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Natural Course or Missed Block? A SARS-CoV-2 Case Report

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Abstract: ***It's not about virus per se, it's not about getting confined to hospital room boundaries, ITS ABOUT thousands of lives in and around you getting affected by sudden change in natural progression of COVID-19 virus behavior on day 7-10. Here we report a 35 year healthcare professional on regular monitoring and follow up gets entangled in sudden cytokinin storm on day 10 of illness. CRP AND CT IMAGING plays a pivotal role in early diagnosis and management of cytokinin storm.***

Keywords: Cytokine storm, COVID-19, SARS-CoV2, Inflammation, Lung damage

1. Case Report

35 year old male patient started with Cough and irritation in throat. On DAY 3 he developed f ever high grade (102'f) and started on antibiotics and paracetamol, isolated self. On day 4 CRP 26.4, LDH 265 and rest CBC was normal, Started on medical treatment.

Day 5 to Day 9 were asymptomatic, afebrile and in recovering phase. On **DAY 9) he had** MILD FEVER (100'f) with SPO2 96.

DAY 10 THE DAY WHAT JUST HAPPENED!!!! Patient developed

Generalised body ache and fever, spo2 93 (slight fall from 95)

HR CT chest suggestive of COVID-19 associated pneumonia with total ct severity score of 29/40(SEVERE) WITH CORADS 5.

CRP 192, LDH 526, sr ferritin 1000, d dimer normal.

Patient immediately hospitalised and started with iv steroids, antiviral (inj remsedivir) and anticoagulants.

ON NEXT 2 DAYS patient did struggled with spo2 falling to 88 and breathlessness on exertion but he did respond well to timely intervention.

ON DAY 13 crp dropped to 92 and maintaining sp02 to 93-95.patient recovered well by day 16 and crp dropped to 29.

2. Discussion

Outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was initially identified in Wuhan China in December 2019, and has led to a global pandemic that not witnessed for more than a century. Virus transmission can be limited by only means of social distancing and use of masks.

COVID-19 infection can vary from asymptomatic individuals to patient with fever, dry cough sore throat, loss of smell, taste and headache and accompanied by high rate of human to human transmission. Patients develop atypical upper respiratory tract pneumonia that poses challenge to clinician for management of disease. Sudden and abnormal uncontrolled cytokine production in critically ill COVID-19 pneumonia patients has been observed and this uncontrolled release of cytokine leads to acute exacerbation of symptoms and disease progression leading to morbidity and mortality in few patients [1]. Development of a cytokine storm is a warning sign of disease escalation; COVID-19 disease shares similarities with other viral diseases such as SARS, MERS and influenza in this sense.

A retrospective study of 41 patients with COVID-19 showed that most SARS-CoV-2 infected patients present clinically with mild symptoms, while a minority of patients progressively declined from the infection and eventually died of acute repiratory pneumonia and multi organ involvement[2]. IN view of mortality and morbidity due to sudden cytokine storm here we review factors involved in identification and management of this disease [3].

Role of cytokine storm in progression of SARS COV PNEUMONIA

The secretion of multiple cytokines [IFN-γ, TNF-α], also termed Cytokine Release Syndrome (CRS), is closely related to development of clinical symptoms.

TNF-α can cause flu-like symptoms similar to IFN-γ, with fever, general malaise, and fatigue, but can also cause vascular leakage, cardiomyopathy, lung injury, and acute-phase protein synthesis [4]. IL-6, which is an important target in CRS induced by adoptive cell therapy, can lead to vascular leakage, activation of complement and the coagulation cascade, leading to the characteristic symptoms of severe CRS, such as diffuse intravascular coagulation (DIC) [5, 6]. IL-6 is likely to cause cardiomyopathy by promoting myocardial dysfunction, which is often observed in patients with CRS [7]. Activation of endothelial cells is also one of the hallmarks of severe CRS. Capillary leakage, hypotension and coagulopathy can be result of endothelial dysfunction [8] (Fig. 1). Various studies have shown that Virus-induced immunopathological events play a crucial role in the fatal pneumonia observed after COVID-19 pneumonia infections [9].

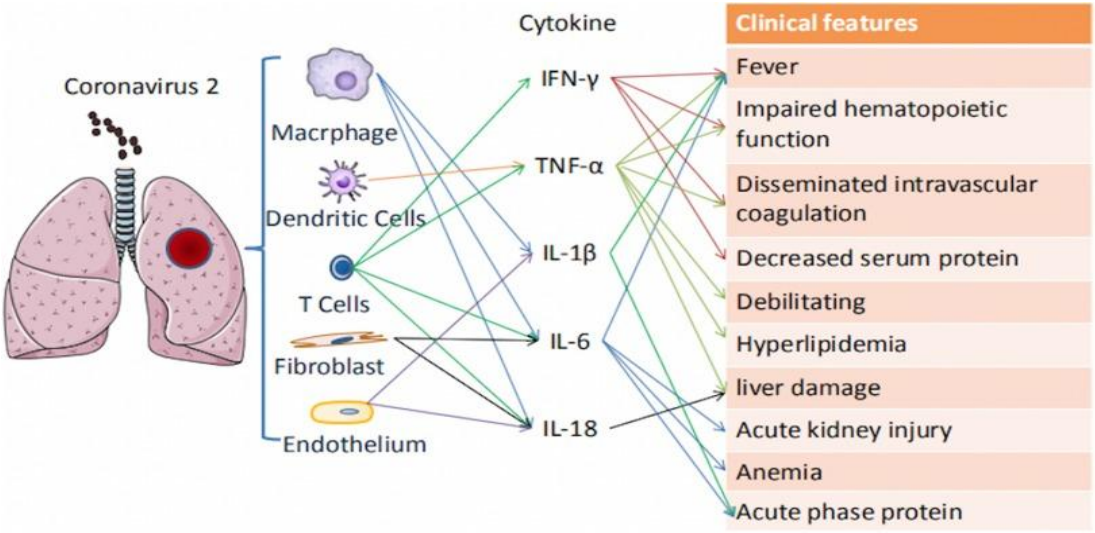


Figure 1: Figure depicting clinical feature and various cytokine receptor

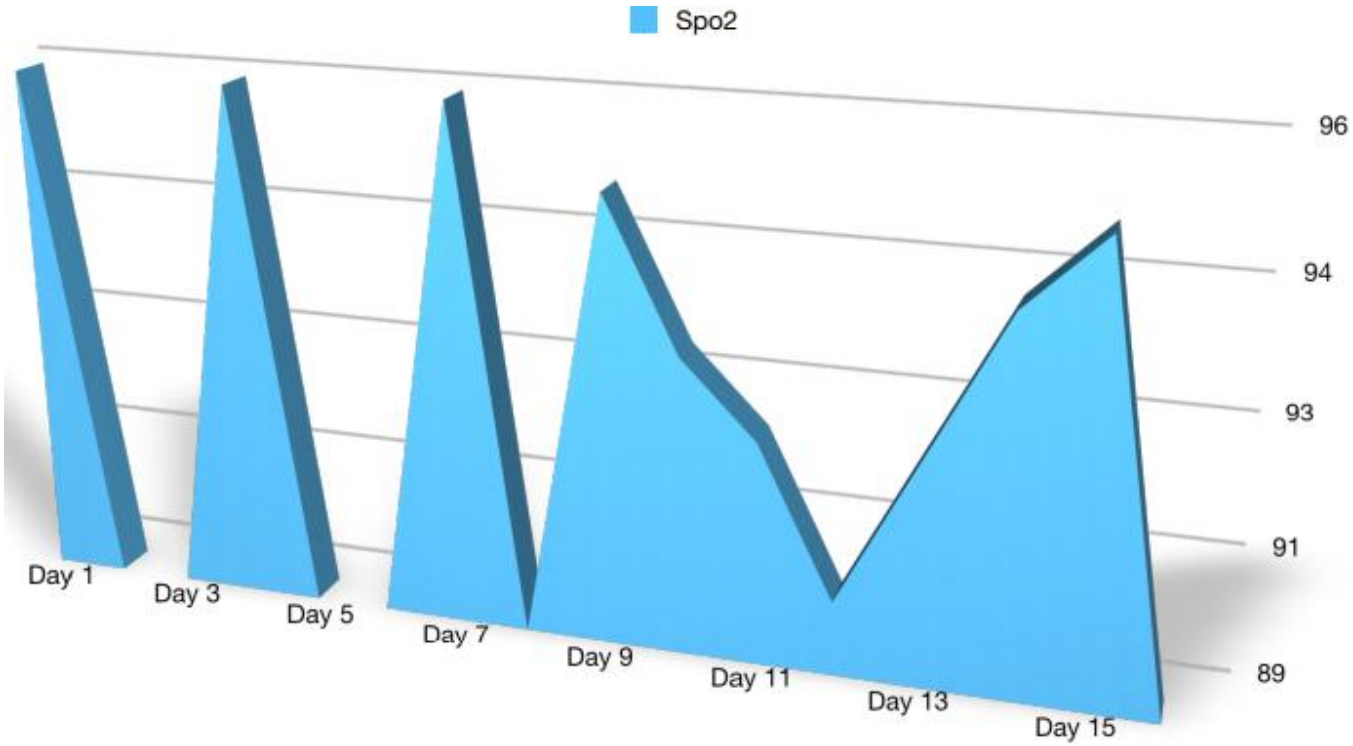
Rapid production and hyperactivation of T cell, macrophages natural killer cell and over 150 inflammatory cytokines and chemical mediators released by immune or non immune cells takes place and make Cytokine storm a potentially vey fatal immune condition [10, 11]. Pro inflammatory factors aberrant release leads to lung epithelial damage and damage of endothelial cell in viral pneumonia which leads to vascular leakage, alveolar edema and hypoxia. Aberrant production of pro-inflammatory factors, containing IL-6, IL-8, IL-1β, and GM-CSF, and chemokines CCL2, CCL-5, IP-10, and CCL3, together with reactive oxygen species during cytokine storm cause acute respiratory distress syndrome leading to pulmonary fibrosis and mortality [12].

High serum pro-inflammatory cytokines like IFN-γ, IL-1, IL-6, IL-12, and TGFβ and chemokines like CCL2, CXCL10, CXCL9, and IL-8 were detected in cases of severe pneumonia compared to patients with uncomplicated SARS [13]. Compared to mild or moderate disease in MERS infection, high levels of serum pro-inflammatory cytokines (IL-6 and IFN-α) and chemokines (IL-8, CXCL- 10, and CCL5) were observed in severe disease, [14]. IL-6 in severe diseased group was found to be 76 % higher than in mild group (30 %) [15, 16]. Clinical chest examination in patients with early phase SARS-COV-2 pneumonia also revealed patchy inflammatory cell infiltration; however, the pathological results in early stage of SARS-COV2 pneumonia require further confirmation [17]. IN conclusion multiple cytokines aberrant release of trigger a cytokine storm that produces immune pathological damage to multiple tissues and organs, even when body immune response seeks to suppress and eradicate the virus (Fig. 1).

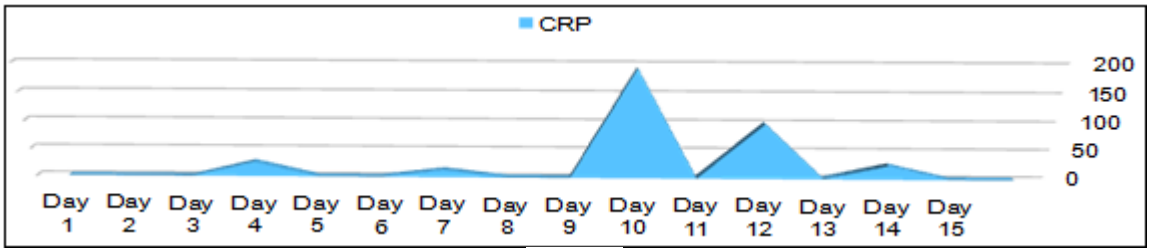
In this present case report patient had sudden rise in symptoms (graph 1) on day 10 of illness and there was sudden spike in crp (table 1, graph 2) jump of almost 10 times. Other parameters like LDH, SR FERRITTIN AND IL-6 were also raised on day of symptom deterioration. In such scenarios there is race with disease progression and timely and momentarily intervention in key to revive such patients.

Table 1

	CRP	Spo2
Day 1		96
Day 2		
Day 3		
Day 4	26	96
Day 5		
Day 6		
Day 7	13	96
Day 8		
Day 9		95
Day 10	192	93
Day 11		92
Day 12	98	90
Day 13		92
Day 14	25	94
Day 15		95

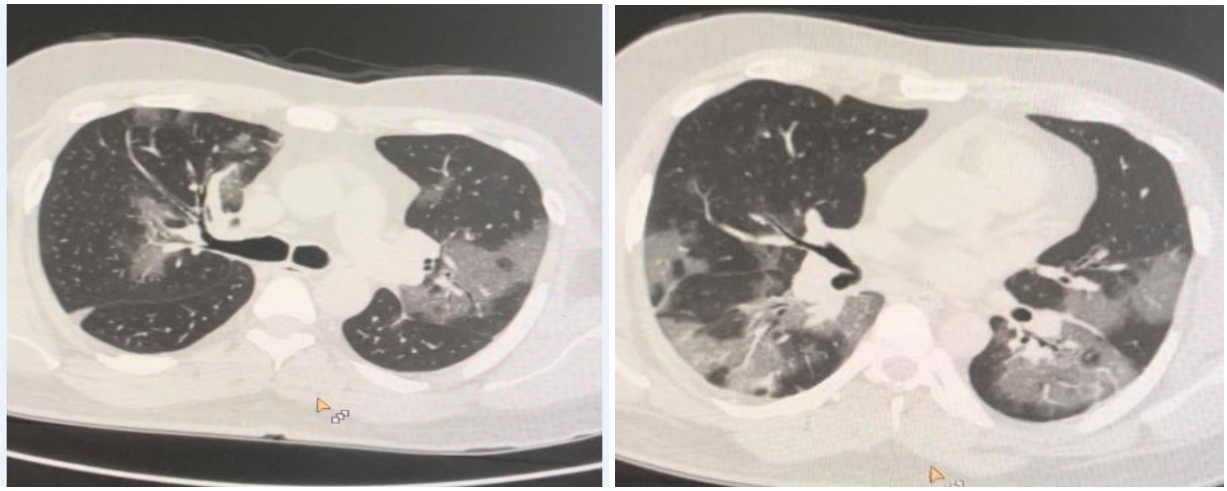


Graph 1



Graph 2

Timely performed High-resolution CT (HRCT) of the THORAX can provide important information regarding the progression of COVID-19 pneumonia and thus helping in its early prognosis and managing progression of COVID-19 pneumonia.



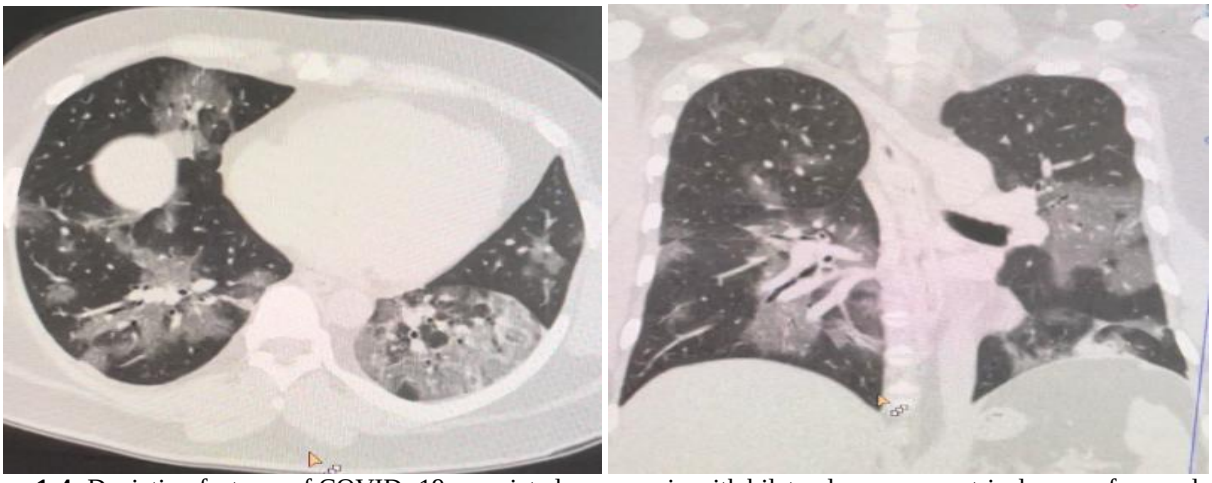


Figure 1-4: Depicting features of COVID -19 associated pneumonia with bilateral near symmetrical areas of ground glass opacification, inter/ intralobular septal thickening and patchy air space opacification in bilateral lung parenchyma giving apico-basal gradient with Total CT severity score of 29/40 (severe).

Close attention should be paid in the treatment of patients with SARS-CoV-2 infection, to limit the impact immune inflammatory factor release, and several effective cytokine storm blockers and therapeutic methods. In the clinical process of COVID-19 pneumonia, there is window period between the diagnosis and the occurrence of MODS which is about 5–7 days. During and after this window period patient can either recover which comprise about 80% but ~20 % of the patients progress to severe pneumonia, with ~ 2 % mortality [18]. To improve the prognosis, we suggest that patients with COVID-19 pneumonia be given targeted focused treatment at the time of diagnosis, in order to block the possibility of a subsequent cytokine storm. The early and timely use of immunological and clinical intervention in the evaluation of patients with MODS may reduce mortality in the most severe and critical patients (Fig. 2, position 2).

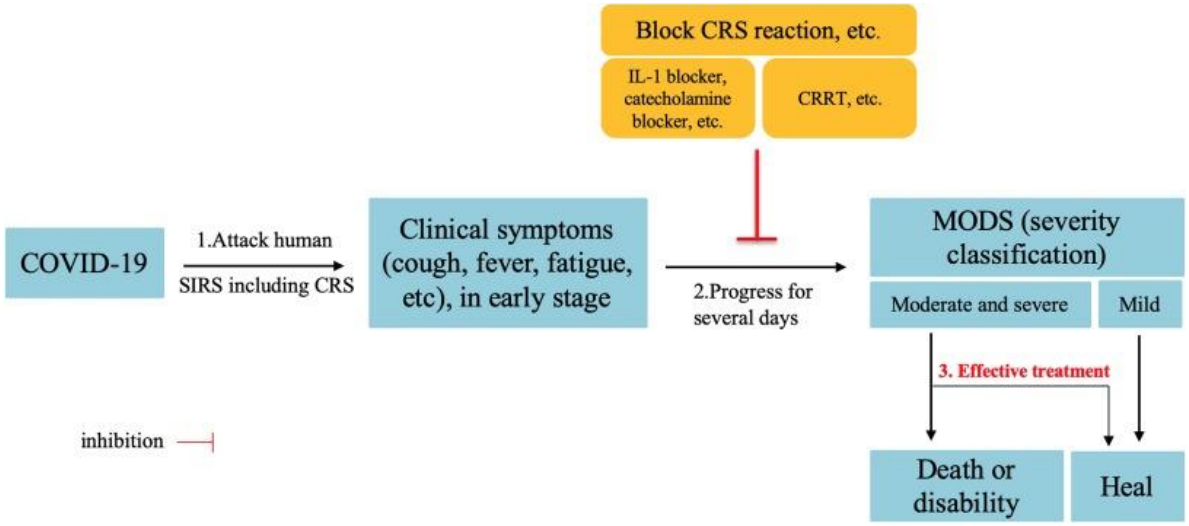


Figure 2: A summary of the process of onset SARS-CoV2 pathogenesis with potential treatment options against the virus-induced cytokine storm

3. Conclusion

After COVID-19 infection, some patients develop systemic inflammatory response syndrome (SIRS) and MODS characterized by the uncontrolled release of inflammatory mediators, giving rise to a cytokine storm that contributes to increased mortality in ARDS. Accurate prediction and targeted intervention is very crucial and life saving during the course of COVID-19 pneumonia will be essential to improve patient survival.

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