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Review Article

Covid-19 Pneumonia Presenting as a 'Typical Radiological Bronchopneumonia' Pattern in Clinical-Radiological-Pathological Phenotype with Transient Hyperglycemia

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Abstract: Radiological phenotypes are radiological patterns or observable characteristics of COVID19 pneumonia. Various phenotypic classifications have been reported in literature. CT severity radiological phenotypes are widely used and universally accepted radiological phenotypic methods. Radiological CT severity phenotypic differentiation has documented very crucial role in initial assessment and during triaging of these cases in indoor and outdoor setting. Typical COVID-19 lung parenchymal involvement described as predominant ground glass opacities (GGOs) and consolidations in peripheral and subpleural portion of any lobe, predominantly involving lower lobes. Atypical Radiological patterns in COVID-19 has been documented as bronchopneumonia, multifocal consolidations, necrotizing pneumonia, cavitations with GGOs with or without consolidations. In present case report, 43-year male, presented with acute febrile respiratory illness with acute hypoxic respiratory failure documented as oxygen saturation of 80% at room air with tachypnea and respiratory distress. HRCT thorax was showing Pleural based, peripheral, central, multifocal patchy, confluent & ill-defined GGOs and consolidations in bilateral lung fields in upper, middle and lower lobes. These typical radiological features suggestive of bronchopneumonia like radiological pattern which was very unusual for typical COVID-19 radiology. His laboratory parameters have shown abnormally raised inflammatory markers like CRP, Ferritin, LDH, D-Dimer and IL-6. Importantly, his random blood sugars were raised with abnormally raised HbA1c levels to label as diabetes mellitus. He was diagnosed with diabetes mellitus this time with COVID-19 illness without use of steroids. He was treated with standardized COVID-19 management institutional protocol with combination of low molecular weight heparin, methylprednisolone, remdesivir, meropenem and teicoplanin. Patient required BIPAP support with higher oxygen requirement with nasals canula for one week due to advanced radiological disease with more anatomical involvement. We have documented successful treatment outcome with use of rational treatment in timely by predicting disease severity with use of composite analysis of clinical, laboratory and radiological markers of illness. Transient hyperglycemia is known to occur and reported after COVID-19 illness due to virus induced inflammatory response and pancreatopathy with beta cell dysfunction. Transient hyperglycemia can be easily managed with insulin during hospitalization and oral anti-diabetic agents after discharge for few weeks. Dietary and lifestyle modification will help in majority with complete reversal of abnormally high sugar levels with restoration of normal HbA1c levels to non-diabetic range.

Keywords: COVID-19 Pneumonia, HRCT thorax, Inflammatory markers, COVID-19 RT PCR, IL-6, CRP, LDH, D-Dimer.

INTRODUCTION

COVID-19 pneumonia is heterogeneous disease with variable effect on lung parenchyma, airways and vasculature leading to long term effects on lung functions. Although Lung is the primary target organ involvement in corona virus disease-19 (COVID-19), many patients were shown pulmonary and extrapulmonary manifestations of diseases variably during all three waves, which occurred as resultant pathophysiological effects of immune activation pathway and direct virus induced lung damage [1, 2]. COVID-19 is a coronavirus-related disease, its etiological agent was discovered in the middle of the 20th century, its epidemics-pandemics has created a health burden in the early 21st century, but evidence are coming up with its correlation with "Russian or Asiatic

flu" of late 19th century [3]. Like the Influenza virus-related global pandemic in 1918 (early 20th century), a Spanish flu which has multiple waves in ongoing pandemic lasted for almost 5 years, currently ongoing COVID-19 pandemic has documented 3–5 waves globally lasted over a period of 3 years [3]. During the first wave, the majority of affected COVID-19 cases were having extrapulmonary involvement as compared to pulmonary, while in the second wave, the predominant pattern was pulmonary. Cardiovascular involvement was seen more often in the first wave as compared to the second wave, and the rational for the same was not known, and medical experts believed as "Wuhan variant virus has more thrombogenic activation syndrome" as compared to Delta variant coronavirus [4]. In the first wave, extrapulmonary manifestations as pseudo acute coronary syndrome, pulmonary thromboembolism, and stroke were documented in a greater number of cases as compared to the second wave. Rapidly evolving pneumonia or "accelerated acute respiratory distress syndrome" (ARDS) was more commonly documented in the second wave, i.e., the larger number of cases were presented with rapidly deteriorating radiological and clinical laboratory parameters as increased computed tomography severity score, worsened oxygenation, increased inflammatory markers like CRP [4-7], LDH [8-11], Ferritin [12-15], IL-6 [16-21] and D-Dimer [22-26]. In present case report we have observed bronchopneumonia like radiological pattern in HRCT thorax in COVID-19 pneumonia as a clinical radiological pathological phenotype.

Case Summary

43-year-old, male, teacher by occupation admitted with complaints of cough, fever and shortness of breath of acute onset during second wave of COVID-19 pandemic. He had taken oral antibiotics and antipyretics with cough suppressants for similar complaints from his family physicians. He has done his COVID-19 RT PCR testing at covid care facility (CCC) and found his results were RT PCR positive. He was isolated at covid care center and offered medical treatment. His illness worsened with high grade fever and increases cough with chest discomfort and shortness of breath increased with grade IV. His family members brought to our center for further treatment. His relatives brought patient to our center with HRCT thorax which has showed typical bronchopneumonia pattern.

HRCT findings are: [Image 1-4]

1. Pleural based, peripheral, central, multifocal patchy, confluent & ill-defined GGOs and consolidations in bilateral lung fields in upper, middle and lower lobes
2. Axonal or central to peripheral, pleural based, patchy, confluent, opacity with well-defined to ill-defined margins, GGOs and consolidation with line of demarcation between normal and abnormal lung in bilateral upper and lower lobes
3. Pleural based patchy, multifocal, confluent opacities of consolidation with necrosis with line of demarcation, involving central to peripheral areas of lung parenchyma in both lower lobes
4. Multifocal, ill-defined to well defined consolidation with line of demarcation in bilateral lower lobes. Pleural based and central patchy consolidations in bilateral middle lobes with few GGOs randomly distributed in central and peripheral parts.
5. Although line of demarcation is present, limiting sign is not very classically documented in HRCT imaging due to ill defined and confluence opacities as observed in bronchopneumonia.

We have documented clinical examination findings as increased respiratory rate to 28 breaths per minute, heart rate 122 per minute, blood pressure 100/68 mm hg and oxygen saturation as 80% at room air and 88% with oxygen support with nasal canula @ 4 liters per minute & 96% with BIPAP support with oxygen flow 12 liters per minute. His respiratory system examination revealed vesicular breath sounds in bilateral lung fields with adventitious sounds as bilateral crepitations heard over mammary, axillary, interscapular, and infrascapular area. Other systemic examinations were normal.

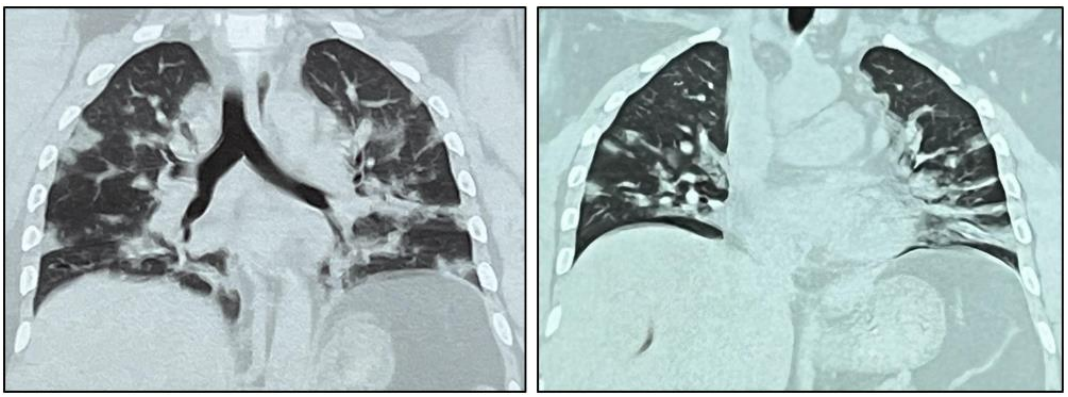

Image 1: HRCT thorax showing pleural based, peripheral, central, multifocal patchy, confluent & ill-defined GGOs and consolidations in bilateral lung fields

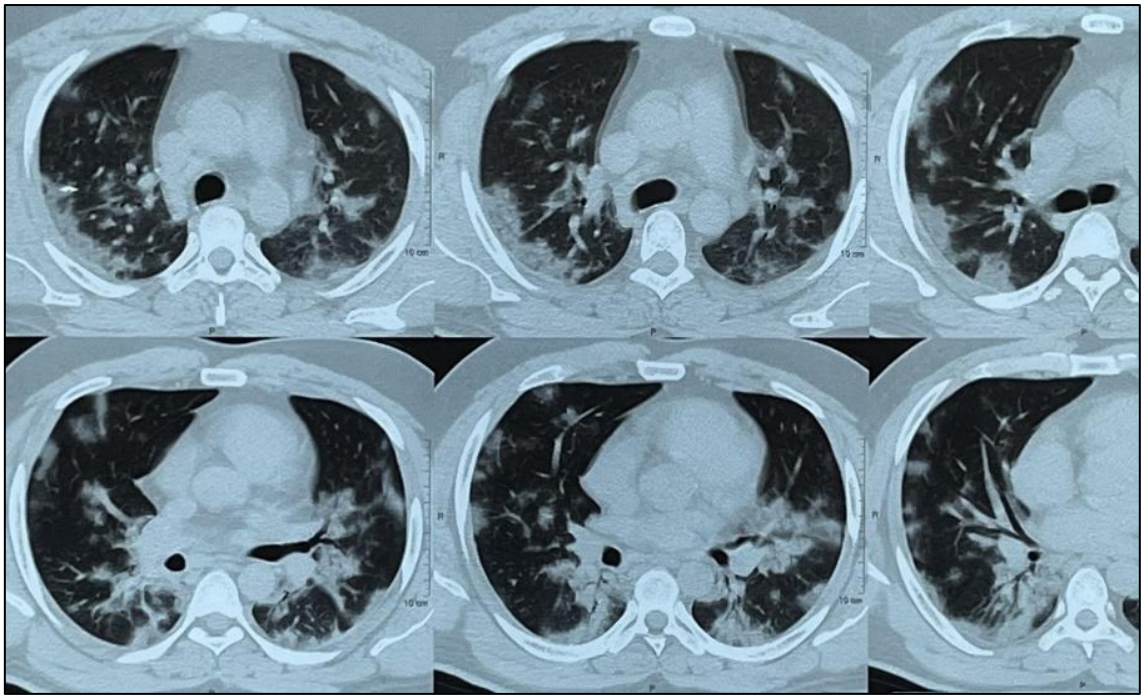

Image 2: HRCT thorax showing peripheral, axonal at some points, pleural based opacity with GGO and consolidation with line of demarcation between normal and abnormal lung in bilateral upper and lower lobes

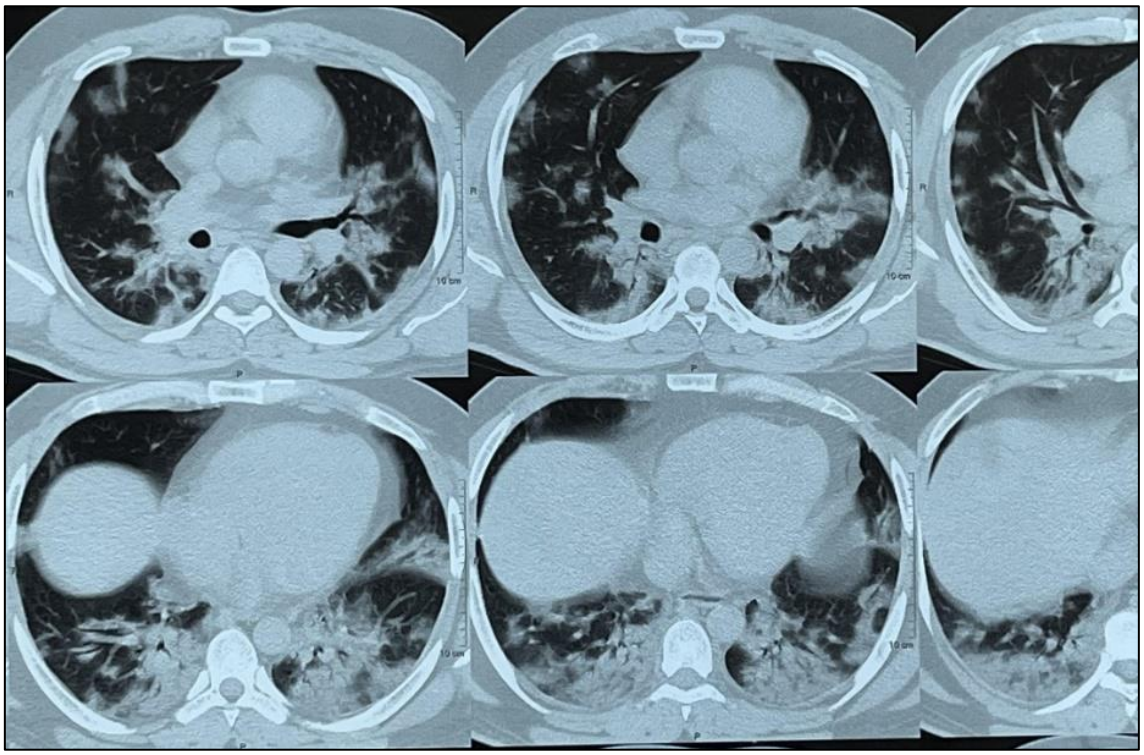

Image 3: HRCT thorax showing pleural based patchy, multifocal, confluent opacities of consolidation with necrosis with line of demarcation, involving central to peripheral areas of lung parenchyma in both lower lobes

Laboratory parameters during hospitalization at entry point as Haemoglobin 13.8 gm%, total white blood cells 3200/mm^3, Polymorphs 62%, Platelet count as 114000/uL, CRP-92 mg/L (0-6 mg/L), random blood sugar level-286 mg% HbA1C 9.8 %, LDH 1328 IU/L (70-470 IU/L). Serum biochemistry examinations for liver and kidney functions were normal. Other inflammatory markers such as ferritin 1398 ng/ml (5-250 ng/ml in males), IL-6 was 242 pg/ml (0.00-7.00 pg/ml), D-dimer was 1128 ng/ml (<500 ng/ml).

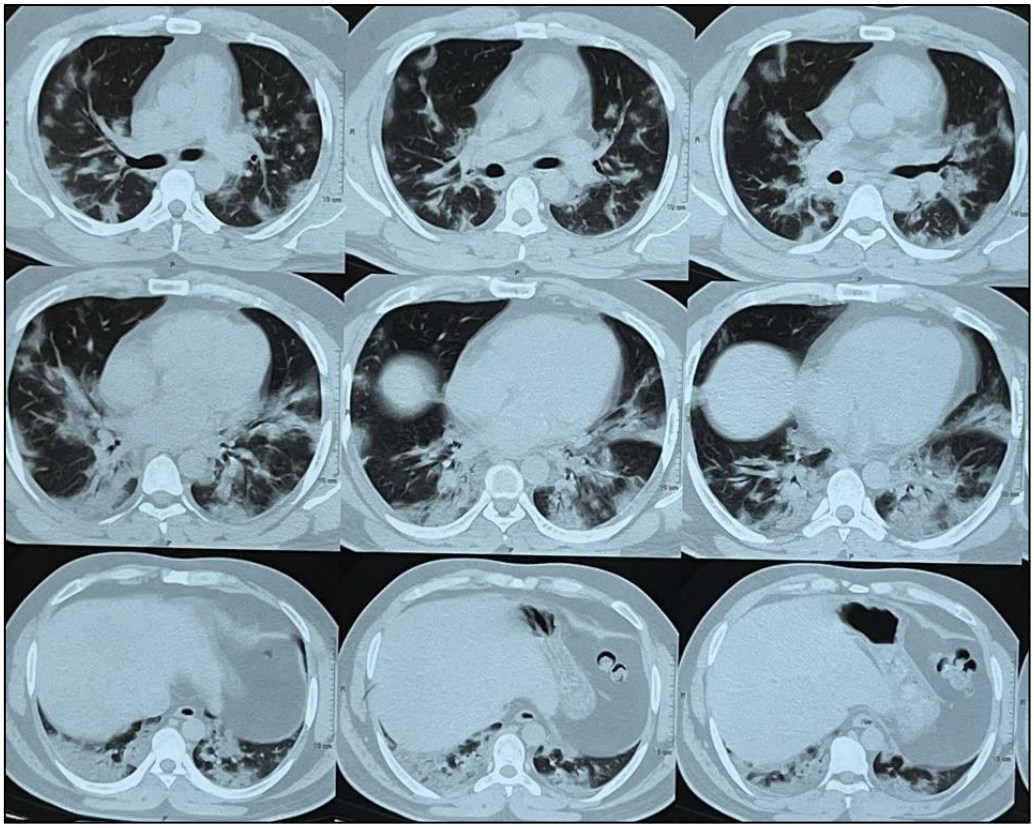

Image 4: HRCT thorax showing multifocal, ill-defined to well defined consolidation with line of demarcation in bilateral lower lobes. Pleural based and central patchy consolidations in bilateral middle lobes with few GGOs

He was treated in Intensive care unit with BIPAP with oxygen supplementation @ 12 liters per minute with target Spo2 of 91%, intravenous antibiotics meropenem 1-gram intravenous infusion three times and teicoplanin 400 mg daily infusions, injection methylprednisolone 40 mg intravenous three times, Remdesivir injection 200 mg bolus on day 1 and 100 mg infusion OD for 4 days, low molecular weight heparin with short acting regular insulin according to blood sugar level. His clinical stability documented after three days of treatment with resolution of fever, suppression of cough and decrease in chest discomfort with significant amount of decrease in shortness of breath. His oxygen requirement decreased to 4 liters on day 5 and 1 liter on day 10. His vital parameters were maintained to normal without oxygen supplementation on day 15 of hospitalization. He was discharged on oral medicines after 16 days of medical treatment in hospitalization, seven days in intensive care unit and eight days in indoor unit. He was advised for oral rivaroxaban 2.5 mg daily orally for thromboprophylaxis and vildagliptin plus metformin (50+500) BD daily for diabetes control. He was advised for strict monitoring of blood sugar levels monthly. His lung functions assessment done at three months of discharge from hospital, which has showed restrictive lung functions in spirometry analysis and due to minimal symptoms of breathlessness; we have offered him pulmonary rehabilitation and breathing exercises for three months. His respiratory symptoms were improved significantly after three months with normal lung functions in spirometry tests. His blood sugar level was controlled in normal range after three months, dose pf vildagliptin was reduced to OD, and observed normal blood sugar level with normal HbA1c of 5.1% after six months of therapy. Thus, he was having ‘transient hyperglycemia and diabetes mellitus’ related to COVID-19 related endocrine complications and pancreatopathy due to acute inflammatory response in virus related disease. Chest radiological examination was normal, done at six months.

DISCUSSION

COVID-19 pandemic is over now and we are in great peace of relief after three years. This pandemic has observed significant impact on quality of life globally and the put unforgettable imprints on history of mankind. Reason for more havoc in this pandemic was less studied virus by medical scientists regarding its pathophysiology, available treatment options and lack of effective vaccine to tackle this dragon. Immune dysregulation has documented during course of active viremia, during recovery of viral illness and after post viral phase. Immune dysregulation occurs in ‘selected group’ of cases irrespective of disease severity and vaccination status and observed in cases with negligible illness to advanced one mandates further research [27, 28]. HCQ was tried initially for prophylaxis treatment of COVID-19 due to its anti-inflammatory properties but has not shown any dramatic results. WHO has removed HCQ from the treatment plan after many trial results with

disappointing outcomes. HCQ is a drug with multiple beneficial pleiotropic effects such as immunomodulatory effects which regulates immunological responses that inhibit dysregulated immune system. Revisiting this old drug with 'versatile effects' can be used as treatment option for short time as frontline molecule for Long covid when no definitive options are available after consideration of risk benefit ratio which is a cost-effective treatment option [27]. L-Arginine is amino acid with multiple beneficial effects such as immunomodulatory effects which will regulates immunological response in inhibit dysregulated immune system additional to its universally known antioxidant, vasodilatory and regenerative and cellular proliferation effects on immune cells. These Immunomodulatory and or diseases modifying effects of L-Arginine makes it the future candidate with 'game changer' role for management of Long covid resulting from immune dysregulation as a core pathophysiologic pathway of this Dragon Pandemic [28].

Infodemic' is a pandemic of misinformation spread in a pandemic manner regarding health issues of global concern. Globally, Infodemic is rapidly rising and more adverse outcomes are observed in social, economic and family lives. Infodemic is reported first time during SARS in 2003 & now during evolution of COVID-19 pandemic in 2020. Infodemic is more rapidly spreading pandemic than any communicable disease due to its ultrafast method of transmission by means of electronic & social media in the form of print or digital platform. Here, in Infodemic, the culprit is 'misinformation' spread without any scientific evidence regarding health issues of global concern. During COVID-19 pandemic infodemic evolved parallel with actual natural viral disaster and documented comparable effects on mankind globally [29].

Immune dysregulation is known to occur after natural COVID-19. Altered homeostasis between Th1 and Th2 interplay is a real issue of concern. Immune dysfunction as Th1 and Th2 dysregulation is usually restored after other respiratory viral infections by our own reboot system as in the "Tomorrow never dies" situation [30].

Composite index is combination clinical, radiological and laboratory inflammatory marker assessment. Combination of any two abnormalities were observed crucial role in early suspicion, diagnosis, monitoring, and recognition of complications, management and disposition of patients. Composite index rather than single biomarkers may provide more reliable information. Availability and cost issues cannot be ignored. It would be impossible for clinicians to consolidate and critically analyse the enormous data that is continuously added to the COVID-19 literature to extract practically useful information for the benefit of patients. Still, as of now Composite index should be considered as 'point of care test' to honour successful treatment outcome and prevent mortality and morbidity due to this "Dragon Pandemic" [31, 32].

Now the robust data is available for role of various inflammatory markers in initial assessment of cases which are associated with direct or indirect virus-related lung injury. Apart from lung involvement, proportionate number of cases were shown systemic manifestations due to activation of inflammatory pathway and inflammatory surge resulting in to pulmonary and extrapulmonary effects which have significant impact on final outcome. All these effects can be easily picked up by timely analysis of inflammatory markers. Now these markers are also called as 'inflammatory biomarkers.' Various inflammatory markers such as CRP, Ferritin, LDH, D-dimer and IL-6 were exuberantly used during workup of COVID-19 cases worldwide and reported their valuable role in initial assessment, predicting severity, guiding or triaging hospitalization, predicting need of interventions during hospitalization, analysing final outcome, predicting post recovery outcome and possibility of long covid manifestations [4-26].

Dengue-COVID-19 overlap is clinical syndrome with overlapping clinical and laboratory workup of both the illnesses. High index of suspicion is must in all covid cases in tropical settings where dengue is endemic; and all cases with leukopenia and thrombocytopenia with fever should be screened for dengue serology. False positive dengue serology or dengue antigen cross-reactivity is known to occur in underlying COVID-19 illness, and have impact on clinical outcome as it will result in delay in covid appropriate treatment initiation and many cases require intensive care unit treatment due to progressed covid pneumonia. Covid-19 and Dengue antigenic cross-reactivity has significant association with lung fibrosis as a resultant pathophysiological effect of the immune activation pathway; and these cases required longer oxygen supplementation and anti-fibrotics in follow up. 'Dengue-COVID-19 overlap' is very frequently documented in tropical settings and disease of concern in critical care settings; as the natural trend of this entity is different and has an impact on clinical outcome if diagnosis is delayed. Both diseases may behave like 'two sides of the same coin', and rational for coexistent pathology were still undetermined [33-37].

TB and COVID-19 are rare combinations and always suspect in tropical countries like India where the burden of TB is high, and in the pandemic era, all lung infiltrates should be screened for COVID-19 lung involvement [38]. Neurovascular complications such as stroke, venous thrombosis, encephalopathy, and vasculitis is documented in various studies. Authors have documented, embolic stroke in this case in COVID-19 secondary to hypercoagulability and cardiomyopathy [39]. Authors have reported Dyselectrolytemia as result of pulmonary involvement in COVID-19 disease is

reason for recurrent syncope. Although syncope is a vague neurological manifestation of many neurological and non-neurological illnesses, it is well documented in viral illnesses such as flu and COVID; recurrent syncopal episodes need further workup [40].

Radiological phenotypes are radiological patterns or observable characteristics of COVID-19 pneumonia. Robust data is available regarding role of HRCT in COVID-19 pneumonia and we have evaluated role of radiological phenotypes in assessing severity, predicting response to therapy and final outcome in COVID-19 pneumonia. Radiological patterns or phenotypes have documented important role in assessing disease severity in COVID-19 pneumonia. Easy to treat and Difficult to treat phenotypes help in triaging the cases at entry point in correlation with clinical and laboratory inflammatory markers analysis. Phenotypic categorization is simple, sensitive and guided during treatment planning in indoor units. Presence or absence of GGOs, consolidations and crazy paving with necrosis were key radiological markers in categorizing these phenotypes. Clinical-radiological-pathological phenotypes-five types as classical GGOs, consolidations, Bronchopneumonia, Necrotizing pneumonia and cavitating. Radiological phenotyping should be correlated with clinical and laboratory parameters for accurate analysis of severity assessment, duration illness prediction and inflammatory markers workup. Phenotyping will also help in monitoring of COVID-19 pneumonia cases and guide for necessary timely interventions in indoor units to have successful treatment outcome. Post covid fibrosis is reversible and should be labelled as sequalae due to near total reversible nature [41-45]. Radiological CT severity Phenotypic categorization is a simple, sensitive and more widely studied and universally accepted classification system. Limitation of this method is its 'static and only' radiological assessment criteria and not 'dynamic and clinical and laboratory parameters' included 'composite index' criteria which is temporal assessment over a period of time as disease process evolves and not a single point assessment. Radiological CT severity phenotypes will predict disease severity as per the anatomical extent of disease and this actually either overestimate in severe category and underestimates in mild category. Thus, quote 'one size fit to all' will not suit conventional CT severity scoring tools and phenotypes [45].

The Radiological Society of North America expert consensus proposed four categories to report chest CT findings attributed to COVID-19 (typical, indeterminate, atypical and negative for pneumonia) [46] shown in Table 1.

Table 1: Proposed reporting categories for CT findings related to COVID-19

COVID-19 pneumonia Imaging classification	CT findings	Differential diagnosis
CT mimickers of typical COVID-19 Commonly reported imaging features of greater specificity for COVID-19 pneumonia	Typical findings are: 1. Peripheral, bilateral, GGO with or without consolidation or crazy-paving 2. Multifocal GGO of rounded morphology with or without consolidation or crazy-paving 3. Reverse halo sign or other findings of organizing pneumonia	1. Influenza pneumonia 2. SARS and MERS pneumonia 3. Organizing pneumonia 4. Connective tissue disease (RA) 5. Drug toxicity 6. Acute interstitial pneumonia
CT mimickers of indeterminate COVID-19 Commonly reported imaging features of greater specificity for COVID-19 pneumonia	Absence of typical features AND presence of: 1. Multifocal, diffuse, perihilar or unilateral GGO with or without consolidation 2. Lacking of specific distribution 3. Non-rounded or non-peripheral GGO	1. Other causes of viral pneumonia 2. Atypical bacterial infections 3. Pneumocystis infection 4. Pulmonary edema 5. ARDS 6. Acute hypersensitivity pneumonitis, 7. Eosinophilic pneumonia 8. Diffuse alveolar hemorrhage 9. Pulmonary alveolar proteinosis
Conditions presented by clinical scenarios that mimic COVID-19 but with atypical CT features Uncommonly or not reported CT features	Absence of typical or indeterminate features AND presence of: 1. Isolated lobar or segmental consolidation without GGO 2. Discrete small nodules (centrilobular or "tree in-bud") 3. Lung cavitation 4. Smooth interlobular septal thickening with pleural effusion	Alternative diagnoses rather than COVID-19 should be considered such as typical bacterial pneumonia, TB or other non-infective processes

Coronavirus disease 2019 (COVID-19) is the first coronavirus-related global pandemic caused by a novel severe acute respiratory syndrome coronavirus-2, and rapid evolution of the pandemic has resulted in fast-track developments in antivirals, medical management, and vaccination for use to prevent morbidity and mortality. As of today, different institutional treatment protocols and respective national guidelines have been evolved worldwide with team of medical experts and recommended for combinations of antiviral, antibiotics, steroids, and anticoagulants with variable outcomes. Medical evidence suggests that the beneficial role of

combo therapy as combination of antiviral, anticoagulants, and steroids has shown mortality and morbidity benefit across the globe. Robust data are available regarding the usefulness of Remdesivir in COVID-19 pneumonia with variable efficacy and its use has been documented with shortened hospital stay without mortality benefit. Remdesivir led to a shorter median time from randomization to recovery (10 days, vs. 15 days with placebo) and may have reduced the time to hospital discharge (12 days vs. 17 days) but did not show a mortality benefit [47, 48].

Vaccination is one of the most effective interventions to substantially reduce severe disease and death due to SARS-CoV-2 infection. To date, treatments for COVID-19 are mainly targeted symptomatic treatment and supportive therapy. Currently, one of the most effective strategies for mitigating COVID-19 pandemic is global vaccination that can create an immune barrier among population to attenuate the speed and scope of SARS-CoV-2 transmission. In this systematic review and meta-analysis of 18 peer-reviewed studies, which included nearly 7 million individuals, we found evidence of waning immunity against SARS-CoV-2 infection from a high of 83% at one month to 22% at five months or longer after being fully vaccinated. Similar trends were observed for symptomatic COVID-19. VE against SARS-CoV-2 infection declined more rapidly in individuals ≥ age 65 years but was less than 50% in all age groups by month five [49]. Few cases received vaccine before second wave; and those received covid vaccine were required intensive care unit hospitalizations as 'breakthrough infections' with more virulent delta variant. That was real turnup and aversion to vaccines from the community and majority were nodding for vaccination. Few cases received covid vaccine developed minor allergic reactions and some documented major adverse events. Reversible rheumatological disease without life threatening emergencies were documented after covid vaccination [50, 51].

Pulmonary functions abnormality in post-COVID-19 pneumonia cases has been documented and should be assessed cautiously to have successful treatment outcome. Spirometry is cost-effective, non-invasive, easily available, sensitive tool for assessment lung function in post COVID care setting and it will help management of these cases by assessing response to treatment. Restrictive lung disease is the predominant lung function impairment in post-COVID-19 recovered lung pneumonia cases. Age above 50 years, male gender, DM, High CT severity, longer duration of illness, proper timing of initiation of BIPAP/NIV therapy, has documented significant impact on post-COVID lung functions at 12 weeks assessment. All post-COVID cases need lung functions assessment by spirometry to predict the course of underlying lung pathology and targeting interventions accordingly [52, 53].

Lung fibrosis in post-covid 19 cases is documented in interim follow up at three months of discharge form hospital and should be assessed cautiously to have successful treatment outcome. Age above 50 years, male gender, Diabetes, High CT severity, longer duration of illness, proper timing of initiation of BIPAP/NIV therapy, and its early use in comorbid class has documented significant impact on post covid lung fibrosis [54-56]. Antifibrotics were exuberantly used to treat post covid lung complications. Lung is the primary target organ in COVID-19 disease with diverse clinical and radiological presentations and outcome. It has caused minimal to moderate lung disease in some patients and in some cases caused deadly acute respiratory distress syndrome (ARDS). COVID-19 disease caused lung damage by direct virus induced alveolar damage, cytokine induced alveolar and vascular damage and microvascular thrombosis resulting into acute hypoxic respiratory failure. COVID-19 pneumonia evolved over period of three weeks in cases with ARDS as natural course of illness. Usually, ARDS resolves by fibrosis or resolution as final outcome. Similarly, in COVID-19 recovered cases of advanced disease or those suffering from ARDS are having post covid lung disease. Lung fibrosis is final radiological outcome of COVID-19 pneumonia documented in proportionately majority of cases. Post COVID lung fibrosis is considered as worrisome radiological complication observed during early phase of pandemic. Antifibrotics such as Nintedanib and Pirfenidone were used to treat post covid lung complications such as fibrosis. Both drugs were shown good antifibrotic property in clinical trials for fibrotic lung disease and observed positive outcome in restoring lung parenchyma. Time trends of final radiological outcome has evolved over months with or without treatment with antifibrotics and steroids. Importantly, Post covid lung fibrosis resolved more than fifty percent cases in six months and nearly in all cases after one year. Thus, antifibrotics were used irrationally in fibrosing lung condition of reversible type [54-59]. Post COVID lung fibrosis is considered as 'health issue of great concern' initially in post pandemic phase of first wave, and due to its resolving nature over time period; now considered as 'sigh with relief' due to its reversible pathophysiology. Post COVID sequel is minimal residual effects of COVID-19 lung disease irrespective of disease severity in past. Authors recommend to use term post COVID sequel over post COVID lung fibrosis [58, 59].

Long COVID is more prevalent chronic health care issue in post COVID care settings. We are in great piece of relief due to nearly end of this deadly pandemic which has caused significant change in routine of entire globe. Long COVID is an unpredicted sequel of COVID-19 disease documented nearly in half cases globally. Long COVID is multisystem syndrome with nonspecific symptoms and organic signs of unidentified pathology occurs after COVID-19 disease. Long COVID symptoms has been documented in 'selected' cases

irrespective of disease severity or hospitalization and possible link remains unknown. Long COVID symptoms has significant impact on quality of life in those cases suffered from disease in recent past and lingering to almost two years since infection. Importantly, not all cases of COVID-19 were shown long COVID symptoms. Most common long COVID symptoms as joint pain, fatigability, chest discomfort, shortness of breath, hair loss, chest pain, weight gain, anxiety/depression & memory impairment. Pathophysiology resulting into long COVID manifestations is still not completely validated. Researchers have reported 'immune dysregulation', 'autoimmunity', 'antigenic mimicry' & 'coagulation abnormalities' are probable pathophysiological mechanism for long COVID. Some of the long COVID effects shown complete reversibility including post COVID lung fibrosis. Reboot system to restore immune dysregulation and recovery in long COVID is real concern. Long COVID symptoms cases are more health conscious and usually follows pattern of doctor shopping due to underestimation by family physicians either due to lack of suspicion or lack of knowledge regarding treatment protocol. Still, we are not having right answer for exact duration of long COVID symptoms and when it will show complete reversibility. Further, it needs 'birds eye vision' to pick up and manage cases with long COVID manifestations during routine care in rehabilitation unit [60-65] Long covid is observed in selected group of patients and occurs irrespective of severity of covid, irrespective of hospitalization and interventions required during hospitalization. Long covid occurrence is observed in special class of patients which can be predicted early during course of illness by analysing markers. Biochemical markers will help in suspecting chance of occurrences but sequential markers will help in targeting interventions to prevent it and guide in management of long covid. Clinical presentation and immunological patterns are different during different waves due to either genetic makeup or immune pathway alterations resulting into long COVID [66-70]. Pathophysiology resulting into long COVID manifestations is still not completely validated. Researchers have reported 'immune dysregulation' and 'coagulation abnormalities' are probable pathophysiological mechanism for long COVID. Some of the long COVID effects shown complete reversibility including post COVID lung fibrosis. Reboot system to restore immune dysregulation and recovery in long COVID is real concern. Long COVID symptoms cases are more health conscious and usually follows pattern of doctor shopping due to underestimation by family physicians either due to lack of suspicion or lack of knowledge regarding treatment protocol [71, 72]. Immune alteration is documented after natural infection & effect of vaccination in restoring Th1/Th2 interplay is not known. The 'reboot system' or time required to restore 'normalcy' is a real concern as documented as our immune phenomenon.

CONCLUSION

In this case report, a 43-year teacher presented with COVID-19 pandemic related acute respiratory illness with respiratory symptoms and acute hypoxic respiratory failure diagnosed by positive results of RT PCR test. He was having bronchopneumonia like lung parenchymal abnormalities in clinical-radiological-pathological phenotype in HRCT thorax with abnormally raised inflammatory markers. He was treated in intensive care unit with standardised institutional guidelines with combination of remdesivir, methylprednisolone, low molecular weight heparin and antibiotics for COVID-19 protocol with BIPAP with oxygen supplementation and showed excellent response to medical treatment. In this patient we have observed transient hyperglycemia in diabetes range which has completely reversed with oral antidiabetic agents for short term use with improvement in respiratory parameters including spirometry analysis.

Key learning points from this case report are:

1. COVID-19 infection involves a complex interplay of the immunological and inflammatory responses. Inflammatory parameters are closely linked to the COVID-19 severity and mortality. Inflammatory parameters could be used to predict the transition from mild to severe/critical infection in patients of COVID-19.
2. Pulmonary, extrapulmonary and pulmonary-extrapulmonary involvement were documented 'selectively' with genetic makeup of virus variant. Pulmonary were more common with Wuhan and delta variants and extrapulmonary were more frequently reported with omicron and other recent corona virus related variants. Pulmonary and extrapulmonary manifestations were reported with Wuhan variant.
3. Composite index will play a crucial role in early suspicion, diagnosis, monitoring, and recognition of complications, management and disposition of patients. Each of these components in turn can have crucial implications on the healthcare system and the administrative machinery, directly impacting patient care
4. Clinical-radiological-pathological phenotypes were classified in five types as classical GGOs, consolidations, Bronchopneumonia, Necrotizing pneumonia and cavitating. Other phenotypic classifications such as response to treatment phenotype as Easy to treat and difficult to treat, duration of illness phenotype as evolving and evolved, CT severity phenotype as mild, moderate and severe, topographical or anatomical phenotype such as unilateral and bilateral, lastly; final radiological outcome phenotypes as resolving, persistent and progressive phenotype.
5. A broad spectrum of pulmonary conditions demonstrates imaging features that mimic those

of COVID-19 and are difficult to differentiate from it. Awareness of these conditions, careful radiologic analysis and attention to the clinical data are required to prevent an erroneous diagnosis that could potentially adversely impact management and patients' outcome. A correct diagnosis of these conditions may prevent unnecessary hospitalization and reduce strict quarantine measures for all suspected patients that hold significant pressure on healthcare providers and medical infrastructure.

6. HRCT imaging has played a very crucial role in diagnosing early COVID-19 illness with high sensitivity with very good negative predictive value in the first few days of infection. Additionally, radiological extent with anatomical involvement classified as severity has helped in triaging cases in outdoor settings and guided requirement of hospitalization in majority of cases. HRCT imaging has also played a crucial role in analyzing severity with need for aggressive interventions in intensive care units and isolation units in correlation with clinical parameters and timely use of laboratory markers such as IL-6, CRP, D-Dimer, LDH and ferritin.
7. Bronchopneumonia is a typical radiological presentation of COVID-19 pneumonia which is an indicator of advanced radiological disease with worsened clinical and laboratory parameters. We have documented requirements of aggressive interventions such as BIPAP and higher oxygen requirements for longer duration. We have suspected an advanced stage of COVID-19 pneumonia due to characteristic radiological features accompanied by clinical and laboratory criteria. We have documented successful treatment outcomes with standard COVID-19 institutional protocol.
8. Transient diabetes mellitus is known to occur with COVID-19 related endocrine dysfunction, Viral illness related pancreatopathy and with use of systemic steroids as an adjunct to standard management protocol. Oral anti-diabetic therapy for a few weeks to months has shown excellent response and outcome with near complete reversal in Diabetes mellitus. Hence, we labeled these cases as transient hyperglycemia rather than Diabetes mellitus in COVID-19 related hyperglycemia in spite of raised HbA1c level in defining criteria of DM.

Abbreviations

RT PCR-real time reverse transcription polymerase chain, HRCT-high resolution computerised tomography, CRP C-reactive protein, SpO2 oxygen saturation, LDH lactate dehydrogenase, IL-6 Interleukin-6, CT-computerised tomography, SARS-CoV-2 severe acute respiratory syndrome-corona virus-2 BIPAP/NIV-bilevel positive airway pressure/non-invasive ventilation.

Conflicts of Interest: NIL

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