagnosis. Of interest, the patient had pseudohyperkalemia due to the severe leukocytic response to the virus which was confirmed by doing both serum and plasma potassium simultaneously. More clinical and laboratory research is needed to evaluate the inflammatory markers associated with COVID-19 cytokine storm, and hopefully find a mechanism to abort such a storm in the future.

4. Conclusion

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Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There was no conflict of interest among corresponding authors.

Statement of informed consent

Proper informed consents were obtained.

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