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# Early Onset of Pulmonary Fibrosis in a Known Patient of Covid-19 Pneumonia - A Case Report

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**ABSTRACT**--A Known Patient Of COVID-19 Pneumonia , with CORADS - Score of 5 (CORAD-5),treated with standard protocols ,oxygen support and NIV ,could not be weaned off oxygen support. Pulmonary Thromboembolism, was suspected and CT Pulmonary angiogram was ordered.CTPA showed Extensive Pulmonary Fibrosis in a time frame of 16 days.

**Keywords:** COVID-19 Pneumonia , Pulmonary Fibrosis , NIV(Noninvasive ventilation) ,Pulmonary Thromboembolism

## I. INTRODUCTION

In December 2019, reports emerged that a coronavirus that specialists had never before seen in humans had begun to spread among the population of Wuhan , China(1).

The novel coronavirus 2019(COVID-19) also known as severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) is an enveloped RNA virus belonging to the beta-coronaviridae family(2). COVID-19 has been found to be the cause of severe pneumonia and acute respiratory distress syndrome (ARDS) with a significantly high mortality rate(3). It transmits from bats like other virulent coronavirus (Cov)strains such as severe acute respiratory syndrome coronavirus(SARS-COV)and middle East respiratory syndrome coronavirus (MERS-COV) COVID-19 has become the focus of medical world(2).

On March 11th, 2020 World Health Organization assigned to COVID-19 a pandemic status. Although patients initially present with fever with or without respiratory symptoms, various degrees of pulmonary abnormalities develop later in all patients and these can be seen on chest computed tomography(CT) imaging(4).

Here we report a case of elderly male presenting with generalized weakness, headaches, body aches and shortness of breath, later found to be COVID-19 negative through real time polymerase chain reaction(RT-PCR) from nasopharyngeal swab , in spite of chest computed tomography(CT) imaging showing CORADS-score of 5(CORAD-5) at presentation ,which rapidly progressed to post inflammatory pulmonary fibrosis.

## II. CASE REPORT

On August 5th , 2020 a 59-year old male( non-smoker) with a medical history of Hypertension , Diabetes, presented to out-patient department with a history of generalized weakness, headaches and body aches since July 31st,2020 and shortness of breath since August 4th,2020.

The initial physical examination revealed a heart rate of 93 bpm, an oxygen saturation( SpO2) of 70% on ambient air and blood pressure of 110/61 mmHg. He was immediately admitted to a high dependency unit .

He required high flow oxygen(10lpm) through a non rebreathing mask to maintain an oxygen saturation(SpO2) of 92%.He also was put in prone position . A chest X-Ray was performed on August 5th,2020 which showed dense homogenous opacities predominantly of lower lung lobes (figure 1)

Nasopharyngeal swab was sent for covid-19 - Real time polymerase chain reaction test( gold standard ) which panned out negative. The chest CT of this patient on August 5th,2020 showed CORADS score of 5(figure 2) . He was started with Empirical course of Antibiotics ,Antivirals and short course of steroids. However, patient's condition deteriorated on August 5th ,2020 . He was started on NIV with AVAPS mode with IPAP maximum of 16 cm of H2O, minimum of 14 cm of H2O and EPAP of 5 cm of H2O. On 6th day of admission NIV was removed and the patient was then put on 15 lpm of high flow oxygen with which oxygen saturation(SpO2) of 98% was maintained. He was then Weaned off NIV and was put on oxygen support with a requirement of 6lpm of oxygen, with oxygen saturation(SpO2) around 94%. Gradually oxygen requirement reduced from the time of admission ,but a baseline requirement of oxygen was needed with 3 lpm to maintain an

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oxygen saturation(SpO2)of 92%.. On 16th day of admission , in view of the continued support of oxygen, not being able to wean off oxygen support and several episodes of Nocturnal de-saturation observed in the initial days of hospitalization, Pulmonary Thromboembolism was suspected and CT pulmonary angiogram was advised . The report showed no evidence of pulmonary embolism, but it showed rapid onset of extensive Pulmonary fibrosis. On the 20th day , patient was discharged on home oxygen therapy with a requirement of 3 lpm to maintain oxygen saturation(SpO2) of 92% and prescribed anti fibrotic therapy with pirfenidone.

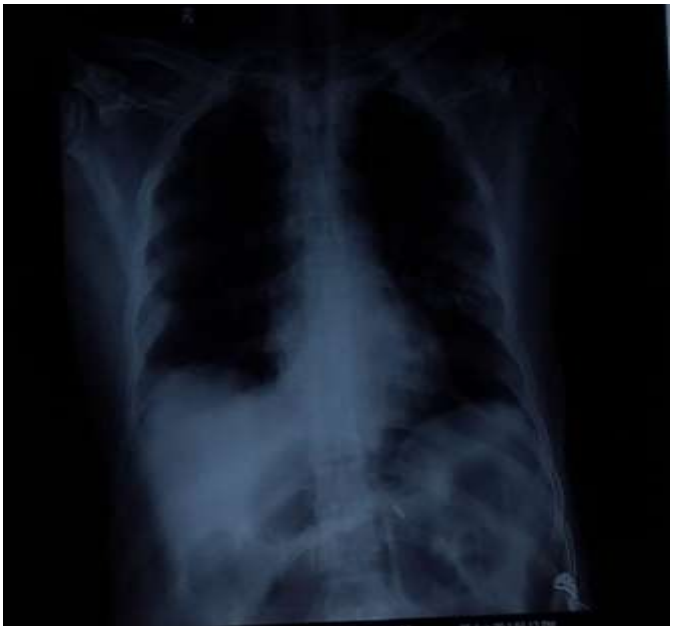

**Figure1 Chest X-ray showing Right Lower zone dense homogenous opacification**

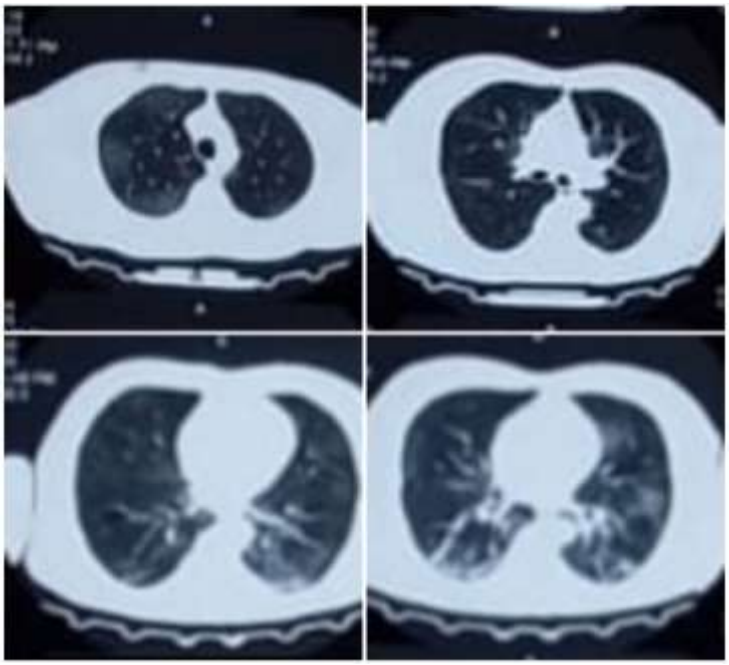

**Figure 2The first CT scan 6 days after symptoms onset showed Bilateral ground glass opacities predominantly involving lower lobes**

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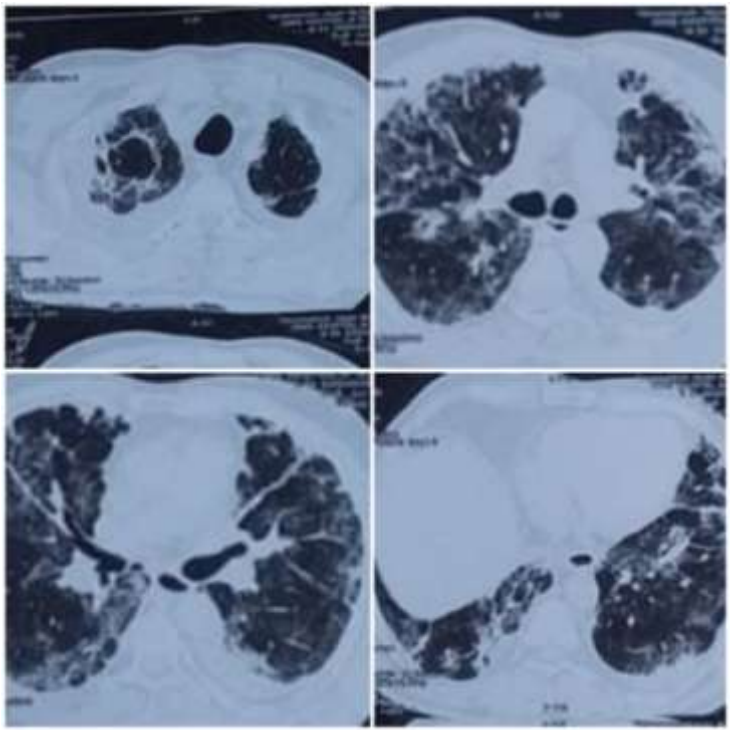

**Figure 3 CTPA scan performed 16days later progressed in to Extensive Pulmonary fibrosis involving all lobes of both lungs**

## III. DISCUSSION

Post-inflammatory pulmonary fibrosis has been categorized as a general diagnostic code used by providers of parenchymal fibrosis(5), which was not rare after viral pneumonia and caused continuous pulmonary function loss , reported in middle east respiratory syndrome(MERS) patients. Similar to SARS-COV, SARS-COV-2 binds to human cells using the angiotensin-converting enzyme 2(ACE 2) as a receptor, which is found in many tissues such as the lung, kidney, heart and intestines (6).Of the 1099 patients with confirmed COVID-19 in the Chinese study by Guan and colleagues(7),173 had severe disease. In this group, the median age was 52 years,100(57.8%) were male, 41(23.7%) had a history of hypertension, 28(16.2%) had diabetes mellitus, and 10(5.8%) had coronary artery disease. Of 67 patients who were admitted to intensive care required mechanical ventilation, or died, the median age was 63 years, 45 ( 67%) were male, and 39(58%) had a co morbidity, of which the most common was hypertension affecting 24 (36%) individuals . Pulmonary fibrosis usually occurs as a consequence of severe and/or prolonged assault to the lung).Excessive deposition of extra cellular matrix occurring in response to the prolonged insult lead to lung fibrosis(8). Alveolar epithelial damage follows the application of the injurious stimulus, and this results in the release of damage-associated molecular patterns(DAMPs) from injured cells. This in addition to pathogen-associated molecular patterns(PAMPs) from microbes, are recognized by alveolar macrophages, leading to a series of downstream transduction, and release of antimicrobial and pro inflammatory cytokines including IL-1 and TNF(9). The presence of air space exudates , alveolar collapse, and interstitial, edema show as ground glass opacity, consolidation , and septal thickening upon chest imaging(10) .Following alveolar injury, fibroblast migration to the site of the injury is stimulated by fibroblast growth factor(FGF), PDGF, TGF- beta and IL-1(11).Fibroblasts synthesized collagen, fibronectin, and ECM ground substance. In addition to disorganized ECM synthesis, myofibroblasts play an additional role in the inflammatory response by secreting IL-1 , IL-6 , IL-8 and monocyte chemo attractive protein -1 (MCP-1)(12).Normally CT changes overline during Early stage (0-4) shows Ground glass opacities, Partial Crazy paving ,with lower number of involved lobes, Progressive Stage (5-8) shows Extension of Groundglass Opacities, Increased Crazy paving Pattern, Peak Stage (10-13) shows

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Consolidation, Absorption Stage(14 days) showed Gradual progression (13).

There is accumulating evidence that a subgroup of patient's with covid-19 develop cytokine storm syndrome leading to increased mortality from the virus induced hyper inflammation(14). The prevalence of post-covid-19 fibrosis will become apparent in time, but early analysis from patients with covid-19 on discharge from hospital suggests a high rate of fibrotic lung function abnormalities. Overall, 51(47%) of 108 patients had impaired gas transfer and 27(25%) had reduced total lung capacity(15). In a study of 62 patients by Zhou Et Al, fibrotic changes were seen on chest CT scans in 21(33.9%) patients , with this finding more likely to occur in advanced-phase disease (8-14 days after the onset of symptoms) than early phase of the disease ( <7 days after the onset of symptoms)(16) .

Suggesting that, to be effective any potential anti fibrotic intervention should be considered within the first week of ARDS onset(17).The rationale for using anti fibrotic therapy is based on the spectrum of pulmonary fibrotic disease observed in COVID-19, ranging from fibrosis associated with organizing pneumonia to severe acute lung injury, in which there is evolution to widespread fibrotic change(18). On March 30th, 2020 , Vicore Pharma submitted a clinical trial application for C21(an agonist of AT2R) in IPF and this drug has been given approval for a phase 2 study in COVID-19(19).Pirfenidone reduces serum and lung IL-6 concentrations in murine models of pulmonary fibrosis, providing further biological rationale for the use of pirfenidone in COVID-19(20).

Given the scale of the COVID-19 pandemic and the number of people requiring invasive ventilation worldwide, post COVID-19 fibrosis is likely to be a substantial problem. Ultimately the interstitial lung disease community should pull together to investigate the long term consequences of COVID-19 and develop evidence based strategies to deal with this emerging problem.

## IV. CONCLUSION

SARS-COV-2 has continued to spread across the world, infecting millions of individuals in the process. Like previous human coronavirus outbreaks, pulmonary fibrosis has been recognized as a potential sequela among survivors. Virus-induced lung injury , immune response, and attempts at healing are central to the process of fibrogenesis .With no proven effective targeted therapy against pulmonary fibrosis, risk reduction measures should be directed at limiting illness severity and protecting the lung from other incidental injuries.

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