VOLUME - 9, ISSUE - 12, DECEMBER - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Medical Science

EFFECTIVENESS OF TOCILIZUMAB IN PATIENTS WITH SERIOUS COVID-19 PNEUMONIA: PRESENTATION OF A RECOVERED PATIENT CASE.

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ABSTRACT

SUMMARY: On March 11, 2020, the disease caused by coronavirus 2019 (COVID-19), by SARSCoV-2 initially reported in Wuhan, China in December 2019, was characterized as a pandemic by the World Health Organization (WHO) spreading Worldwide. The COVID-19 virus causes diverse clinical manifestations, including respiratory conditions, from the common cold to severe pneumonia with respiratory distress syndrome (ARDS), septic shock, and multi-organ failure. The case of an adult patient with rapid clinical-radiological progression of COVID-19 pneumonia is presented, in whom the compassionate use of interleukin-6 receptor blocker (Tocilizumab) was proposed for the management of his pathology.

OBJECTIVE: Describe Tocilizumab as pharmacological therapy against Covid-19, by presenting a clinical case

DESIGN: Prospective, observational in a single center.

METHODOLOGY: This is a systematic review of the efficacy of Tocilizumab in patients with pneumonia affected by Covid-19, emphasizing its clinical characteristics and short-term complications. The information and images obtained belong to the medical staff in charge of the case, whose reinforcements are provided by the Excel, Word and JPG statistical package.

KEYWORDS : Tocilizumab, Covid-19.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19, for its acronym in English Coronavirus Disease 2019) is a respiratory disease of humans caused by a new coronavirus identified with the acronym SARSCoV-2. On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. Most of the infections occur person to person, being highly transmissible. The symptoms vary from asymptomatic cases to febrile symptoms with cough and respiratory distress, pneumonia and respiratory distress. It can also be accompanied by gastrointestinal disturbances. The department of internal medicine at Harvard Medical School Brigham Hospital has postulated a clinical-therapeutic classification of the disease that divides its course into different stages and in turn identifies two overlapping but different pathological subsets, triggered the first one by the virus and the second by the host's response to the virus. The stages in turn are as follows: Stage I (mild), early infection: The initial stage occurs at the time of inoculation and early establishment of the disease. During this period, the virus multiplies and takes up residence in the host, focusing primarily on the respiratory system. Stage II pulmonary involvement: In the second stage of the disease, lung involvement is established, viral multiplication and localized inflammation in the lung is the norm. Patients develop viral pneumonia, with cough, fever, and possibly hypoxia (defined as a PaO2 / FiO2 of 300mmHg, imaging (chest x-ray or CT scan) reveals bilateral infiltrates or ground glass opacities. Blood tests reveal increased of lymphopenia, together with the elevation of transaminases, the treatment would consist mainly of supportive measures because a specific antiviral treatment has not yet been established, although it would be at this stage that they would theoretically show a greater degree of efficacy. Stage III (severe) of systemic hyperinflammation: A minority of patients with COVID-19 will progress to the third and most severe stage of the disease, which manifests as a syndrome of extrapulmonary systemic hyperinflammation. In general, the prognosis and recovery of this critical stage of the disease is poor, and rapid recognition and deployment of such therapy may have the highest yield. Currently, the treatment of COVID-19 is symptomatic and supportive, and there is no specific curative drug scheme. Treatments with different drugs have been proposed based on the extrapolation of their effectiveness in similar conditions. One of these described treatments is the use of tocilizumab.

CASE PRESENTATION

A 52-year-old male patient, with no personal pathological history, refers to a previous evaluation for respiratory symptoms (photo1). They send outpatient treatment with Ivermectin, Azithromycin, amoxicillin / clavulanate, prednisone and enoxaparin. With general malaise, thermal rise quantified at 38 °, liquid stools on multiple occasions, sporadic dry cough and dyspnea on medium efforts, due to high suspicion of symptoms compatible with pneumonia, he was admitted to the health unit. Upon arrival a chest tomography is performed (photo 1), in addition a complete analysis is performed and a nasopharyngeal swab sample is

taken for SARS COV 2.

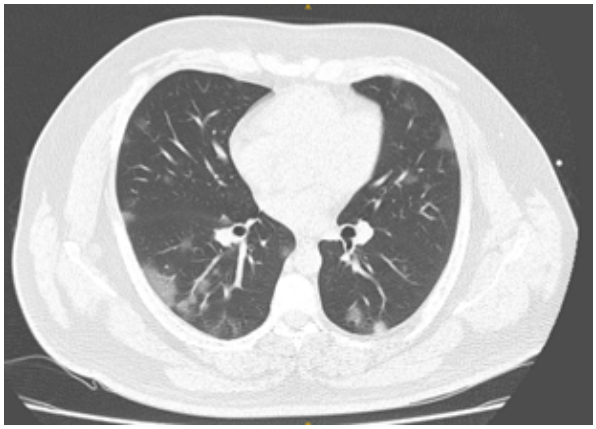

Photo 1. Ground glass opacities in both lung fields.

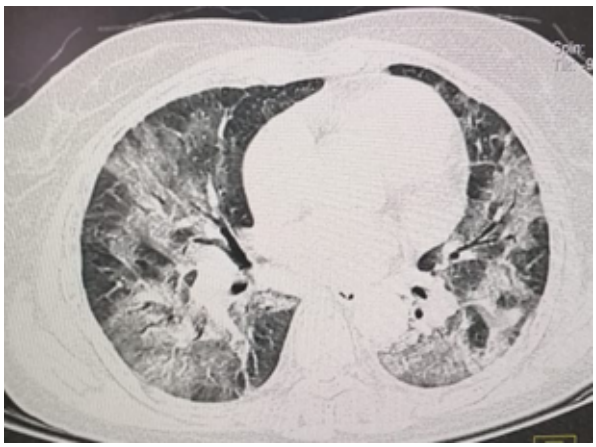

Photo 2. Diffuse ground glass opacities with a tendency to consolidate.

Evidenced in the analysis of leukocytes 6410, neutrophils 91.6%, lymphocytes 4.5%, hemoglobin 17.6 mg / dl, hematocrit 51%, platelets 153000, urea 42.8 mg / dl, creatinine 0.89 mg / dl, total bilirubin 0.57 mg / dl, direct bilirubin 0.24 mg / dl, indirect bilirubin 0.36 mg / dl, GGT 249 U / l, LDH 318 U / l, TGP 85 U / l, TGO 55 U / l, sodium 140, potassium 3.65, chlorine 104, Polymerase Chain Reaction 9.19, PCR-RT Positive.

Patient remains tachypneic, use of accessory muscles, before the worsening of respiratory failure a chest tomography is performed (photo 3), the ICU is consulted where admission is decided with a diagnosis of Severe Berlin Respiratory Distress Syndrome.

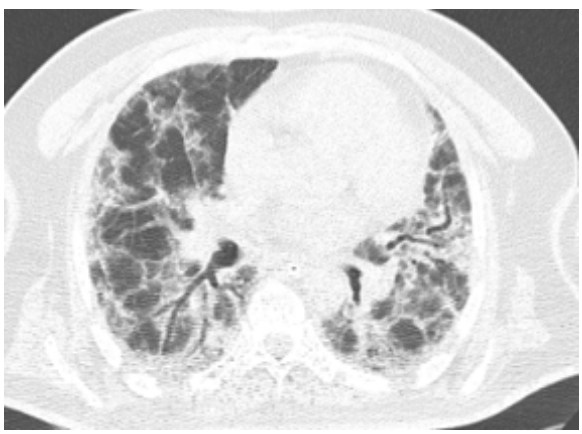

Photo 3. Opacities in diffuse ground glass. Traction bronchiectasis, CO-RADS 6

As a coronavirus treatment, ampicillin plus sulbactam 4/10, dexamethasone 5/5, azithromycin 5/5 were maintained, since there was no improvement from the respiratory point of view, it was decided to prescribe Tocilizumab 2/2.

During his stay in the unit with stationary evolution, febrile peaks did not subside due to suspicion of bacterial superinfection, therefore, cultures were requested, the same as reported in a tracheal aspirate Serratia Marcescens AMP C + Escherichia Coli and urinary tract infection associated with klebsiella oxytoca blee catheter , with analytical control of leukocytes 14.71, neutrophils 90 / dl for which a treatment based on meropenem 10/10, amikacin 5/5 is prescribed.

Regarding respiratory management, it is managed with protective ventilation 07/16/20, it began with invasive mechanical ventilation, on 08/05/2020 with evidence of a decrease in ventilatory parameters, with improvement in oxygenation indices, thus progressing in Ventilatory weaning being extubated with good tolerance until 08/08/2020 orotracheal re-intubation was decided, on 08/09/2020 a percutaneous tracheostomy guided by bronchoscopy was performed due to polyneuropathy, mechanical ventilation was disconnected 11/8, being used oxygen therapy at high flows. As a complication, I present a left pneumothorax resolved with placement of a thoracotomy.

Serratia Marcescens AMP C + Pseudomona Aeruginosa resistant to carbapenem + Enterococcus Faecalis was caused by pneumonia associated with cultured health care, which is why it was de-escalated to Ceftazidime / avibactam 7/7.

From the hemodynamic point of view, the patient required vasoactive agents due to septic shock from a pulmonary focus. He was managed with norepinephrine.

Finally, the patient was discharged with a tracheostomy removed due to tolerance after being closed for 24 hours, with oxygen at low flows 2 liters per minute, chest X-ray without infiltrates (photo 5). Patient with important sequelae due to underlying pathology and prolonged stay in ICU (pulmonary and motor) for which outpatient follow-up is performed.

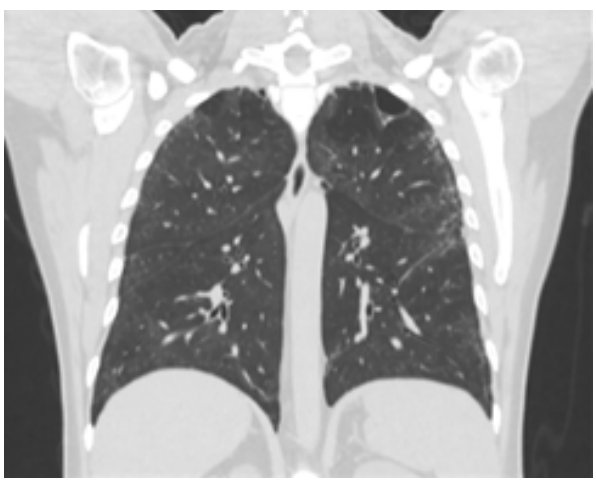

Photo 4. Coronal section: Ground glass image distributed peripherally in a smaller quantity compared to previous plates. Cystic bronchiectasis in the lung apices.

DISCUSSION

Tocilizumab is the only humanized monoclonal anti IL-6 antibody. Due to the participation of interleukin 6 in the Cytokine Release Syndrome ("cytokine storm") it was inferred that the blockade of the IL-6 receptor could inhibit the release of cytokines and therefore avoid the advanced phase of hyperinflammation that characterizes COVID-19 is severe

and can lead to irreversible harm, including death.

The health regulatory agencies of China, Italy and the USA have authorized the use of anti-IL6 agents in patients with respiratory distress syndrome (ARDS) associated with COVID19 virus infection, and large-scale randomized clinical trials have even begun in the countries. mentioned. In a Chinese study with 21 patients who received Tocilizumab in a single arm, there was improvement in 75% (15/21) of them, including two patients who came off mechanical ventilation within a few days.

Tocilizumab was administered early in the ICU course, usually on the day of admission for ICU support, and a median of 9 days from the onset of self-reported symptoms. Therefore, it is necessary to study whether the early administration of tocilizumab at the time of hospital admission could improve outcomes and decrease the overall use of resources.

A study published in 'The Lancet' used clear evidence that the use of tocilizumab is associated with an improvement in median overall survival from the time of admission compared to patients not receiving tocilizumab. In a post-hoc analysis, patients with baseline C-reactive protein levels of 15 mg / dl or higher were more likely to show improved survival associated with tocilizumab, while no relationship was seen in patients with lower protein C levels. reactive.

It is evident that in our clinical case presented, despite the bacterial superinfection to multiple causative agents, a prolonged stay in the ICU patient overcomes the infection and at the moment there is notable remission of the disease, for which it is documented in our experience that Tocilizumab in early phases reduce mortality and there is a notable improvement from the tomographic and clinical point of view.

CONCLUSIONS

Currently there are no studies with results available on the use of TCZ in patients with COVID-19, limiting themselves to anecdotal information in patients from China and Italy. In this sense, we have the study by Xu et al. the WHO describes how the majority of patients experienced improvement in various parameters (oxygen requirement, lung radiological image, lymphocyte count, C-reactive protein) without significant adverse events. On the other hand, patients with COVID-19 who required ICU support and who received tocilizumab had a reduced mortality.

Thus, tocilizumab appears to be among the first potentially successful treatments for patients with severe COVID-19 who require support in the ICU, pending confirmation from an ongoing randomized trial.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest.

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