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Colchicine May not be Preventive in COVID-19 Pneumonia: Case Report

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Abstract

The recent outbreak of Coronavirus Disease 2019 (COVID-19) continues to evolve in many countries and pose life-threatening clinical issues to global public health. There is no vaccine or therapeutic proven options to prevent COVID-19 infection. It has been speculated that some immunomodulating drugs may have an effect on the progression of this infection. It is reasonable that colchicine may be tested in the context of COVID-19 to detect its immunomodulatory effects which may prevent acute respiratory distress syndrome. We discussed a case with COVID-19 pneumonia using colchicine successfully treated and reviewed the literature.

Keywords: COVID-19; Colchicine; Pneumonia; LDH

Abbreviations

WBC: White Blood Cell; C-RP: C-Reactive Protein; LDH: Lactate Dehydrogenase; BUN: Blood Urea Nitrogen; sCr: serum Creatinine; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) or Coronavirus Disease 2019 (COVID-19) by named the World Health Organization is a newly emerged disease that has become a global public health challenge. The search for drugs against COVID-19 is continuing. This new viral infection characterized by dry cough, fever, dyspnea, fatigue, and lymphopenia, which can be complicated by interstitial pneumonia leading to severe Acute Respiratory Distress Syndrome (ARDS) which results from an unmodulated inflammatory response and leads to death [1,2].

Because specific drugs to treat SARS-CoV-2 have not yet been revealed. Currently several potential drugs are used for COVID-19 patients; however, none of the therapies have been proven to be completely effective. Antiviral therapy for SARS-CoV-2 and immunosuppressive treatment have to continue concomitantly for preserve vital organ functions. Immunomodulating drugs such as hydroxychloroquine, chloroquine, tocilizumab (an anti-interleukin-6 receptor antibody), are widely used in different stages of the disease since high uncontrolled inflammation is responsible for deaths [3-7].

Colchicine is utilized for the treatment of gout, Behçet's Disease, and also for prevention of pericarditis and Familial Mediterranean Fever (FMF). Colchicine disrupts the microtubule formation and reduces chemotaxis, phagocytosis, and migration of neutrophils [5]. Therefore, it is reasonable that colchicine may be tested in the context of COVID-19 to detect its immunomodulatory effects which may prevent Acute Respiratory Distress Syndrome (ARDS).

At the present time, several randomized studies regarding colchicine in COVID-19 patients have been announced. Nevertheless there are opposite opinions claim that colchicine doesn't prevent ARDS moreover may be harmful for patients with COVID-19 [6]. In this case, we report a patient who has been under colchicine treatment for three years and diagnosed COVID-19 pneumonia and recovered without any complications associated with COVID-19 infection.

Case Presentation

A 38 years, Caucasian, old female patient admitted to emergency unit complaining of cough and fever for 2 days. The patient is a nurse and she has been active working in hospital. She had been diagnosed rheumatoid arthritis and been using colchicine 1 mg/day for three years.

On admission, the patient had cough, and her vital signs were as follows: Arterial blood

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Table 1: Clinical laboratory results.

Parameters	1st day	3rd day	6th day	9th day
WBC (10^3/uL)	7.13	5	6.52	7.22
Lymphocyte (10^3/uL)	1.5	1.72	2.07	2.03
Neutrophil (10^3/uL)	5.12	2.97	3.84	4.4
Hemoglobine (g/dL)	12.5	10.6	11.1	10.9
Platelets (10^3/uL)	226	178	225	229
C-RP (mg/dL)	0.2	0.2	2.2	0.6
Procalcitonin (ng/mL)	<0.05	<0.05	<0.05	<0.05
D-Dimer (ng/mL)	388.71	778.9	571	455
Ferritin (ng/mL)	39.29	89.9	95	97
Fibrinogen (mg/dL)	334	336	405	473
LDH (U/L)	135	138	224	152
BUN (mg/dL)	19.26	12.8	10.7	19
sCr (mg/dL)	0.66	0.58	0.54	0.62
AST (u/L)	21	19	87	37
ALT (u/L)	16	14	89	24
Albumin (g/L)	42	36	37	38
Troponin I (ng/mL)	0.001	0.003	0.001	0

pressure, 100/70 mmHg; heart rate, 73 beats/min; body temperature, 37.3°C; respiratory rate, 20 breaths/min and oxygen saturations of 99% on room air. Physical examination was unremarkable. Chest CT (Computer Tomography) scan revealed ground-glass opacification at lower lobes of lungs. COVID-19 was confirmed by Polymerase Chain Reaction (PCR). Laboratory findings revealed white blood cell count 7.13×10^3/uL, lymphocyte 1.5×10^3 u/L, c-reactive protein (C-RP) 0.2 mg/dL and procalcitonine <0.05 ng/mL. D-dimer level was 388.71 ng/mL, and ferritin was detected 39.29 ng/mL, Fibrinogen was 348 mg/dL, while lactate dehydrogenase level was 135 U/L on admission. The laboratory findings are given in Table 1 during the patient's follow-up in the hospital. Hydroxychloroquine 400 mg/day, azithromycin 250 mg/day, enoxaparin 4000 units per day were started for COVID-19 pneumonia. Colchicine therapy was maintained unchanged. On the 4th day of her hospitalization CT scan showed progression, although her vital parameters were stable. Favipiravir treatment 1200 mg per day was started. Hydroxychloroquine and azithromycin ended up in 5 days. Enoxaparin dosage was raised up to 8000 units per day. After completing five days of favipiravir therapy as her clinical and laboratory findings were stable, she was discharged from the hospital.

Discussion

Colchicine has been approved for gout, Behcet's Disease and familial Mediterranean fever. Colchicine is a lipid-soluble alkaloid which within 24 h to 72 h of oral administration accumulates in granulocytes and monocytes. Colchicine reaches much higher concentrations within leukocytes than in plasma and persists there for several days after ingestion. In recent years, colchicine has attracted attention in the management of cardiovascular diseases by suppressing their inflammatory component [7]. Its mechanism of action is thought to be the potent inhibitor of tubulin polymerization and microtubule generation and, possibly, effects on cellular adhesion molecules, inflammatory chemokines, and the inflammasome. Colchicine may inhibit activation of NLRP3 inflammasome and additionally may inhibit directly the synthesis of TNF-α, IL-1β, and IL-6 [5,7]. Colchicine is an antimitotic substance that blocks cell division during metaphase [5]. Also, COVID-19 enters the cell using the Angiotensin-Converting Enzyme 2 (ACE2) as a host receptor and causes infection. Especially, in low cytosolic pH the virus increases its entry into the cell by penetrating to ACE2 [8]. Although colchicine is known to play an important role in intracellular protein traffic and has poor binding to microtubules at alkaline pH, its effect on the penetration of the virus into the ACE2 receptor is controversial [7,9]. All these compounds enhance the inflammatory process and are responsible for alveolar damage, interstitial infiltration, and ARDS. Therefore some authors suggest that colchicine may decrease the tissue damage in COVID-19 pneumonia by these pathways and can be used in patients with increased risk of ARDS [10].

However, it has been suggested that colchicine may be effective in COVID-19 infection and reduce cytokine storm seen during the COVID-19 infection. Cumhur et al. [6] disagree with this suggestion and claim that since colchicine does not decrease intracellular pH enough, there will be a high viral load leads to more severe cytokine storms [6]. In addition toxic doses of colchicine affect alveolar type II pneumocytes, inhibiting the release of surfactants and causing ARDS and also toxic doses leads to DIC and multiorgan failure [11]. So that the colchicine treatment in COVID-19 pneumonia may increase the risk of ARDS and DIC [6].

A trial has been done in Israel with patients under treatment of hydroxychloroquine or colchicine and COVID-19 test was performed. There was no significant difference between the groups found positive and negative [12]. Also there are several trials investigating the efficacy of conventional therapeutic doses of colchicine have been registered for the treatment of COVID-19 (NCT04322682, NCT04328480, NCT04326790).

In this case we report a patient under treatment of colchicine because of rheumatoid arthritis for three years and diagnosed COVID-19 pneumonia. In our case, severe complication of pneumonia like ARDS was not observed. We think that this result may be related to early detection of pneumonia and early antiviral therapy. It is interesting in that it has been shown that colchicine does not prevent the development of COVID-19 pneumonia, even if this specific case. Patient was a nurse and she was in the high-risk group for the infection so just by this case we cannot reach a definite conclusion for general population. More data's and results of the ongoing trials are awaited to decide whether colchicine will take place in therapeutic protocols for COVID-19 infection.

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