

Bronchoscopy Manifestation In Severe COVID-19 Patient: Case Series

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Case Report

Keywords: bronchoscopy, severe COVID-19, mucus plug

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Bronchoscopy Manifestation In Severe COVID-19 Patient: Case Series

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Short Title: Bronchoscopy Manifestation In Severe Covid-19 Patient

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Abstract

Background: Severe manifestation of COVID-19 are identical with significant inflammation and associated with high mortality due to severe hypoxemia. Bronchoscopy's role in the management of COVID-19 patients is still controversial and minimally evaluated

Case presentation: Our case series reported unique bronchoscopy presentation. Three patients with COVID-19 were confirmed by PCR nasopharyngeal swab suddenly complain of progressive dyspnea and impending respiratory failure not respond with oxygen therapy. An emergency bronchoscopy was performed. All three patient had a normal bronchial wall without inflammation and edema but showed significant thick and copious mucus plug resulting in sudden desaturation. Patient showed significant clinical improvement following bronchoscopy intervention showed by clinical and chest x-ray improvement.

Conclusion : Deteriorating severe COVID-19 patient can have normal bronchial mucosa in bronchoscopy and showed marked thick and copious mucus plug. Bronchial washing and suction can be a life-saving modality as therapeutic effort. Significant improvements following the bronchial washing and suction was seen. Bronchoscopy should be performed with precaution and sufficient personal protective equipment to prevent infection transmission.

Keywords: bronchoscopy, severe COVID-19, mucus plug

Background

COVID-19 is an emerging disease with unexpected phenotypes. ^[1] Bronchoscopy's role in the management of COVID-19 patients is still controversial and minimally evaluated. Bronchoscopy is an aerosol-generating procedure thus poses a high risk of infection to proximate healthcare staffs. ^[2] On the other hand, bronchoscopy can be a lifesaving treatment modality in COVID-19 patients. There are few mechanism reported underlying COVID-19 hypoxemia, such as diffusion disturbance, V/Q mismatch, and shunting. ^{[3]-[5]}

Diffusion disturbance due to pulmonary edema was commonly reported in COVID-19. ^[5] COVID-19 tends to associated with inflammation with pulmonary ARDS features due to inflammation and pulmonary edema manifest as edema, hyperemic mucosa and redness in bronchoalveolar lavage fluid. ^[6] In this case series, we report unique bronchoscopy findings in three COVID-19 patients with sudden deterioration and impending respiratory failure but had normal bronchial mucosa in bronchoscopy and showed marked thick and copious mucus plug and significant improvements following the bronchial washing and suction. This propose a new hypoxemia mechanism and role of bronchoscopy in COVID-19 management.

Case Presentation

Case 1

Mr. S was referred to our hospital due to fever, cough, and dyspnea 11 days prior to admission. Other medical history was remarkable. Nasopharyngeal swab was positive for severe acute respiratory distress syndrome Coronavirus-2 (SARS-CoV-2). Chest X-ray (CXR) showed inhomogeneous opacities in middle-lower right lung. Laboratory examination showed leukocytosis, increased liver enzymes, and increased D-dimer of 35.20. Blood gas analysis (BGA) results were pH 7.42, pCO₂ 45.5 mmHg, pO₂ 83 mmHg, BE 6, HCO₃⁻ 30.1 mEq/L with non rebreathing mask (NRM) 15 litres per minute. Patient underwent clinical deterioration and emergency bronchoscopy was performed. Bronchoscopy showed thick mucus plug. Chest X-Ray showed improvement following bronchoscopy (shown in Fig. 1). Blood gas analysis after bronchoscopy results were pH 7.48, pCO₂ 42.2 mmHg, pO₂ 133 mmHg, BE 9, HCO₃⁻ 31.9 mEq/L with nasal cannula 3 litres per minute. Nnasopharyngeal swab on day 8 and 9 following admission were negative and discharge 3 days later. Bronchial fluid culture showed *Candida albicans* and no bacterial growth.

Case 2

Mr. C was admitted to hospital due to fever, cough, and dyspnea in the last 1 week. Other medical history was remarkable. Nasopharyngeal swab was positive for SARS-CoV-2. Laboratory result showed BGA with pH 7.5, pO₂ 106 mmHg, pCO₂ 33.3 mmHg, HCO₃⁻ 28.7 mEq/L, BE 6, O₂ saturation 99% with NRM 15 litres per minute, elevated liver enzyme, severe hyponatremia, increased CRP-Hs of 144.61 mg/L, and normal procalcitonin. Chest X-ray found bilateral pneumonia and atelectasis. Patient was admitted to intensive care unit, but his condition clinically deteriorates despite adequate support. Bronchoscopy was done and found normal mucous, bronchial mucosa was not hyperemic or fragile. The only abnormality was mucous plug on the lower right lobe. Post bronchoscopy CXR

revealed significant improvement (shown in Fig. 2), BGA improved with pH 7.49, pO₂ 109 mmHg, pCO₂ 37.4 mmHg, HCO₃⁻ 28.9 mEq/L, BE 5, O₂ saturation 99%. Patient's clinical condition and general appearance improved significantly after bronchoscopy. Patient were treated with N-acetylcysteine 200 mg twice daily, tocilizumab 200 mg once daily for 2 days, fluconazole 200 mg twice daily, acetylsalicylic acid 80 mg once daily, clopidogrel 75 mg once daily, cefoperazone sulbactam 2 grams twice daily. Nasopharyngeal swab was negative for SARS-CoV-2 on day 20 and discharge 1 week later.

Case 3

Mr. J was admitted to hospital due to breathing discomfort. Other medical history was remarkable. Nasopharyngeal swab was positive for SARS-CoV-2. General condition was mild despite severe hypoxemia on BGA. Laboratory examinations showed normal routine blood count and high CRP of 114 mg/L. Chest computed tomography (CT) scan revealed diffuse ground glass appearance. The patient was treated with unfractionated heparin 250 unit/hour for 3 days, oseltamivir 75 mg twice daily, tocilizumab 400 mg once daily for 2 days, cefoperazone sulbactam 2 grams twice daily, N-acetylcysteine 200 mg three times daily, levofloxacin 500 mg once daily, and fluconazole 200 mg twice daily.

Follow-up nasopharyngeal swab was negative for SARS-CoV-2 on day 19. However, the patient suddenly developed worsening shortness of breath. Blood gas analysis showed pH 7.5, pO₂ 57 mmHg, pCO₂ 29 mmHg, HCO₃⁻ 29 mEq/L, and BE 0.4. Chest X-Ray showed atelectasis and pneumothorax. The patient underwent urgent bronchoscopy and a water sealed drain was inserted. Bronchoscopy showed mucous plug at right and left main bronchus orifice. One day after the bronchoscopy procedure, CXR showed significant improvement (shown in Fig. 3. a-d), with BGA findings pH 7.5, pO₂ 98 mmHg, pCO₂ 35 mmHg, HCO₃⁻ 29 mEq/L, BE 4.

On day 26 the patient again suddenly developed worsening shortness of breath. Chest X-Ray showed atelectasis, hence the second bronchoscopy was performed. Bronchoscopy showed thick mucous plug, similar to first bronchoscopy (shown in Fig. 3. e-h). Bronchoalveolar lavage culture showed *Acinetobacter baumannii*, sensitive to cefoperazone sulbactam, amikacin, and tigecycline. Despite insignificant CXR improvement after the second bronchoscopy, the patient had significant clinical improvement, continued with extubation and walking rehabilitation.

Discussion and Conclusions

The role of bronchoscopy in COVID-19 is still controversial. Bronchoscopy is a multimodal tool for diagnosis and treatment in various conditions. In the case of COVID-19, bronchoscopy poses risks to both patients and health care providers when performed without appropriate precautions.^[7]

Multiple guidelines have reported on various indications for bronchoscopy, such as lobar or entire lung atelectasis due to mucous plug, facilitating tracheostomy, and life-saving intervention due to significant hemoptysis, stenosis, foreign body, or severe airway obstruction. Other possible indications included inconclusive non-invasive COVID-19 testing, the concern of an alternative etiology of respiratory disease which would change the management (especially in immune-

compromised), and suspicion of super-infection. ^[8] To the best of author knowledge, this is the first case series regarding the use of bronchoscopy in COVID-19 patients.

All patients in this case report were categorized as severe confirmed COVID-19 infection according to the Chinese Center for Disease Control and Prevention (CDC) classification due to shortness of breath and lung infiltrates more than 50%. ^[9] These findings suggested impending life threatening condition, in which a life-saving intervention was warranted. The patients in this case series underwent emergency bronchoscopy due to atelectasis and severe airway obstruction, manifested by significant desaturation and clinical deterioration. Bronchoscopy findings demonstrated thick mucus plug in all three patients. Bronchial washing for mucus plug clearance was done as therapeutic effort.

Several hypoxemia mechanisms have been reported in COVID-19 infection. Hypoxemia at the early COVID-19 stage can be caused by diffusion disturbance. Infection causes localized alveolar and interstitial edema, especially at the interface of pulmonary structures with different elastic characteristics. ^[10] In advanced stage, alveolar collapse will occur when pulmonary edema progress with concomitant loss of surfactant and superimposed pressure. Alveolar collapse will create intrapulmonary shunting in non ventilated lung. Continued pulmonary edema will increase lung weight and dependent atelectasis which exacerbate shunting fraction and decreases oxygenation which cannot be corrected by increasing FiO₂. ^[11] Another reported mechanism is V/Q mismatch due to intravascular microembolism

In regards to the bronchoscopy findings, pulmonary edema will demonstrate redness in bronchoalveolar lavage (BAL) fluid) ^[12] These characteristic findings seemed to be shared with other types of coronavirus, such as severe acute respiratory syndrome (SARS).^[12] Interestingly, bronchial wall's mucous membrane in these patients appeared to be intact, non-hyperemic, and no swollen bronchus was seen. These findings contradicted with previous report regarding bronchoscopy findings of COVID-19, where it was stated that bronchoscopy would show extensive bronchial mucosal hyperemia, swollen bronchial mucosa, mucous-like secretions in the lumen, jelly-like sputum blocking the airway in critically ill patients^[6] and pulmonary edema. ^[12]

Clear fluid BAL in our cases suggested that pulmonary edema might not the major pathological process that causes clinical deterioration in our patients. Other different course and causes of hypoxemia should be considered.

In light of recent publications, it has been reported that mucous plug may have a significant role in causing hypoxemia in COVID-19 patient. Post-mortem COVID-19 autopsy showed fibromyxoid exudation and the formation of thick mucous plugs.^{[13],[14]} Mucogenesis in COVID-19 remains unclear. SARS-Cov-2 hyperstimulate respiratory mucosa through type I hypersensitivity which trigger inflammatory biomarkers. ^[15] Inflammation triggers neutrophil chemotaxis. Lung-infiltrating neutrophils produce neutrophil extracellular traps (NETs) which increase mucus accumulation and rigidity. ^[16] COVID-19 infection causes ciliary dyskinesia which impaired mucociliary clearance. ^[17]

Mucus must have good viscosity and elasticity for optimal interaction with cilia and effective mucociliary clearance. ^[18] Mucus hypersecretion causes mucus plug formation. ^[15] Mucous plug can partially or completely obstruct one or more airways, hence should be considered as one of the significant problem in COVID-19 patient as it may worsen shunting and cause desaturation due to

further atelectasis and providing suitable environment bacterial superinfection.^[19] Thus bronchoscopy can be considered as therapeutic measures in patients with significant mucous plug formation which is evidenced by infiltrate and/or atelectasis in CXR.

All patients in this case had significant desaturation, and CXR revealed atelectasis and consolidation. After bronchial washing and suction, all patient showed significant improvement on both clinical and CXR. There was no marked adverse event in these patients. Nevertheless, bronchoscopy should be performed with precaution and sufficient personal protective equipment to prevent infection transmission.^[20]

In conclusion, bronchoscopy has a potentially special role in COVID-19 treatment approach. Patients with COVID-19 may have a normal bronchial wall without inflammation and edema. Although severe COVID-19 patients may show normal bronchial mucosa, but severe mucous plug can cause significant clinical deterioration due to shunting. Thick and copious mucous obstruction should be reckoned in a case of sudden and / or progressive desaturation. Bronchoscopy can be a life-saving modality as therapeutic effort.

Abbreviations

AABIP	: American Association for Bronchology and Interventional Pulmonology
BAL	: bronchoalveolar lavage
BGA	: Blood gas analysis
CDC	: Center for Disease Control and Prevention
CT	: computed tomography
CXR	: Chest X-ray
MOD	: multiple organ dysfunction
MOF	: multiple organ failure
NETs	: neutrophil extracellular traps
NRM	: non rebreathing mask
SARS	: severe acute respiratory syndrome
SARS-CoV-2	: severe acute respiratory distress syndrome Coronavirus-2

Declarations

- Ethical approval and Consent to participate

The study was approved by Ethical committee of Siloam Hospital (No.696/SHLV-HA/X/2020) and written consent was obtained from all patients

- Consent for publication

All patients gave written consent for their personal or clinical details along with any identifying images to be published in this study. These patients have not been reported in any other submission by us or anyone else.

- Availability of data and materials

The data are available from the corresponding author on reasonable request.

- Competing interests

The authors have no conflicts of interest to declare

- Funding

There was no specific funding sources

- Authors' contributions

A.W, J.S, A.S.S, N.P.L, S.S.S undertook conception, analysis, interpretation. All authors have read, improved, and approved the final version of the manuscript.

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References

1. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Crit Care*. 2020;24:154.
2. Luo F, Darwiche K, Singh S, Torrego A, Steinfort DP, Gasparini S, et al. Performing Bronchoscopy in Times of the COVID-19 Pandemic: Practice Statement from an International Expert Panel. *Respiration*. 2020;99(5):417–22.
3. Masi P, Bagate F, d’Humières T, Al-Assaad L, Abou Chakra L, Derumeaux G, et al. Is hypoxemia explained by intracardiac or intrapulmonary shunt in COVID-19-related acute respiratory distress syndrome? *Ann Intensive Care*. Springer International Publishing; 2020;10(1):4–6.
4. Santamarina MG, Boisier D, Contreras R, Baque M, Volpacchio M, Beddings I. COVID-19: A hypothesis regarding the ventilation-perfusion mismatch. *Crit Care*. *Critical Care*; 2020;24(1):4–7.
5. Archer SL, Sharp WW, Weir EK. Differentiating COVID-19 Pneumonia from Acute Respiratory Distress Syndrome and High Altitude Pulmonary Edema: Therapeutic Implications. *Circulation*. 2020;142(2):101–4.
6. First Affiliated Hospital - Zhejiang University School of Medicine. Handbook of COVID-19 Prevention and Treatment - The First Affiliated Hospital, Zhejiang University School of Medicine Compiled According to Clinical Experience. 2020. 22 p.
7. Ost DE. Bronchoscopy in the Age of COVID-19. *J Bronchology Interv Pulmonol*. 2020;00(00):1–3.
8. Lentz RJ, Colt H. Summarizing societal guidelines regarding bronchoscopy during the COVID-19

- pandemic. *Respirology*. 2020;1–4.
9. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and Prevention. *JAMA - J Am Med Assoc*. 2020;323(13):1239–42.
 10. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med*. Springer Berlin Heidelberg; 2020;46(6):1099–102.
 11. Dhont S, Derom E, Van Braeckel E, Depuydt P, Lambrecht BN. The pathophysiology of ‘happy’ hypoxemia in COVID-19. *Respir Res*. 2020;21(1):198.
 12. Brand V den, Leijten haagmans L, Riel V, Martina. Pathology of Experimental SARS Coronavirus Infection in cats and ferrets. *Vet Pathol*. 2008;562:551–62.
 13. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. Elsevier Ltd; 2020;8(4):420–2.
 14. Konopka KE, Wilson A, Myers JL. Postmortem Lung Findings in a Patient With Asthma and Coronavirus Disease 2019. *Chest*. Elsevier Inc; 2020;1–3.
 15. Khashkhasha HK, Elhadi M. A hypothesis on the role of the human immune system in covid-19. *Med Hypotheses*. 2020;143(January):110066.
 16. Earhart AP, Holliday ZM, Hofmann H V., Schrum AG. Consideration of dornase alfa for the treatment of severe COVID-19 acute respiratory distress syndrome. *New Microbes New Infect*. Elsevier Ltd; 2020;35:100689.
 17. Skalny A V., Tinkov LR, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, et al. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). *Int J Mol Med*. 2020;46(1):17–26.
 18. Pieterse A, Hanekom SD. Criteria for enhancing mucus transport: a systematic scoping review. *Multidiscip Respir Med*. 2018;13(22):1–12.
 19. Panchabhai TS, Mukhopadhyay S, Sehgal S, Bandyopadhyay D, Erzurum SC, Mehta AC. Plugs of the Air Passages: A Clinicopathologic Review. *Chest*. Elsevier Inc; 2016;150(5):1141–57.
 20. Torrego A, Pajares V, Fernández-Arias C, Vera P, Mancebo J. Bronchoscopy in Patients with COVID-19 with Invasive Mechanical Ventilation: A Single-Center Experience. *Am J Respir Crit Care Med*. 2020;202(2):284–7.

Figure Legends

- 1 Fig. 1. (a) Chest X-ray of Patient 1 (Mr. S) before bronchoscopy showed middle-lower right lung
2 opacity, (b) Chest X-ray after bronchoscopy showed improvement lower right lung opacity, (c)
3 bronchoscopy image before bronchial washing showed thick mucus plug, (d) after suction and
4 bronchial washing showed clear mucosa
- 5 Fig. 2. (a) Chest X-ray of Patient 2 (Mr. C) before bronchoscopy, (b) after bronchial suction and
6 washing showed bilateral opacity improvement, (c) bronchoscopy showed thick mucus plug
- 7 Fig. 3. (a) Chest X-ray of Patient 3 (Mr. J) before bronchoscopy showed right pneumothorax and
8 right lower lobe atelectasis; (b) post-bronchoscopy showed improvement on right lower lobe
9 atelectasis, (c) first bronchoscopy showed thick mucus plug, (d) first bronchoscopy showed normal
10 mucosa following bronchial washing, (e) Chest X-ray of patient 3 showed recurrent atelectasis 1 week
11 after the first bronchoscopy, (f) Chest X-ray showed minimal improvement after second
12 bronchoscopy, (g) Second bronchoscopy of Patient 3 before bronchial wash showed thick mucus
13 plug; (h) Second bronchoscopy after bronchial suction and washing showed normal and clear
14 mucosa.

Figures

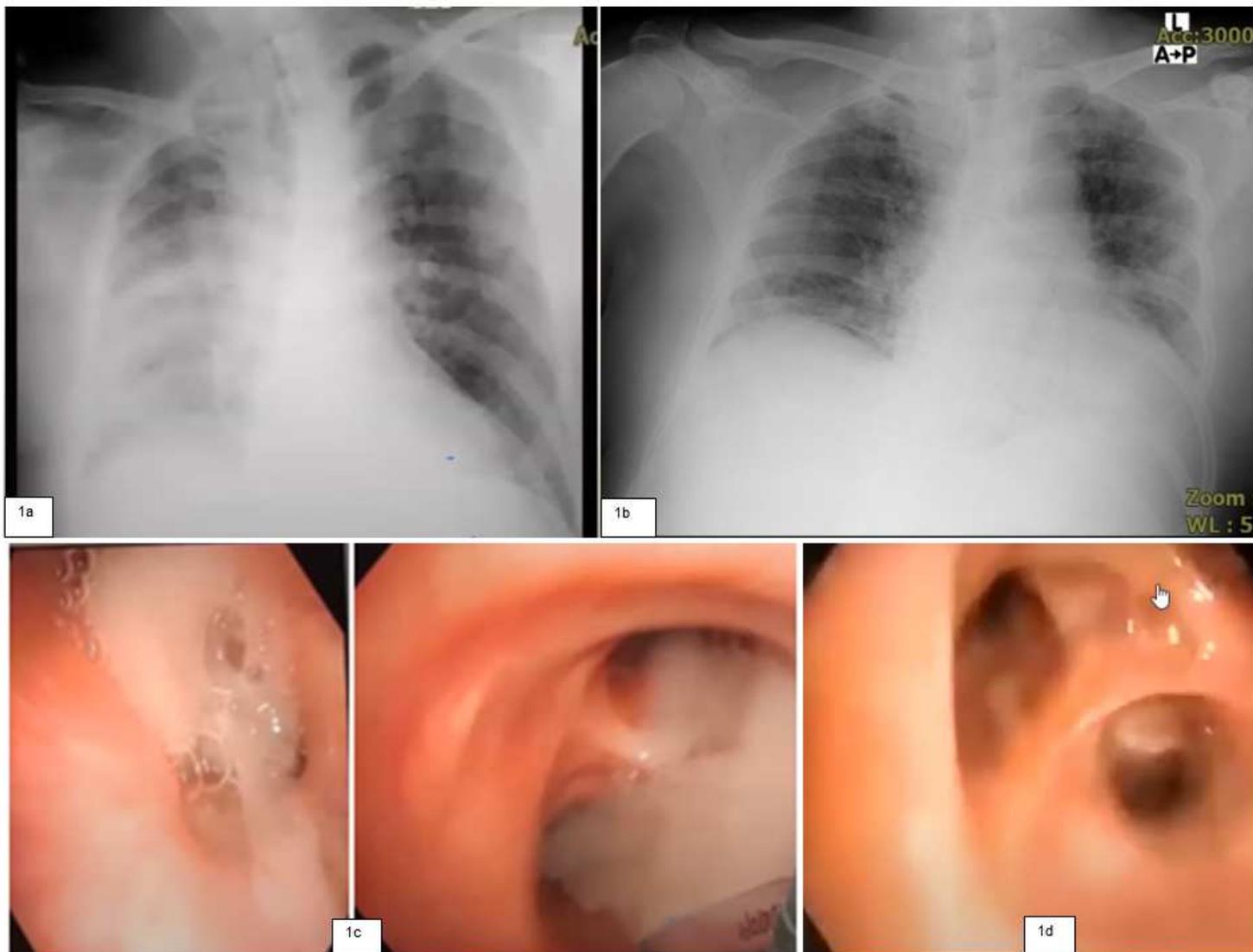


Figure 1

(a) Chest X-ray of Patient 1 (Mr. S) before bronchoscopy showed middle-lower right lung opacity, (b) Chest X-ray after bronchoscopy showed improvement lower right lung opacity, (c) bronchoscopy image before bronchial washing showed thick mucus plug, (d) after suction and bronchial washing showed clear mucosa

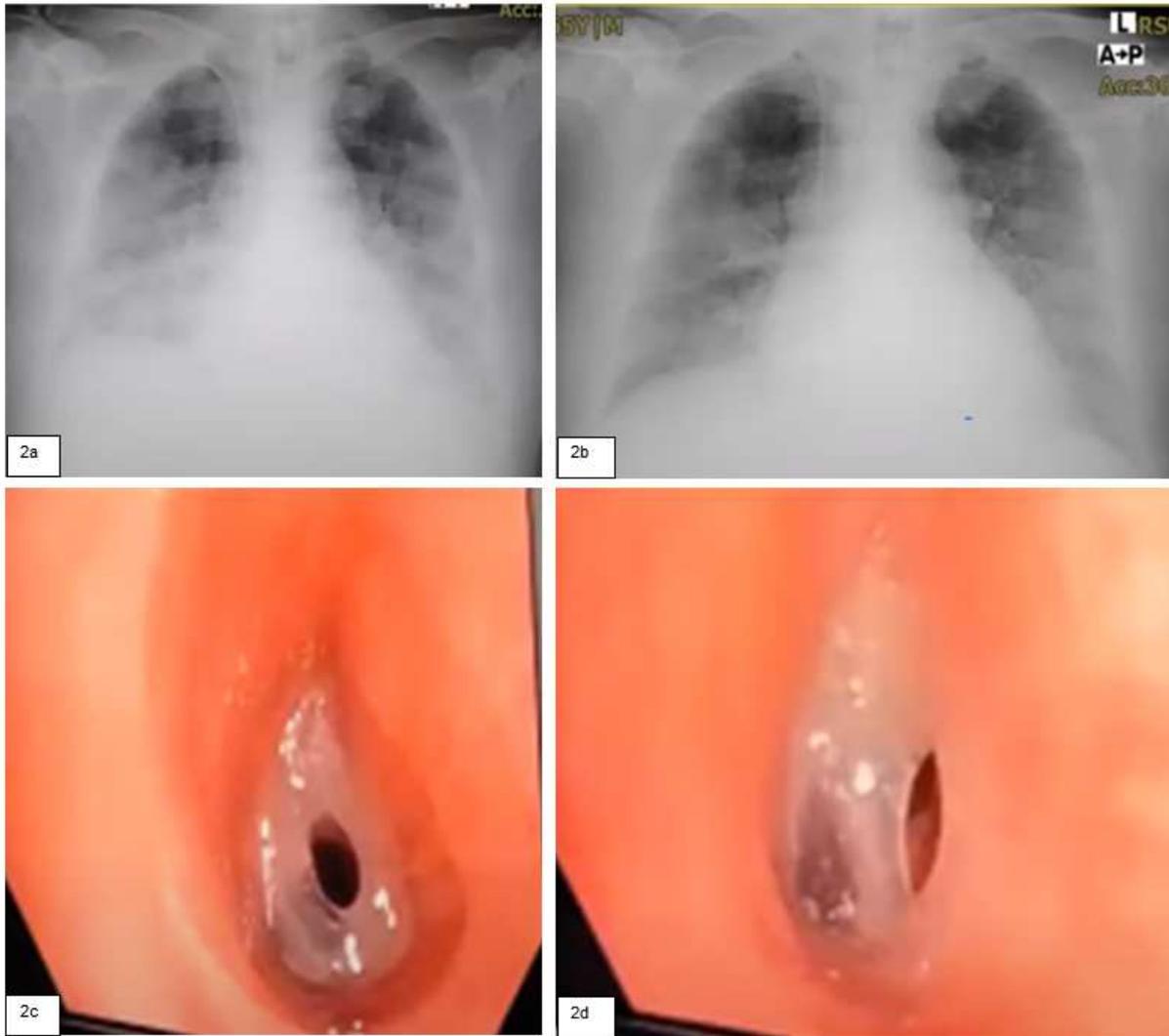


Figure 2

(a) Chest X-ray of Patient 2 (Mr. C) before bronchoscopy, (b) after bronchial suction and washing showed bilateral opacity improvement, (c) bronchoscopy showed thick mucus plug

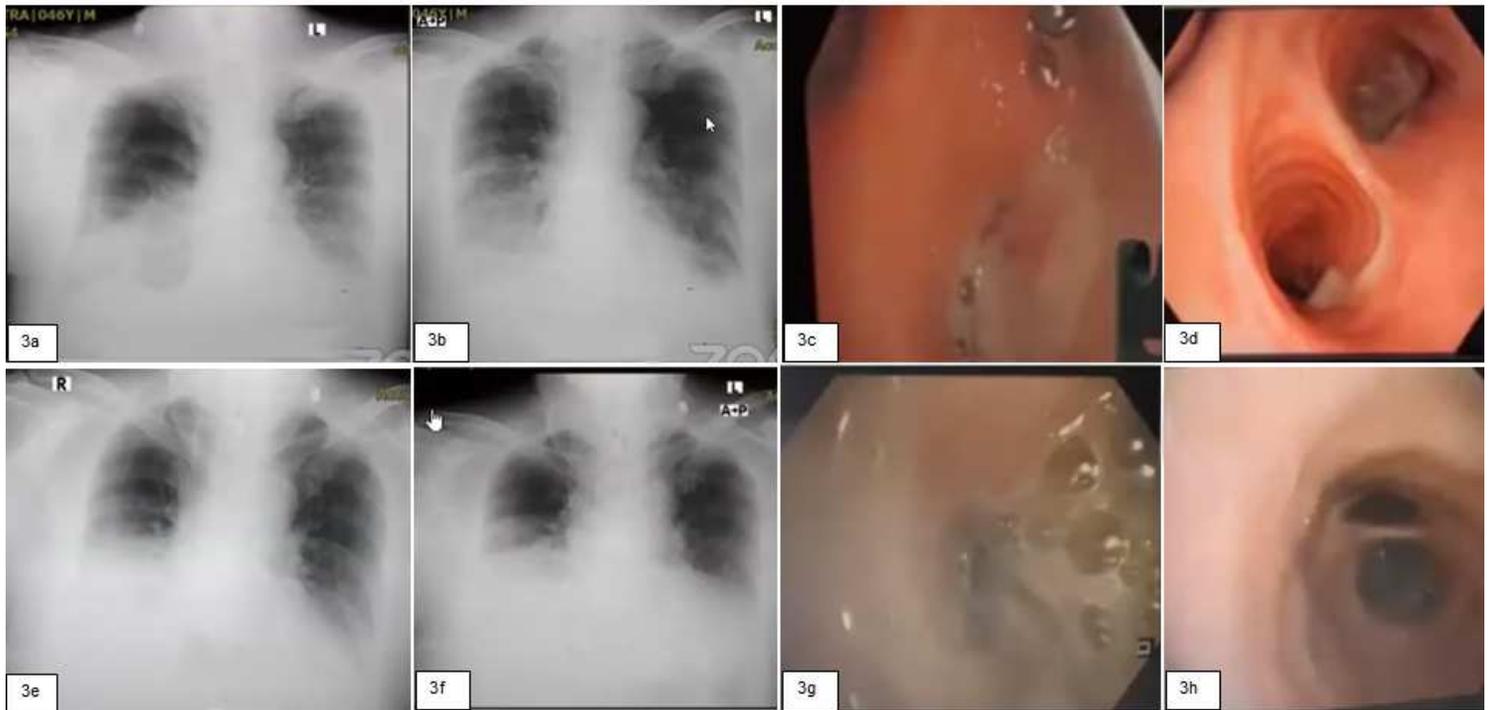


Figure 3

(a) Chest X-ray of Patient 3 (Mr. J) before bronchoscopy showed right pneumothorax and right lower lobe atelectasis; (b) post-bronchoscopy showed improvement on right lower lobe atelectasis, (c) first bronchoscopy showed thick mucus plug, (d) first bronchoscopy showed normal mucosa following bronchial washing, (e) Chest X-ray of patient 3 showed recurrent atelectasis 1 week after the first bronchoscopy, (f) Chest X-ray showed minimal improvement after second bronchoscopy, (g) Second bronchoscopy of Patient 3 before bronchial wash showed thick mucus plug; (h) Second bronchoscopy after bronchial suction and washing showed normal and clear mucosa.