

Successful management of a case of SARS-CoV-2 infection in an advanced Rheumatoid Arthritis patient by dose reduction of immunosuppressive medication

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Case Report

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Abstract

Rheumatoid Arthritis (RA) patients usually managed with immunosuppressive agents and they are at a higher risk of infections. There are limited data regarding RA patients with COVID-19. This article reports a RA patient with an acute SARS-CoV-2 infection that successfully managed by dose reduction of immunosuppressive medication.

Introduction

In late 2019, pneumonia due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, which has immediately spread around the world [1]. The major clinical manifestations of COVID-19 include a range from asymptomatic presentation to acute respiratory distress syndrome (ARDS) [2, 3]. The disease has more sequels in >60 years older patients and those who have comorbidities, such as pulmonary diseases, chronic kidney diseases, diabetes, and also impaired immune systems [4-6]. Rheumatoid Arthritis (RA) is a chronic autoimmune inflammatory disorder that affects joints more than other parts and sometimes associated with the number of comorbidities [7]. The treatment strategy of RA is based on Disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids, hence RA patients have a higher risk of infection, including the COVID-19 [7]. However, limited data are available about the severe case of COVID-19 in Rheumatoid Arthritis (RA) patients [8-12]. Here we present a complicated case of SARS-CoV-2 infection in a 49-year-old female.

Case Presentation

A 49 years-old woman admitted to the hospital (Valiye Asr hospital, Iran, Fars, Fasa) at 11, March 2020 with a dry cough, fever, myalgia, respiratory distress, dizziness and nausea. Though O₂ Saturation (SPO₂%) was low (%) on the admission, O₂ nebulizer administered (O₂ 5 lit/min), which resulted in the correction of O₂ Saturation (87%) very soon (Table 1 and Supplementary Figure 1, A, B, and C and Supplementary table 1). Four days before admission, she had only dry cough without other symptoms. She declared no sign of reduced smell and taste senses. Before admission, she had a history of contact with her two daughters, her husband, and 1-year-old grandchildren, that all of them were positive for COVID-19 by real-time PCR test. She was the only member of her family with severe respiratory problems that needed to be hospitalized (and also the only person with RA in her family), whiles the rest of the family showed mild symptoms and quarantined at home. The Chest x-rays on the first day of hospitalization showed pneumonia signs alongside with bilateral ground-glass pattern, vascular dilation, and traction bronchiectasis in the middle and secondary lobes (Figure 1, A, B, and C). Positive Real-time PCR tests confirmed the SARS-CoV-2 infection. Laboratory findings on admission was a very low WBC count and reduced number of platelets, elevated ESR and PT (Table 1 and Supplementary table 2 and Supplementary Figures 4). The patient's first ECG revealed an ST-elevation (Supplementary Figure 2) that may be resulted in ST-Elevation Myocardial Infarction (STEMI). Because the cardiovascular events are

among the most common cause of death in RA patients, the patient had a very sensitive condition to manage with intensive care strategy.

Therapy with Hydroxychloroquine was started on the 1st day and continued for 10 days. Oseltamivir was added on the 2nd day and continued for 6 days. The patient's nausea was controlled by Ranitidine, Ondansetron, and Pantoprazole. Kaletra (Lopinavir/Ritonavir 200-50 mg/day and night 2 tab each) was added to the antiviral regimen on the 4th day, continued as the main antiviral medication for 7 days until symptoms relieved. A cluster of Antibiotics was prescribed for the first week because of low WBC count and suppressed immunity to prevent secondary infection. In the following, she was treated with one period of Levofloxacin medication in the last week. Theophylline G and O₂ Nebulizer treatment helped to support the airway and reduce the respiratory symptoms (Table 1 and Supplementary Figure 3). As laboratory findings and symptoms demonstrate, the patient's condition was by the end of 1st week worsened. The WBC and RBC count were reduced (Supplementary Figures 4). Chest CT scans at the 2nd week revealed the destructive effects of inflammation of the infection (Figure 1, D, E, and F). Due to the laboratory findings and symptoms were more similar to the COVID-19 cytopenia, we decided to redesign the treatment. So, the DMARDs and immunosuppressant treatment were omitted. We then discontinued the Ebretex and Nisopred at the 2nd week by dose reduction, only Sulfasalazine was continued. This strategy led to increased WBC count and altered hematologic factors. By reducing the symptoms, the patient was discharged with a stable condition and quarantined for 14 days at home. Her real-time PCR was negative on day 21. The last CT scan showed a significant reduction in GGO on day 35 (Figure 1, G, H, and I).

Discussion

The patient's RA disease diagnosed 15 years ago with pain in her distal joints and her disease was under control by receiving conventional treatments (first-line treatments) as conventional Disease-modifying antirheumatic drugs (csDMARDs) medication (Ebretex (methotrexate) 15mg/week Thursdays and Fridays, Sulfasazin 1000mg/day), Ipravent 20 mg, vitamin D- calcium(1 tab/day) and corticosteroids (Nisopred 5 mg/day).

The results of this case have shown that a gradual reduction of immunosuppressive drugs led to decline the disease severity. Immunosuppressive medication in RA patients (e.g., csDMARDs and corticosteroids) in the course of SARS-CoV-2 infection may be as a double-edged sword [13]. Managing the RA disease with the lowest possible dose of csDMARDs besides antiviral therapy against SARS-CoV-2 could be an effective strategy for treatment of COVID-19 in RA patients.

Previous studies demonstrated the increased risk of infection as an adverse effect of corticosteroids [14, 15]. Our report also confirms this fact. Although some previous studies clarified that receiving Methotrexate is not associated with increased risk of infection in RA patient, previous findings are inconsistent with the results of our study [16, 17]. On the other hand, the most important cause of lung tissue damage and respiratory distress is due to the cytokine release storm (CRS) caused by the immune

system in response to SARS-CoV-2. Patients with RA who are being treated with immunosuppressive drugs such as corticosteroids and methotrexate have weakened immune systems, and this weakness puts forward this theory that they are safe from CRS and its destructive effects [18]. This is not confirmed in our case.

In this case report, all the family members were infected with the virus at the same time, only this patient with RA presented with severe respiratory symptoms and needed to be admitted to hospital. These conditions may indicate that a defect in the immune system caused by rheumatoid arthritis or as a result of medication has led the patient to acute respiratory illness caused by contamination with COVID 19 [8].

The immunosuppressive medication in RA patients in the course of SARS-CoV-2 infection may be like a double-edged effect. Managing the RA disease with the lowest possible dose of csDMARDs besides antiviral therapy against SARS-CoV-2 and managing infection symptoms could help to gain better clinical results.

Abbreviations

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

COVID-19: coronavirus disease 2019

ARDS: acute respiratory distress syndrome

RA: Rheumatoid Arthritis

DMARDs: Disease-modifying anti-rheumatic drugs

GGO: ground glass opacity

STEMI: ST-Elevation Myocardial Infarction

Declarations

ETHICS STATEMENTS

Informed consent was obtained from the participant for the publication of this case report. The study approved by the Ethics Committee of Jahrom University of Medical Sciences, Jahrom, Iran.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the Supplementary Material.

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Conflicts of Interest: The authors declare no competing interests.

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AUTHOR CONTRIBUTIONS

AB, MAB and AA designed the study. AB and MAB wrote the draft of the manuscript. AB and FF collected data and performed analyses. RR, FF, and AA supervised the study. AA revised the manuscript for submission.

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Tables

Table1: The patient's information, laboratory data, treatment and outcome.

Case Demographic information

Age	49
Gender	female
Background disease condition (Rheumatoid Arthritis)	
Year of RA diagnosed	16 (years)
CPK	90 days BI:+2
Last CD4 T cell count (cells per μ L)	90 days BI: 8.8
ESR	90 days BI: 50
RA medication before the infection	Immunosuppressive Ebetrex: 15mg/ twice weekly, Sulfasazin 1000mg/day corticosteroids (Nisopred 5 mg/day) Ca-D (1tablet PO-QD) Folic acid (1tab PO-QD)
MCV	90 days BI:97.3
MCHC	90 days BI :31.1
Clinical findings	
Duration of symptoms, days	BI :4 days
Temperature	OA: 38.2 DD:37
Symptoms	BI: dry cough OA: Headache, dry cough, fever, myalgia, chest pain , <i>respiratory distress</i> , dizziness Dd and HQ: dry cough, chest pain PI: mild chest pain
Quarantine time after discharge from hospital	14 days
Negative RT-PCR covid-19 test time	28 days after hospitalization
Duration of treatment	21 days
Blood pressure (mm Hg)	OA:110/70 DD:110/70
Respiratory rate (breaths per min)	OA: 25 DD:18
Heart rate (beats per min)	OA:90 DD:78
Chest CT scan findings	OA: Bilateral ground-glass opacities vascular dilation and traction bronchiectasis DD: developed Bilateral ground-glass opacities vascular dilation and traction bronchiectasis PI: mild ground-glass opacities
O2 saturation in ambient air	OA: 64% DD:98%
Red Blood cell count	BI:4.1(10^6 Mic) OA:4.2(10^6 Mic) DD:3.51
Hemoglobin(g/dL)	BI: 12.4 OA:12.6 DD:11.6
White blood cell count	OA:3.6 (10^3 Mic) DD:7.6 (10^3 Mic)
Lymphocyte	OA:30 % DD:31%
Neutrophil	OA:59% DD: 55 %
Platelets (cells per 10^3 /L)	BI:363(10^3 Mic) OA:130 DD:489
PT (ctrl = 13.5)	OA:12.9 sec
PTT (ctrl= 30)	OA:37.6 sec
C-Reactive Protein (mg/L)	OA:+1
ESR (1 hr)	BI:50 OA: 30
Severity of the infection at admission	Severe
Treatment during covid-19	

Antiviral Medication regimen	Hydroxychloroquine 200mg PO (Q12h) Tamiflu po (75 mg-12h) Lopinavir /ritonavir (200-50 mg Kaletra day and night 2 tab each)
Antibiotic	Imipenem (500 mg IV-Q8h) Vancomycin (1g IV-Q12h) levofloxacin (in home quarantine 750mg PO-Q24h)
Admitted to an intensive care unit	No
Invasive or non-invasive mechanical ventilation	yes
Corticosteroids	Yes (prednisolone 5 mg -QD)
RA medication	Immunosuppressive Ebetrex: 15mg/ twice weekly, Sulfasazin 1000mg/day Corticosteroids (Nisopred 5 mg/day)
Symptom control medication	Apotel (1Ampol IV if temperature>38 degree of centigrade) Ondansetron (4mg IV-stat) Pantoprazole (40 mg PO -Q12h) Promethazine (10mg PO-TID) Ranitidine (50mg IV-TID) Theophylline G (syrup 5cc PO-TID) Ca-D (1tablet PO-QD) Folic acid (1tab PO-QD) Ipraterium bromide (in home quarantine if feel shortness of breath)
Outcome	Cured

OA: On Admission; DD: Day of discharge from the hospital; PI: Post Infection; BI: Before Infection; HQ: Home quarantine.

Figures

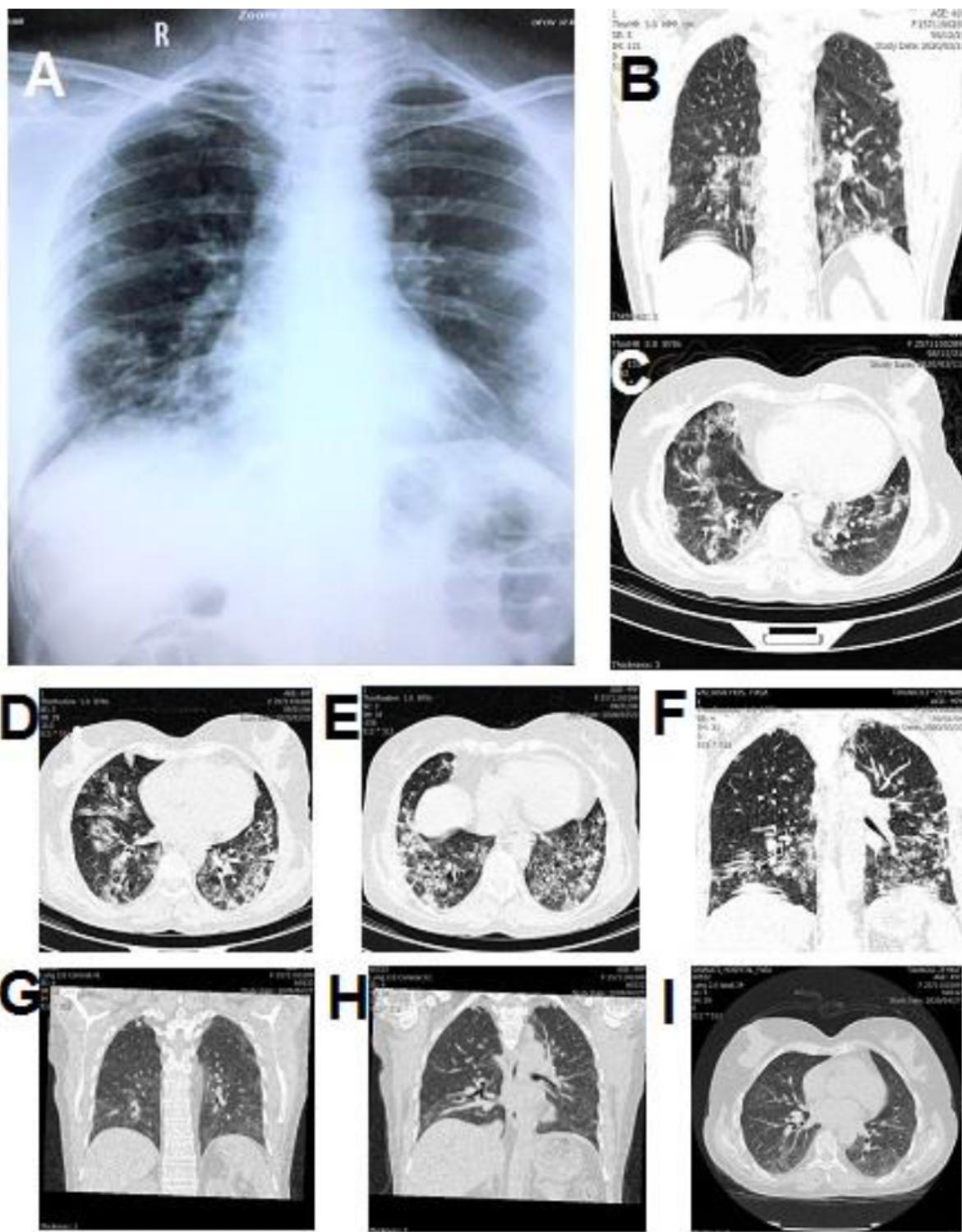


Figure 1

A: Chest x-rays on day of hospitalization showed transparency and bilateral lung involvement in the middle and secondary lobes. B: coronal section and C: axial section: Chest x-ray on day of hospitalization at 11/0/2020 showed transparency GGO and bilateral lung involvement in the middle and lower lobes. D, E, and F: CT scans at day 14 showed worsening and increased symptoms of lung involvement, GGO, and infiltrates. G, H, and I: CT scans at day 26/0/2020 showed further progression of the findings.

consolidation and visible intralobular lines (crazy paving pattern). G, H, and I: CT scans on day 35 showed a significant reduction in GGO.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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