Long COVID Mimicking Interstitial Lung Disease: A Case Series

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ABSTRACT: Interstitial lung diseases (ILD) can occur due to various known or unknown causes. They usually present with dry cough and exertional dyspnea. On radiology usual findings are ground glass opacities (GGO’s), reticular shadows, nodules etc. Some patients after acute COVID-19 (coronavirus disease 2019) suffer from persistent symptoms/manifestations. These have been called ‘Long COVID’. Long COVID also has radiological features like GGO’s, nodules and reticulations. Further, patients even without history of acute COVID-19, can also present with ‘Long COVID’. In the present case series, we describe three such cases with no history of having suffered from COVID-19, presenting with ILD like features and diagnosed as Long COVID. We infer from these cases that ‘Long COVID’ can both clinically and radiologically mimic ILD’s. Hence, emphasizing the fact that in the present COVID-19 pandemic situation, ‘Long COVID should be a differential diagnosis to be considered while making a new diagnosis of ILD.

KEYWORDS: SARS-CoV-2, Interstitial Lung Disease, COVID19, IgG, COVID-19 RT-PCR Testing.

Introduction
Pulmonary interstitium, referred to as supportive tissue around the alveoli, is commonly involved in interstitial lung diseases (ILDs) [1].

Involvement of pulmonary interstitium can occur due to some known and other unknown aetiologies [2].

Organic and inorganic dust, various drugs and infections can cause one or the other form of ILD [3].

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) has emerged as a potentially hazardous infection in the recent times [4].

Lungs are among the most commonly involved organs [5].

The severity of the disease can range from mild symptoms to a life-threatening infection [6,7].

COVID-19 (Coronavirus Disease 2019) infection of the lungs shows various CT (Computed Tomography) manifestations mimicking ILD including ground glass opacities, septal thickening and/or reticulations, crazy paving pattern and nodules [8].

Although these findings are more common in severe COVID 19, cases with mild disease can also have such features [9].

In this case series we describe three patients without any history suggestive of acute COVID and presentation similar to interstitial lung diseases, but were subsequently confirmed as cases of ‘Long COVID’ [10].

The present work was part of project approved by the Institute Human Ethics Committee (IHEC).

Cases
We had three patients presenting to us with history of dry cough and insidious onset exertional breathlessness.

The duration of symptoms varied from 6-10 weeks.

None of them had any history of prior respiratory ailments. Clinical-radiological findings were suggestive of ILD (Table 1).

RT-PCR for COVID-19 was negative in all three patients.

All serological investigations for ruling out various ILD were negative.

In view of the current COVID-19 pandemic status, the patients were subjected to IgG antibodies test against SARS-COV-2, which was found to be positive in all three of them.

Based on above findings, these patients were diagnosed as ‘Long COVID’.

They were started on short course of systemic corticosteroids.

Post-treatment clinical and radiological profile of all three patients showed improvement.

Also, a written informed consent was obtained from all the patients before publication of their data.
**Table 1. Comparison of various parameters among three cases.**

| Parameters                          | Case 1            | Case 2                        | Case 3                        |
|-------------------------------------|-------------------|-------------------------------|-------------------------------|
| **Age (Years)**                     | 56                | 65                            | 53                            |
| **Gender**                          | Male              | Male                          | Male                          |
| **Diabetes Mellitus (Duration)**    | No                | Yes (15 years)                | Yes (16 years)                |
| **Hypertension (Duration)**         | No                | No                            | Yes (2 years)                 |
| **Symptoms**                        | Cough and exertional dyspnea for 6 weeks | Cough, exertional dyspnea and chest pain for 8 weeks | Cough and exertional dyspnea for 10 weeks |
| **Auscultatory findings**           | Bilateral infrascapular inspiratory fine crepts | Bilateral infrascapular inspiratory fine crepts | Bilateral infrascapular inspiratory fine crepts |
| **Baseline Chest X-ray**            | Bilateral diffuse reticulations (Figure 1a) | Bilateral lower zone reticulations | Bilateral lower zone reticulations |
| **Baseline CT Chest**               | Diffuse patches of ground glass opacities (GGOs) (Figure 2 a) | Bilateral peripheral GGOs in lower lobes (Figure 3 a) | Bilateral lower lobe reticulations (Figure 4 a) |
| **COVID Antibody level**            | 2.10              | 4.0                           | 5.4                           |
| **Treatment given**                 | Oral corticosteroids in tapering doses for 4 weeks | Oral corticosteroids in tapering doses for 2 weeks | Oral corticosteroids in tapering doses for 2 weeks |
| **Post treatment Radiology**        | Clearing of reticulations & GGOs (Figures 1b & 2b) | Clearing of GGOs (Figure 3 b) | Clearing of reticulations (Figure 4 b) |

*Figure 1. (a), Case 1 Chest X-ray (posteroanterior view) showing bilateral diffuse reticulations; (b), Case 1 showing clearing of reticulations after 7 weeks.*
Figure 2. (a), Case 1 CT scan of chest showing patchy areas of ground glass opacities. (b), Case 1 showing clearing of ground glass opacities after 7 weeks.

Figure 3. (a), Case 2 CT scan of chest showing diffuse ground glass opacities with interstitial thickening; (b), Case 2 showing clearing of ground glass opacities after 10 weeks.

Figure 4. (a), Case 3 CT scan of chest showing bilateral lower lobe reticulations; (b), Case 3 showing clearing of reticulations after 12 weeks.
Discussion

Corona Virus Disease 2019 (COVID 19) has emerged as a public health emergency [11]. The disease severity can range from mild infection to a severe one [12]. Patients suffering from severe disease are more at risk of developing complications including lung fibrosis. But in the literature, cases have been reported of patient with mild diseases having severe cardiorespiratory complications including sudden death [9].

Patients with mild infection have minimal symptoms or are often asymptomatic. And the infection can go unrecognized until some complications develop.

Our case series highlights the importance of this fact. We described 3 cases, who presented to the hospital with a short history of respiratory symptoms and evidence of lung fibrosis. All of them had tested negative for the SARS-CoV-2 by RT-PCR.

On presentation these patients had dry cough, exertional dyspnea, bibasilar crepitations on auscultation, bilateral reticulations on chest radiography and ground glass opacities in CT scan of the chest. Hence, ILD was the probable diagnosis in these cases.

But considering the current COVID pandemic situation the possibility of COVID 19 infection as a differential diagnosis was also kept. IgG antibodies against SARS-CoV-2 were found to be positive in all the cases, confirming a diagnosis of past COVID-19 infection with residual disease i.e., ‘Long COVID’.

ILD are an important differential diagnosis of patients with exertional dyspnea, dry cough and bilateral reticular/ground glass shadows on radiology, when infections/malignancy have been ruled out.

Interstitial lung involvement in sarcoidosis, acute hypersensitivity pneumonitis, eosinophilic pneumonias and idiopathic interstitial pneumonias can show ground glass opacities [13]. The common radiographic patterns observed in Long COVID includes diffuse reticulations, diffuse nodular shadows and diffuse ground glass opacities [14]. These radiologic patterns hence, mimic those seen in ILDs.

Whereas the treatment guidelines are defined in the literature for most of the ILDs, not much literature evidence is available for the pharmacological management of ‘Long COVID’.

So, it is very important to diagnose long COVID patient before labelling it as some idiopathic form of ILD based on the radiology. Idiopathic form of ILD is termed when no underlying cause or association is found.

In the present pandemic, many patients are recovering from the COVID and are suffering from manifestations of Long COVID.

All the three patients in the present case series did not have any symptoms/history suggestive of acute COVID. Despite this they had manifestations of ‘Long COVID’ as confirmed by suggestive radiology and positive serology for SARS-CoV-2.

This case series highlights the importance of considering ‘Long COVID’ disease as a differential to the diseases with interstitial involvement with short history at presentation. After making a diagnosis of long COVID, these patients were treated with tapering doses of systemic corticosteroids which helped in clinical and radiological recovery.

Other studies have also found similar outcomes on usage of systemic corticosteroids in long COVID patients [15-17].

There were limitations in the present study. Firstly, owning to the COVID pandemic situation bronchoscopy and pulmonary function tests could not be performed in these patients. Secondly, this is a small sample observation and would benefit from large scale studies. Further, a longer duration follow up would add to the observations.

Conclusion

The clinical and radiological presentation of ‘Long COVID’ resembles that of ILD’s. Further asymptomatic COVID infection can also manifest signs and symptoms of ‘Long COVID’.

Therefore, in the current COVID-19 pandemic situation, patients with short history of respiratory symptoms and radiological features suggestive of ILD’s—‘Long COVID’ should also be ruled out, before making a diagnosis of ILD.

Conflict of Interest

None to declare.
References
1. King TE. Clinical Advances in the Diagnosis and Therapy of the Interstitial Lung Diseases. Am J Respir Crit Care Med, 2005, 172(3):268-279.
2. Kreuter M, Herth FJF, Wacker M, Leidl R, Hellmann A, Pfeifer M, Behr J, Witt S, Kauschka D, Mall M, Günther A, Markart P. Exploring Clinical and Epidemiological Characteristics of Interstitial Lung Diseases: Rationale, Aims, and Design of a Nationwide Prospective Registry-The EXCITING-ILD Registry. Biomed Res Int, 2015, 2015:123876.
3. Bourke SJ. Interstitial lung disease: progress and problems. Postgrad Med J, 2006, 82(970):494-499.
4. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou y, Shi J, Zhou M, Wu B, Yang Z, Zhang C, Yue J, Zhang Z, Renz H, Liu X, Xie J, Xie M, Zhao J. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol, 2020, 146(1):110-118.
5. Gaviatopoulou M, Korompoki E, Fotiou D, Ntanasis-Stathopoulos I, Psaltopoulou T, Kastritis E, Terpos E, Dimopoulos MA. Organ-specific manifestations of COVID-19 infection. Clin Exp Med, 2020, 20(4):493-506.
6. Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract, 2021, 75(3):e13746.
7. Lamprecht B. Is there a post-COVID syndrome? Pneumologe (Berl), 2020, 1-4.
8. Kwee TC, Kwee RM. Chest CT in COVID-19: What the Radiologist Needs to Know. Radiographics, 2020, 40(7):1848-1865.
9. Suess C, Hausmann R. Gross and histopathological pulmonary findings in a COVID-19 associated death during isolation. Int J Legal Med, 2020, 134(4):1285-1290.
10. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19, 2020; NICE guideline (NG188)[online]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK567263/ [Accessed: 04.03.2021].
11. Noor AU, Maqbool F, Bhatti ZA, Khan AU. Epidemiology of COVID-19 Pandemic: Recovery and mortality ratio around the globe. Pak J Med Sci, 2020, 36(COVID-19-S4):S79-84.
12. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. Int J Infect Dis, 2020, 95:304-307.
13. Bradley B, Branley HM, Egan JJ, Greaves MS, Hansell DM, Harrison NK, Hirani N, Hubbard R, Lake F, Millar AB, Wallace WAH, Wells AU, Whyte MK, Wilsher ML, British Thoracic Society Interstitial Lung Disease Guideline Group, British Thoracic Society Standards of Care Committee, Thoracic Society of Australia, New Zealand Thoracic Society, Irish Thoracic Society. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax, 2008, 63(Suppl5):v1-58.
14. Goel N, Goyal N, Kumar R. Clinico-radiological evaluation of post COVID-19 at a tertiary pulmonary care centre in Delhi, India. Monaldi Arch Chest Dis, 2021, doi: 10.4081/monaldi.2021.1682 (Epub ahead of print).
15. Myall KJ, Mukherjee B, Castanheira AM, Lam J, Benedetti G, Mak SM, Preston R, Thillai M, Dewar A, Molyneaux PL, West AG. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. Ann Am Thorac Soc, 2021, 18(5):799-806.
16. Goel N, Goyal N, Kumar R. Insights in the management of long COVID-19: preliminary observations. Indian J Chest Dis Allied Sci, 2021, 63(2):65-73.
17. Goel N, Goyal N, Spalgaia S, Mrigpuri P, Menon B, Kumar R. Protracted non-invasive ventilation for severe hypoxemic respiratory failure in Long COVID: a case series. Crit. Care Innov, 2021, 4(3):20-26.