The second wave of desaturation in COVID-19

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Abstract

After a complete symptomatic recovery after COVID-19 pneumonia, the second phase of desaturation is a new phenomenon that is being increasingly observed. Two possible mechanisms behind it can be a continued subclinical infection and lung fibrosis. We have presented a case with the former mechanism, who responded well to steroids.

Key Clinical Message:

A second wave of dyspnea and desaturation is being observed post COVID-19 pneumonia and ARDS. It may be secondary to an ongoing lung inflammation or fibrosis after COVID-19 infection. Steroids may have a role in the management of the inflammation.

Introduction:

In late 2019, a novel corona virus, severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), was identified in the human body and led to a pandemic [1]. Understanding the spectrum of this disease, it's prevention and optimal clinical management is the current focus of physicians and researchers around the globe. Many drugs have been and are being investigated for their role in the management of COVID-19 infection. Remdesevir has shown potential in decreasing hospital stay among COVID-19 infected patients [2]. Dexamethasone has shown a mortality benefit in severe COVID-19 [3]. However, the current management of SARS-CoV-2 pneumonia and ARDS focuses mainly on providing supportive measures [4].

The clinical course in COVID-19 varies from asymptomatic disease to fulminant ARDS [5]. There is anecdotal evidence about persisting dyspnea following treatment of COVID-19. Post-COVID pulmonary fibrosis is hypothesized to be one of the etiologies behind this phenomenon [6].Also, post- treatment; an asymptomatic patient may develop a subclinical infectious process. This subclinical infection may lead to a second phase of desaturation. There are currently no guidelines on the treatment of this second phase of desaturation. We present a case monitored the response of steroids in our patient who had desaturation secondary to an ongoing residual subclinical inflammation after he was treated for COVID-19 pneumonia. Our patient had an excellent response to steroids; hence we postulate that steroids can be a potential treatment for such patients.

Case Presentation:

A 53-year-old gentleman with a past medical history of diabetes mellitus, hypertension, and dyslipidemia, presented to the hospital with one day history of dyspnea. He was treated for COVID-19 pneumonia and was discharged one day prior to his readmission. His initial presentation was with dyspnea, fever, fatigue, and a dry cough. Investigation revealed a positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) with bilateral infiltrates on Chest Xray (CXR) [Figure 1a].

Initially he required 3-4 L of oxygen to maintain saturation, but the requirement increased in the subsequent days and reached up to 13 Liters of oxygen via non-rebreather (NRB) mask. He was treated with favipravir and dexamethasone for 10 days, according to the local guidelines at the time. The patient gradually improved, and his oxygen requirement decreased. He was discharged from the hospital in an asymptomatic condition, saturating 100 percent on room air. His repeated SARS-CoV-2 RT-PCR as negative.

One day after discharge, the patient presented with a new onset shortness of breath at rest and exertion. He was requiring 2-3 Liters of oxygen to maintain saturation (SPO^2) above 94 %, and was tachypneic (26 breaths per minute). He was afebrile and did not have any other symptoms. Chest examination revealed bi-basal crackles, with rest of the physical exam unremarkable.

A Chest Xray (CXR) was repeated and did not show significant changes comparing to the previous one [Figure 1b]. A CT pulmonary angiography showed no evidence of pulmonary embolism. However, it was significant for extensive bilateral patchy areas of ground glass opacities and patchy areas of consolidations with air bronchograms [Figure 2].

He was tested again for COIVD-19, but the RT-PCR result came negative, ruling out a possibility of reinfection. The sepsis workup did not reveal any bacterial growth (including Mycoplasma pneumonia, Legionella pneumophila and Chlamydia pneumonia). Nasopharyngeal PCR for common respiratory viruses (including Influenza, Parainfluenza, Respiratory syncytial virus and Middle East respiratory syndrome coronavirus) were negative. A bronchoscopy performed to rule out tuberculosis (TB), eosinophilic pneumonia or pulmonary hemorrhage was unrevealing.

As the patient continued to have desaturation, a multidisciplinary team decided to start a trail of 60 mg prednisolone for 2 weeks. He responded very well, and oxygen requirement decreased. He was off oxygen at rest in two days and was discharged with a follow-up in pulmonary clinic.

Repeated CXR after 2 weeks from discharge showed significant regression on bilateral infiltrate [Figure 1c]. Pulmonary Function Test (PFT) was done, which showed a restrictive pattern with decreased Diffusing capacity for carbon monoxide (DLCO) [Figure 3]. A 6 minutes walking test showed a vivid improvement compared to his previous condition where was not able to complete more than 3 minutes of walking.

Discussion:

COVID-19 infection has a wide spectrum of clinical course and can involve various organs. Lungs are the most common organs involved. Presenting complains include a dry cough, fever, myalgias, headache, dyspnea, sore throat, diarrhea, vomiting, ageusia and anosmia [7]. Most cases of COVID-19 infection are mild to moderate, whereas around 20 % progress to severe and critical illness. The long-term Respiratory sequelae of COVID 19 infection remains unclear, and may depend on disease presentation [8].

The greater part of research related to SARS-CoV-2 focuses on the management. To date, the treatment is largely supportive. Many drugs have been and are being investigated for this purpose, including hydroxychloroquine, Interleukin-6 pathway inhibitors such as tocilizumab, convalescent plasma, remdesivir and dexamethasone [2, 3, 9-11]. Among all the tested treatment modalities, the most promising results are from remdesivir and dexamethasone, as the preliminary reports show a reduction in hospital stay from the former and a reduced mortality by the latter.

The RECOVERY trial is investigating the role of dexamethasone in SARS-CoV-2 infection. Initial results show a decreased 28-day mortality in the treatment arm. However, this effect is seen only in the subset of patients requiring invasive and non-invasive mechanical ventilation [3]. Consequently, current guidelines recommend the use of dexamethasone only in moderate to severely ill patients [12].

In some patients, a second phase of dyspnea is seen after an interval asymptomatic recovery phase in patients successfully treated for COVID-19 pneumonia or ARDS. We propose two possible mechanisms behind this, post-infection fibrotic changes in the lungs or a continued subclinical infective process which becomes symptomatic again after some time. Fibrotic lung changes are reported in survivors with COVID-19

pneumonia and abnormalities in lung function have been detected in COVID-19 patients shortly after the discharge from the hospital [6, 13] . Our patient suffered from ongoing lung damage despite viral clearance and symptomatic recovery. This resulted in chronic lung changes as the pulmonary function test revealed a restrictive pattern with decreased diffusion capacity.

Pulmonary fibrosis usually occurs secondary to dysregulated healing process. Chronic inflammation can lead to fibrosis. The changes in the cellular and molecular environment in the lung tissue secondary to viral infection as in COVID are the key factors behind the fibrosis [14].

The ongoing damage takes place in the tissues secondary to the inflammation leading to an over expression of inflammatory cytokines, including transforming growth factor-1 , tumor necrosis factor-a (TNF-a), interleukin-1, and interleukin-6 (IL-6). This in turn stimulates the proliferation of type 2 alveolar cell and increase in fibroblast recruitment [15, 16]. Eventually, the cascade can lead to an increase the production and deposition of extracellular matrix (ECM), impairing gas exchange and hence leading to hypoxemia [16].

The long-term reversible and irreversible respiratory sequelae of COVID-19- remain obscure, as does the patient population at a high risk to develop them. Our patient had an excellent recovery with steroids. Authors are of the view that a large scale randomized controlled trial is required to establish the efficacy of steroids in post-COVID-19 recurrent dyspnea.

Conclusion:

The second wave of desaturation after resolution of symptoms post-COVID-19 treatment is a rare phenomenon. It can be secondary to an ongoing subclinical infection or due to fibrosis. The role of steroids is not studied in this scenario. Our patient had a dramatic response to steroids indicating a possible role in reducing the post infection inflammation. Larger studies are needed to investigate the management of post-COVID-19 desaturation.

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None

Author contributions

Conceptualization: FA, AA

Patient consent: Mohd A

Literature review: FA, AB, ZY, Mohd A, Mousa A, AE, AA

Manuscript writing: FA, ZY, Mohd A

Radiology part in writing and images: AB

Critical review and modifications: FA**,** ZY, AE, AA

Final review and approval: FA, AB, ZY, Mohd A, Mousa A, AE, AA

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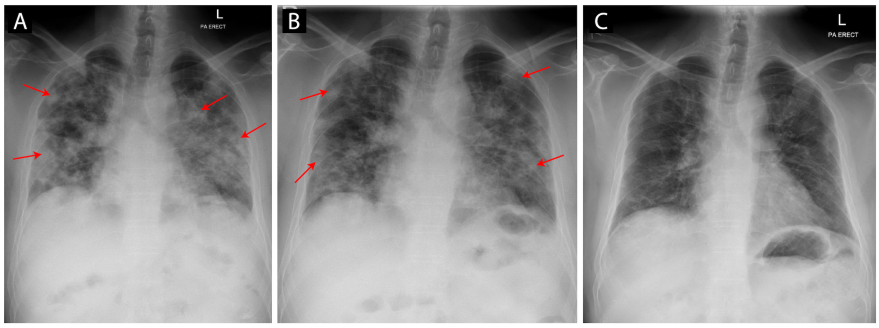
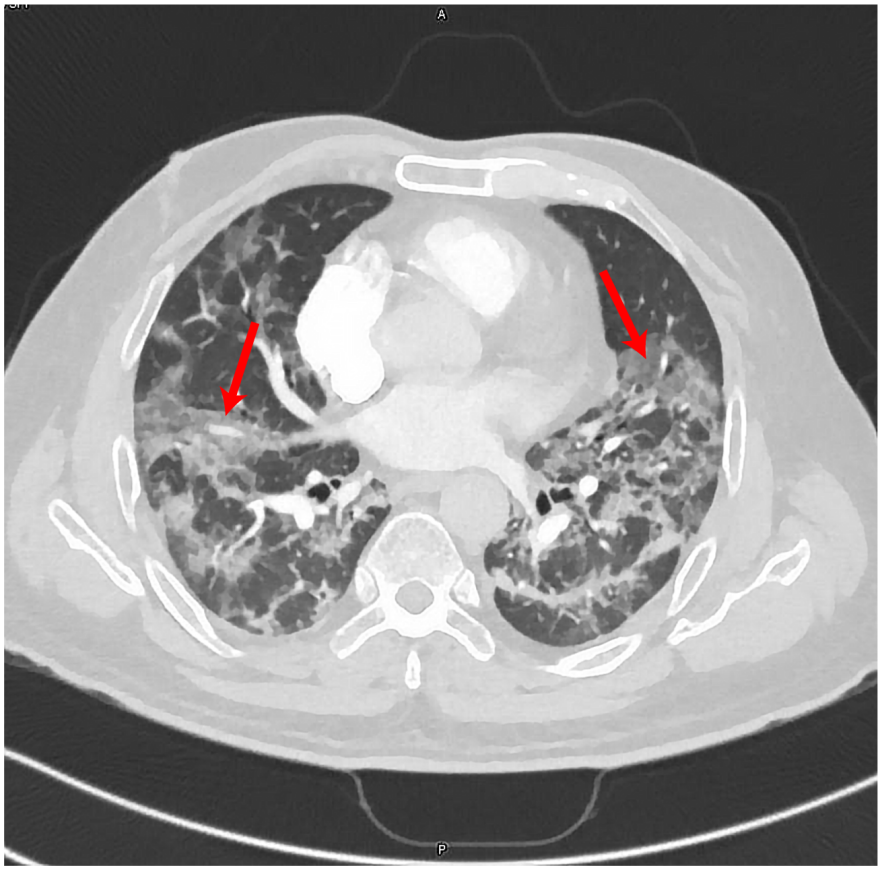
Figures:

Figure 1. CXR of patient (1a: at the time of COVID-19, showing bilateral infiltrates, 1b: at the time of second admission, showing similar changes, 1c: in follow-up clinic with improvement in infiltrates).

Figure 2. CT pulmonary angiogram, showing post infection changes

Figure 3. Pulmonary Function Test (PFT), revealing a restrictive pattern with decreased Diffusing capacity for carbon monoxide (DLCO).



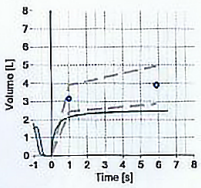


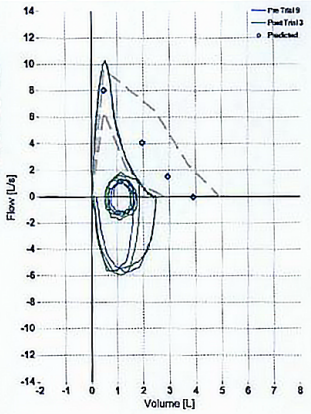
FVL

Tidal

Test Date: 9/16/2020 12:52:33 PM Predicted: Knudson, 1983 * 1.00

			Pre Best		Post Best		
Parameter	Pred	LLN	Trial 9	%Pred	Trial 3	%Pred	%Chg
FVC [L]	3.90	2.86	2.48*	63	2.50*	64	1
FEV1 [L]	3.18	2.45	2.15*	68	2.14*	67	0
FEV1/FVC [%]	81.1	70.4	86.8	107	85.6	106	-1
FEF25-75 [L/s]	3.34	1.35	2.78	83	2.64	79	-5
PEF [L/s]	8.04	-	10.23	127	10.34	129	1
FET [s]	-	-	5.9	-	6.5	-	11





DLCO

Test Date: 9/16/2020 1:02:20 PM Predicted: Miller, 1960 * 1.00

Parameter	Pred	LLN	Result	%Pred
DLCO [ml/min/mmHg]	28.6	20.6	19.0*	66
DLadj [ml/min/mmHg]	28.6	20.6	18.8*	66
VA sb [L]	5.00	4.64	3.25*	64
DLCO/VA (KCO) [ml/min/mmHg/L]	4.77	3.57	5.84	122
TLC sb [L]	6.15	4.79	3.40*	55
RV sb [L]	2.02	1.39	0.95*	47

SVC

Test Date: 9/16/2020 12:59:54 PM Predicted: Knudson, 1983 * 1.00

			Pre Best	
Parameter	Pred	LLN	Trial 2	%Pred
VC [L]	3.90	2.86	2.53*	65
VCex [L]	3.90	2.86	2.53*	65
VCin [L]	3.90	2.86	-	-
IRV [L]	-	-	0.89	-
IC [L]	-	-	1.91	-
VT [L]	-	-	1.02	-

Comment

Spirometry values shows moderate restriction. Bronchodilator salbutamol (metered dose inhaler -100mcg) given 2 puffs administered via aerochamber. Following administration of bronchodilators, there is no significant improvement.
Moderate reduction in diffusion values. The diffusing capacity was not corrected for the patient's hemoglobin.
This preliminary report should not be used clinically unless reviewed and signed by a physician.