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Happy hypoxia in COVID-19: The paradoxical killer

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ABSTRACT

Coronavirus Infectious Disease 2019 is an infectious disease with alarming international concern. It has led to a pandemic with profound mortality and morbidity increasing the stress of workload over healthcare all through the world. It presented with a broad spectrum of presentations ranging from a mild asymptomatic infection to acute respiratory distress syndrome. One of a major reason for mortality in COVID-19 is late presentation to the healthcare facility. Happy Hypoxia is a major reason for this late presentation as patient does not have any significant respiratory distress even at low oxygen saturations. Many of such cases only have mild to moderate disease and recover fully however in some cases critical patients with COVID-19 may require ICU admission with high case fatality rate. We report a case series of such patients who did not report to the hospital due to happy hypoxia but later turned out to have severe COVID-19 infection which turned out to be fatal.

Keywords: Coronavirus, COVID-19, happy hypoxia

1. INTRODUCTION

Coronavirus comes from a family of viruses that cause an Illness similar to common cold, Middle East respiratory syndrome, severe acute respiratory syndrome (SARS). The virus is now known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The severity of COVID-19 symptoms can range from very mild to severe. People who are older have a higher risk of serious illness from COVID-19, and the risk increases with age (Wu et al., 2020). People who have existing chronic medical conditions also may have a higher risk of serious illness.

Although much is known about the epidemiology and the clinical characteristics of COVID- 19, little is known about its impact on lung pathophysiology (Scholten et al., 2017). Most patients usually present with significant arterial hypoxemia but without signs of respiratory distress, they do not even verbalize a sense of dyspnea. This phenomenon is referred as silent or 'happy' hypoxemia. Since timely recognition of hypoxemia has such an impact on prognosis and adequate treatment decisions, we are here to offer an overview of the pathophysiological abnormalities present in COVID-19 which might be able to explain the disconnect between hypoxemia and sensation of dyspnea in the Patient.

2. CASE REPORT

Case 1

A 55 years old male presented with complaints of generalised weakness, cough and chest discomfort since ten days. RT-PCR for Covid-19 was done and was found to be positive. There were no complaints of cough, cold, sore throat, fever. No history of palpitations, breathlessness. No history of drug intake, joint pains or rashes was found. On general examination patient had pulse of 88/min and blood pressure was 130/80mmhg. Patient was maintaining a saturation of 87% on room air with no signs of respiratory distress.

Patient was put on 12 litres of oxygen in view of reduced arterial oxygen levels. HRCT Thorax was done which was suggestive of Ill defined multiple patchy ground glass opacities in both lungs with Interlobar septal thickening as described suggestive of infective etiology of atypical viral pneumonia with a corad-6 grading and a CT severity score of 18/25 (figure 1). Lab investigations are mentioned in Table 1. Patient was started on remdesivir, antibiotics, antiplatelets, and other multivitamin supplements.

After 6 days of Admission to the hospital, besides persistent adequate treatment, patient's general condition deteriorated and was unable to maintain saturation and was now in respiratory distress. He was put on Bipap Support however he was still tachypneic and had tachycardia. On day 13 an arterial blood gas analysis revealed paO2 of 48% and no clinical improvement was observed and Patient had to be taken on mechanical ventilator. Despite all medical management the Patient desaturated and succumbed on day 15 of his admission.

Case 2

A 38 Year old male was admitted to the hospital with the complaints of cold and sore throat since 5 days. No history of fever, cough, breathlessness. No complaints of chest pain, palpitations. No history of travel or contact. No history of Comorbidities such as hypertension, diabetes mellitus, tuberculosis or bronchial asthma. An RT-PCR for COVID 19 was done and was found to be positive. On general physical examination Patient was comfortable with a pulse of 102/min, Blood pressure-120/80 mmHg taken in right arm in supine position, spO2 was 85% on room air. An HRCT- thorax was done which was suggestive of multiple peripheral ground glass opacities in bilateral lung fields suggestive of atypical viral pneumonia with a severity score of 15/25 and CORAD 6 (figure 1). All lab investigations done are mentioned in table 1. Patient was started on Remdesivir, Dexamethasone, low molecular weight heparin, Ivermectin and other supportive measures. After 2 days of Hospitalisation patient was not maintaining saturation on oxygen support and hence was taken on Bipap support. On day 4 of his admission patient was intubated and taken on mechanical ventilator in view of falling saturation and gasping state and his arterial blood gas revealed respiratory acidosis along with pao2 of 54 mmhg. On day 7 of admission the patient succumbed even after all supportive measures and treatment.

Case 3

A 49 Year old female was brought to the hospital with the complaints of fever which was low grade and intermittent in nature since 6 days. It was associated with generalized weakness. There were no complaints of cough, cold, breathlessness. No history of palpitations or chest pain. No history of pain in abdomen, nausea, and vomiting. There was no history of any comorbidity such as hypertension, diabetes mellitus, tuberculosis or bronchial asthma. A reverse Transcriptase Polymerase chain reaction was done and was found to be positive. On general physical examination, pulse-78/min, blood pressure-130/90 mmHg taken in right arm in supine position, respiratory rate 24/min, spO2 88% on room air. An HRCT-thorax done was suggestive of bilateral ground glass opacities in peripheral lung fields with a ct severity score of 20/25 (figure 1). Laboratory investigations are as per table 1. Treatment was initiated with antibiotics, antiviral, low molecular weight heparin and steroids in view of her complaints and findings. Patient was put on oxygen support of 15 litres O2 on which she was unable to maintain saturation hence was shifted to non invasive ventilation. In view of repeated fever spikes Patient was started on high grade antibiotics, remdesivir, steroids and other routine supplements. During the course of stay, there was a fall in saturation levels and patient had to be shifted to ventilator. Despite all measures patient succumbed on 23rd day of Admission.

Case 4

A 76 Year old male came to the hospital with the complaints of cough since 6 days which was productive in nature and loss of taste since 7 days. Patient was a known case of type II diabetes mellitus on oral hypoglycaemic agents. No history of fever, cold, breathlessness. No history of chest pain, palpitations. No history of hypertension, bronchial asthma. On General Examination

Patient was afebrile, pulse was 76 beats per minute, regular in rhythm and volume, Blood pressure was 110/70 mm hg in right arm supine position, respiratory rate was 24 breaths per minute and saturation of oxygen was 89% on room air.

Systemic Examination including Chest was unremarkable. Patient's Throat and Nasal Swab for COVID-19 by (RTPCR) was sent and was found to be positive. HRCT Chest was done which revealed multiple ill defined patchy ground glass opacities with consolidation and septal thickening in bilateral lung fields suggestive of viral pneumonia with a CT Severity Score of 20/25 (figure 1). All laboratory investigations are as mentioned in table 1. Patient was started on intravenous antibiotics, remdesivir, low molecular weight heparin and oxygen supplement on 15 litres. However during the course of hospital stay patient was unable to maintain saturation and was started on non invasive ventilation with bipap support. On day 6 of his admission the patient was taken on mechanical ventilator due to his deteriorating condition. After 15 days of his admission the patient succumbed even after all supportive measures.

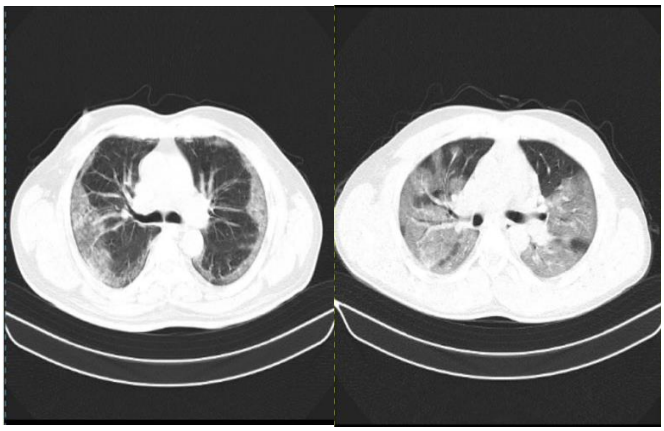
Case 5

A 29 year old female was admitted with the complaints of cough since 8 days which was productive in nature. No complaints of cold, fever, breathlessness. No history of chest pain, palpitations. Patient is a case of hypothyroidism on Tab thyrox 50 MCG OD. No comorbidities such as bronchial asthma, diabetes mellitus, tuberculosis, hypertension. On general examination, patient was afebrile, pulse was 96/min, blood pressure was 100/60 mmHg taken in right arm in supine position, respiratory rate was 20 breaths per minute and oxygen saturation was 84% on room air. An RT-PCR swab was sent which was found to be positive. High resolution CT scan of thorax was done which revealed multiple ill defined patchy ground glass opacities with changes of fibrosis and septal thickening as described above suggestive of infective etiology of atypical viral pneumonia with imaging grading corad-6 with a ct-severity score of 18/25 (figure 1). Laboratory investigations are as mentioned in Table 1.

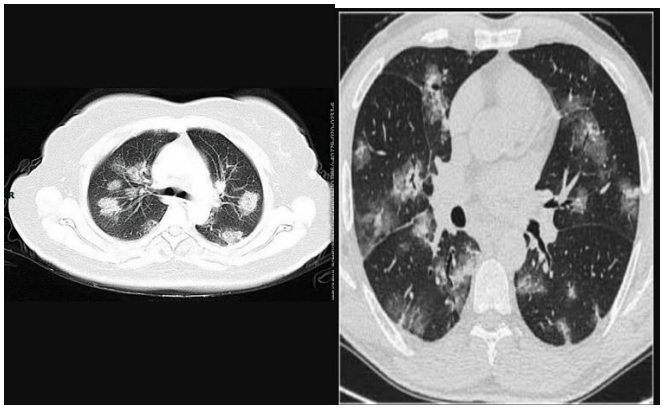
Patient was started on Remdesivir, intravenous antibiotics. Steroids, low molecular weight heparin and was nebulized routinely. After 6 days of hospital stay patient had further fall in saturation and was shifted to non-invasive ventilation. Her condition kept on deteriorating and she ultimately succumbed on day 10 of her admission.

Table 1 showing lab investigations of the Patients

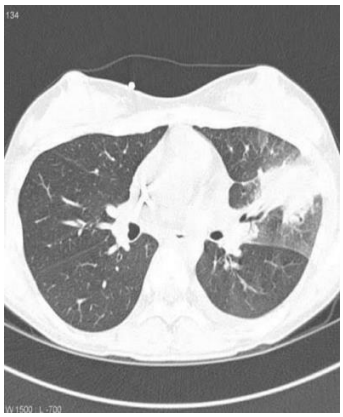
INVESTIGATIONS	CASE-1	CASE-2	CASE-3	CASE-4	CASE-5
CBC	Hb- 8.6gm% Mcv-82 Wbc-11800 Platelet-1.57 lac	Hb-12.6 gm% Mcv-85 Wbc-14003 Platelet-2.4 lac	Hb-11.4gm% Mcv-82 Wbc-6400 Platelet-2.8 lac	Hb-11.2gm% Mcv-76 Wbc-5280 Platelet-1.1 lac	Hb-9.4 Mcv-75 Wbc-380 Platelet-1.63 lac
LFT	Alkaline phosphatise- 78 SGOT-24 SGOT-16 Total bilirubin-0.3	Alkaline phosphatise- 66 SGOT-12 SGOT-26 Total bilirubin-0.5	Alkaline phosphatise- 98 SGOT-33 SGPT-26 Total bilirubin-0.3	Alkaline phosphatise-100 SGOT-82 SGPT-78 Total biirubin-0.6	Alkaline phosphatise-87 SGOT-2 SGPT-16 Total bilirubin-0.9
D-Dimer	7.6	0.6	1.3	2.9	1.2
KFT	Urea-28 Creatinine- 0.6 Potassium- 3.7 Sodium-136	Urea-16 Creatinine-0.8 Potassium-4.6 Sodium-134	Urea-22 Creatinine-1.2 Potassium-4.3 Sodium-146	Urea-34 Creatinine-1.1 Sodium-132 Potassium-4.8	Urea-16 Cretainin -1.1 Sodium-138 Potassium -4.2
Arterial Blood Gas analysis	pH-7.3 Pco2-46 PO2-65 PhCO3-22	pH-7.4 pCo2-38 PO2-84 PhCO3-26	pH-7.38 pCo2-31 pO2-76 PhCO3-27	pH-7.26 pcO2-22 PO2-69 PhCO3-23	pH-7.30 pCo2-21 PO2-77 PhCO3-32



Case 1 Case 2



Case 3 Case 4



Case 5

Figure 1 Showing HRCT of all Cases

3. DISCUSSION

COVID-19 induced pneumonia frequently leads to Hypoxemic Respiratory Failure or Type 1 respiratory failure. This can be accredited to Hypoxia induced constriction of pulmonary vasculature or secondary antiphopholipid syndrome or diffuse intravascular coagulopathy of pulmonary vasculature. Hypoxic pulmonary vasoconstriction is a response to hypoxia to attain homeostasis in the body which occurs in response to diseases like pneumonia. Hypoxia induced constriction occurs of the

pulmonary arteries that supply the affected segments of the lung thus providing perfusion to better ventilated alveoli. This leads to optimization of ventilation/perfusion matching as more blood reaches the adequately ventilated alveoli than the alveoli with reduced ventilation due to the disease. The impairment in this hypoxic pulmonary vasoconstriction is seen in COVID-19 pneumonia (Gattinoni et al., 2020).

This leads to a ventilation and perfusion mismatch (V/Q mismatch) causing persistence of pulmonary blood flow to non ventilated alveoli which can be reflected as a marked increase in P(A-a) gradient of Oxygen. Also there is marked lung edema, loss of surfactant along with superimposed pressure alveolar collapse leading to perfusion of a massive amount of non aerated tissue of the lung. This leads to intra pulmonary shunting. Over time this edema of the lung increases casuing an increase in shunting and reduction in oxygenation of blood. There is intravascular microthrombi formation and reduced lung compliance which further leads to worsening of hypoxia in COVID-19 (Jain et al., 2021). However there is preservation of lung mechanics in the initial course of the disease causing a "Happy Hypoxia" where the hypoxia seen in the saturation of the patient is not matched with his symptoms clinically as the patient remains relatively stable with no respiratory distress.

The abnormalities in gas exchange occur before there is increase in mechanical load of the lung. During the initial days of infection the airway resistance is also less and there is arguably no increase in physiological or anatomical dead space. There is no increase in breathing effort also as the patient's lung mechanics remains to be satisfactory, Relatively high lung compliance explains the absence of breathlessness in the initial stage of COVID pneumonia (Dhont et al., 2020). This happy hypoxia is followed by a stage of rapid deterioration.

As there is progression of disease the areas with consolidation do not inflate easily due to increase in transpulmonary pressures. The volume loss is higher lung volumes. This loss of volume seen in later stages leads to reduced compliance causing laboured breathing pattern. The dynamic compliance of the remaining lung is also effected due to loss of surfactant causing further increase in work of breathing. Furthermore, the Physiological dead space also increases due to reduction in blood flow caused by microthrombi. Therefore with disease progression the dyspnea becomes clinically apparent.

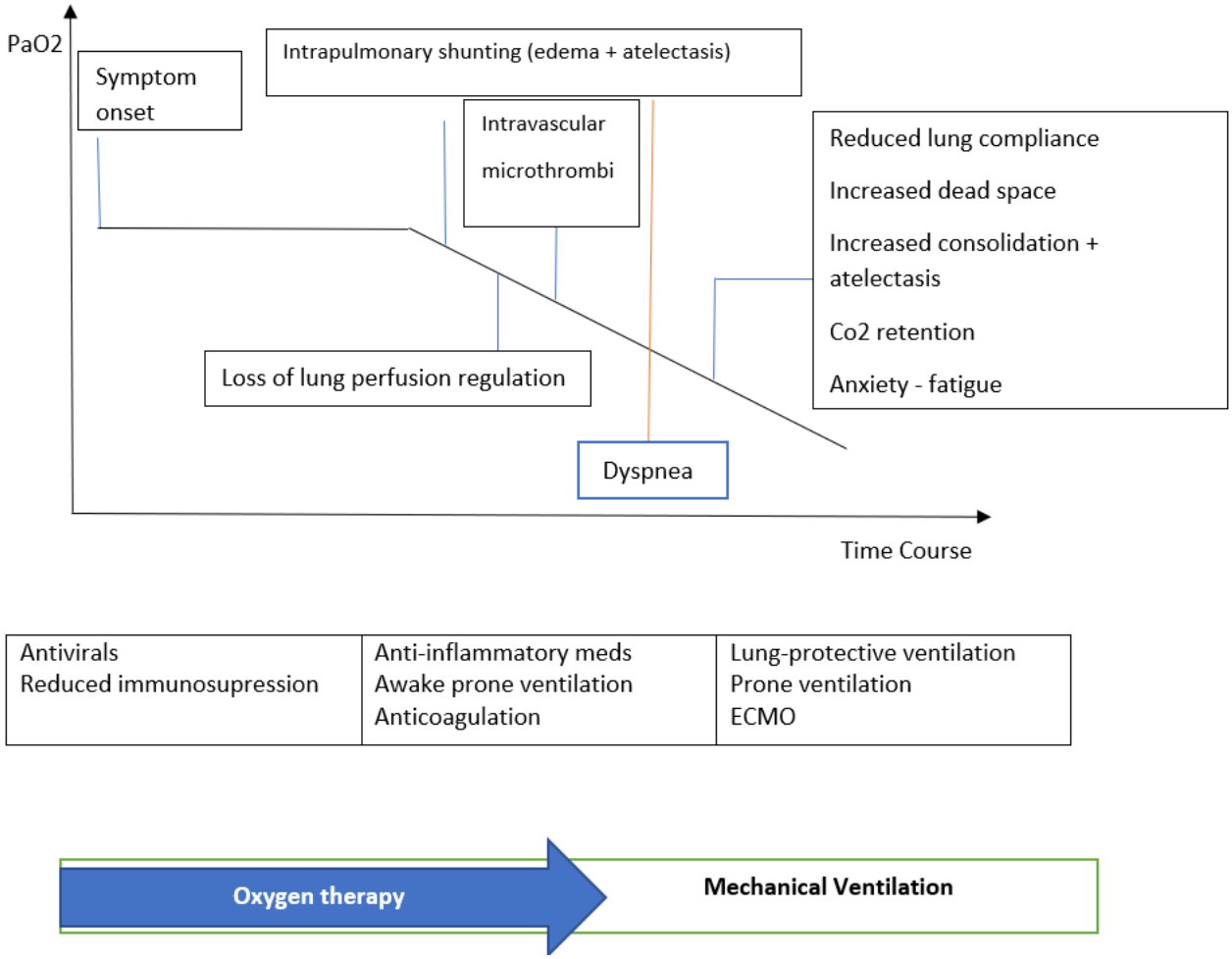


Figure 2 Showing the clinical course of COVID-19 (Source: Dhont et al., 2020)

A Detailed understanding of the clinical course of COVID pneumonia (figure 2) which begins with the happy clinical phase leading on to a rapid deterioration is important for physicians as it emphasises on the importance that the patient and clinicians should be on outlook of this phenomena while treating patients to prevent mortality.

4. CONCLUSION

The remarkable mismatching seen between the hypoxia and a clinically stable patient with happy hypoxia is seen often and physicians should thus not rely on the clinical well being of the patient alone as it can be misguiding at times. This calls for a close monitoring of heart rate, saturation, respiratory rate and signs of hyperventilation. It should be kept in the back of the mind that this clinically happy picture is lead by a rapid deterioration which at times can be fatal as shown by our case series.

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Author's Contribution

All authors have contributed substantially for the concept, assessment and evaluation, data acquisition and development of this work. All authors read and approved the final version of the manuscript.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed Consent

Written & oral informed consent was obtained from the patient in this case report. Additional informed consent was obtained from all individuals from whom identifying information is included in this case report.

Data and materials availability

All data associated with this study are present in the paper.

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