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Case Presentation

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The First Severe Case of COVID-19 Using Extracorporeal Membrane Oxygenation (ECMO) in Shenzhen, China

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Abstract

This is the first confirmed severe case of COVID-19 using ECMO in Shenzhen, China. Patient developed respiratory symptoms at the beginning and deteriorated rapidly from day 7. Intensive interventions were adopted including tracheal intubation, continuous renal replacement therapy (CRRT) and extracorporeal membrane oxygenation (ECMO). Unfortunately, the patient died on day 30 of admission. We found that a large amount of jelly like discharges was accumulated in terminal bronchiole under bronchoscope, which may affect the treatment effect as the main reason.

Keywords: COVID-19; Treatment; ECMO; Case report

Introduction

The atypical pneumonia case, COVID-19, caused by SARS-CoV-2 which was newly named by International Committee on Taxonomy of Viruses (ICTV) [1] was spread widely with 4993470 cases confirmed globally and 84520 in China [2], as of May 23, 2020. Current epidemiologic data indicates that SARS-CoV-2 transmission is occurring from human to human [3-6] except the exposure to the Huanan seafood market in Wuhan, China [7,8]. We report the severe COVID-19 case who traveled through Wuhan, China and describe the clinical features.

Methods

This study was approved by the third People's Hospital of Shenzhen. Written informed consent was obtained from the patient's family for publication of this report and accompanying images.

Case Presentation

On January 14, 2020, a 63-year-old male patient was transferred to the third People's Hospital of Shenzhen by ambulance with a 4-day (from December 28, 2019 to January 1, 2020) staying history in Wuhan, China. On January 9, 2020, he got cough with white phlegm, without cephalalgia, sore throat, rhinorrhoea, fever and feeble. On January 11, 2020, he got fever with temperature at 38.4℃ (101.12 °F), anhelation, and was admitted at Shenzhen People's Hospital. He got chest Computer Tomography (CT) which revealed bronchiectasis with infection. He was prescribed oral administration with oseltamivir 75 mg twice a day and expectorant, defervescence and cough relieving therapies. After symptoms relieving, he went back home. However, two days later, he was sent to hospital with SPO_2 86%. Arterial blood gases indicated PH 7.475, PCO_2 28.3 mmHg, PO_2 69.5 mmHg at oxygen 37% inhalation. After admission to Intensive Care Unit (ICU), the patient received noninvasive mechanical ventilation. Later, the patient received endotracheal intubation with mechanical ventilation and CRRT because of hypoxia and renal failure on January 14. He was potential to be the SARS-CoV-2 infected and transferred to the designated hospital via ambulance.

Apart from a history of Obstructive Sleep Apnea Hypopnea Syndrome (OSAS), the patient was diagnosed with allergic cough 5 years ago and quitted smoking 20 years ago with 20-year smoking history. On admission, the physical examination revealed a body temperature of 37.5℃, blood pressure 125/76 mmHg, pulse of 125 beats per minute, oxygen saturation of 92% while the patient was under mechanical assisted ventilation with 100% oxygen. Lung auscultation reveled rhonchi, and chest radiography indicated diffused interstitial changes and obvious lung consolidation **(Figure 1).** Furthermore, arterial blood gases reveled PH 7.049, PCO_2 76.4mmHg, PO_2 66.2 mmHg, HCO_3^-21.1 mmol/L, BE -9.4 mmol/L, Lac 1.1 mmol/L, FiO_2 80%, and oxygen saturation 82%. Meanwhile, phlegm tested positive with lower Cycle Threshold (Ct) value of 22 for 2019-nCoV RNA by Real-Time-Reverse-Transcriptase-Polymerase-Chain-Reaction (rRT-PCR) assay. The case was notified to Center for Disease Control and Prevention (CDC) of Shenzhen immediately. Although the patient claimed that he had never been to Huanan seafood market and had no contact with ill persons during his travel to Wuhan, China.

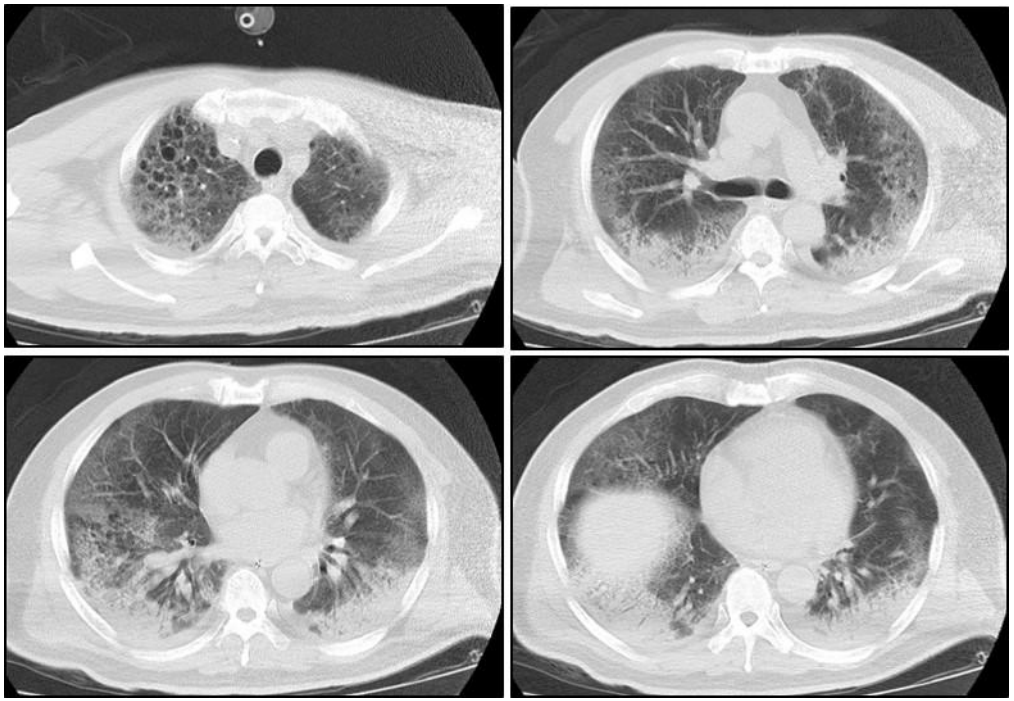

Figure 1: Initial chest computed tomography on admission showed the following characteristics: Interstitial change in the apical segment of bilateral superior lobe. Multiple ground-glass opacities with subpleural distribution. Obvious consolidation in the posterior segment of bilateral lungs.

Treatment during his hospitalization in the third People's Hospital of Shenzhen was largely supportive. The patient received, as needed, antiviral agents consisting of ribavirin, interferon, lopinavir and ritonavir solution. Fortunately, on hospital days 18 and 19 (illness days 24 and 25), RT-PCR revealed Ct value for SARS-CoV-2 RNA converted into negative on nasopharyngeal swab and bronchoalveolar lavage fluid for 2 continual days. Based on the negative value proof, lopinavir and ritonavir solution treatment was terminated on hospital day 21 (illness day 27) **(Table 1).** He also received voriconazole, teicoplanin, meropenem, vancomycin, Polymyxin E, and piperacillin and tazobactam sodium **(Table 2)** as he was infected with different bacteria and/or fungus at different stages during hospitalization. Chest Computed Tomography (CT) also

revealed severe viral pneumonia pervading the whole lung with emphysema on hospital day 9 (illness day 15).

Table 1: Results of real-time-reverse-transcriptase-polymerase-chain-reaction (rRT-PCR) testing for the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *.

	day 1	**day 2**	**day 3**	**day 4**	**day 5**	**day 6**	**day 7**	**day 8**	**day 9**
nasopharyngeal swab	NT	NT	NT	NT	NT	NT	NT	NT	NT
oropharyngeal swab	negative	negative	NT	30	26	negative	NT	negative	33
sputum	22	NT	NT	22.4	NT	NT	28.5	negative	NT
BALF	NT	NT	negative	NT	NT	NT	NT	27.2	NT
	day 10	**day 11**	**day 13**	**day 15**	**day 17**	**day 18**	**day 19**	**day 20**	**day 22**
nasopharyngeal swab	NT	NT	NT	37	NT	negative	negative	negative	NT
oropharyngeal swab	31	NT	26.52	NT	negative	NT	NT	NT	NT
sputum	NT	NT	NT	NT	NT	NT	NT	NT	NT
BALF	NT	27	24.29	31	34	negative	negative	negative	negative

*Lower cycle threshold (Ct) values indicate higher viral loads. BALF denotes bronchoalveolar lavage fluid; NT denotes not detested.

Table 2: Treatment according to days of illness and days of hospitalization, January 9 to February 7, 2020.

	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D 12	D 13	D 14	D1 5	D 16	D 17	D1 8	D 19	D 20	D2 1	D2 2	D 23	D 24
Day of illness	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Drug	ribavirin									lopinavir and ritonavir solution														
	interferon																							
		piperacillin and tazobactam sodium												voriconazole					voriconazole+teicoplanin					
																Polymyxin E								
							meropenem																	
											vancomycin													
								caspofungin																
Event	mechanical assist ventilation													tracheotomy										
	CRRT																							
											ECMO													

There were plenty of proof indicated secondary infection of bacteria and/or fungus, as blood G test presented positive at hospital day 2 of 289.4 pg/ml and day 8 of 424.3 pg/ml (illness days 8 and 14). Sputum smear at hospital days 8, 10, 15 and 16 (illness days 14, 16, 21 and 22), and Bronchoalveolar Lavage Fluid (BALF) smear at hospital day 9 (illness day 15) demonstrated a little fungus spore. Candida was detected in sputum culture on hospital days 9, 10, 12, 18 and 19 (illness days 15, 16, 18, 24 and 25) and in BALF on hospital days 10, 12 and 14 (illness days 16, 18 and 20).

Chest radiography revealed both lungs suffered severe infection with a little hydrothorax before hospital day 10 (illness day 16). However, chest radiography indicated an aggravated infection on hospital day 11 (illness day 17) **(Figure 2A)** than previous images **(Figure 2B).** A Venovenous (VV)-ECMO was applied for lung rest therapy on hospital day 11 (illness day 17) based on hypoxemia and aggravated infection with radiography presentation. The VV-ECMO was commenced with rotational speed at 2800 rpm, blood flow of 3.2 L/minute, gas flow of 5 L/min, FiO_2 of 35% and cistern temperature of 37 ℃.

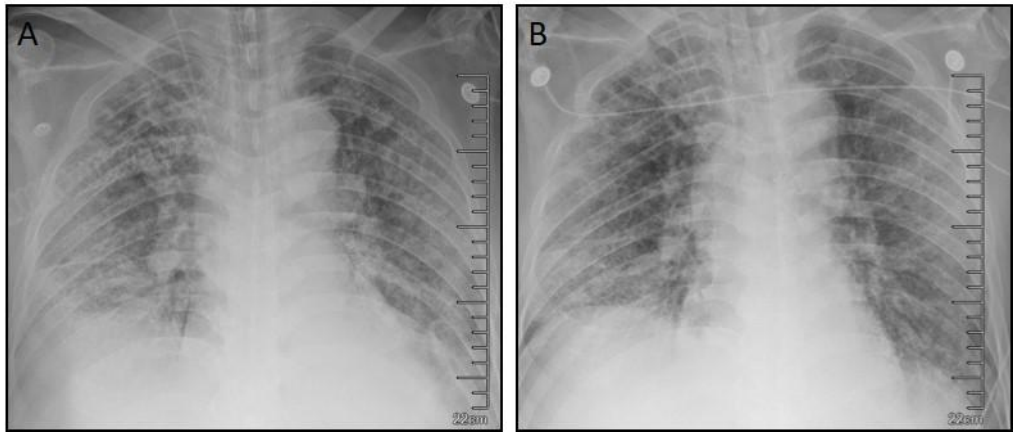

Figure 2: Chest radiograph. (A) Chest radiograph on hospital day 12, the lower lobe of right lung showed an aggravated infection than the previous image. (B) Chest radiograph on hospital day 11.

Arterial gases demonstrated a continuous hypercarbia and hypoxemia **(Figure 3),** though the patient was under mechanical ventilation at prone position and aspiration of sputum every day on admission before hospital day 11 (ECMO day, illness day 17).

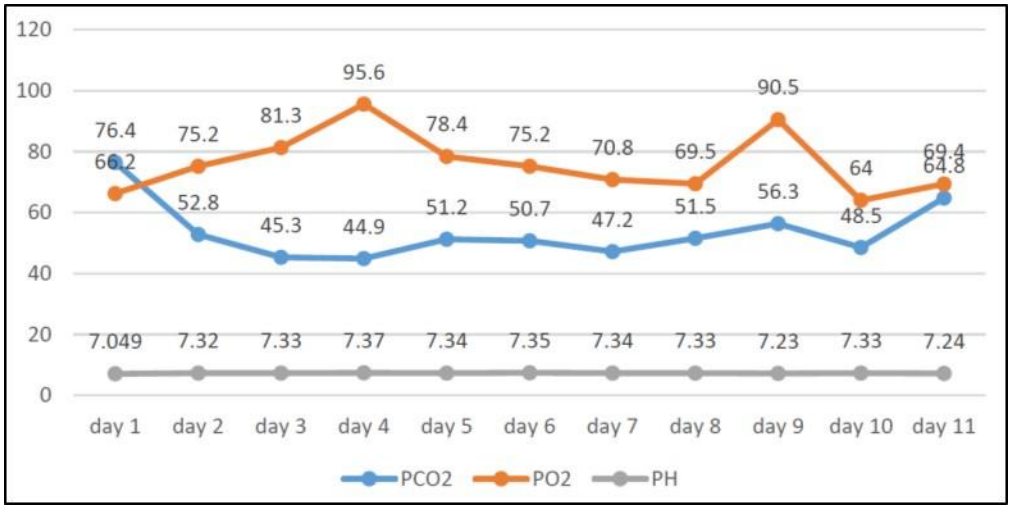

Figure 3: Arterial gases result showed a persistent hypercarbia, hypoxemia and acidemia during mechanical ventilation period.

Counts of immune cells of $CD4^+$ and $CD8^+$ T cells in blood were counted via flow cytometry, and C-Reactive Protein (CRP), High Sensitivity (hs)-CRP and cytokine of interleukin 6 (IL-6) were also defected **(Figure 4),** which indicated the immune response and infection level.

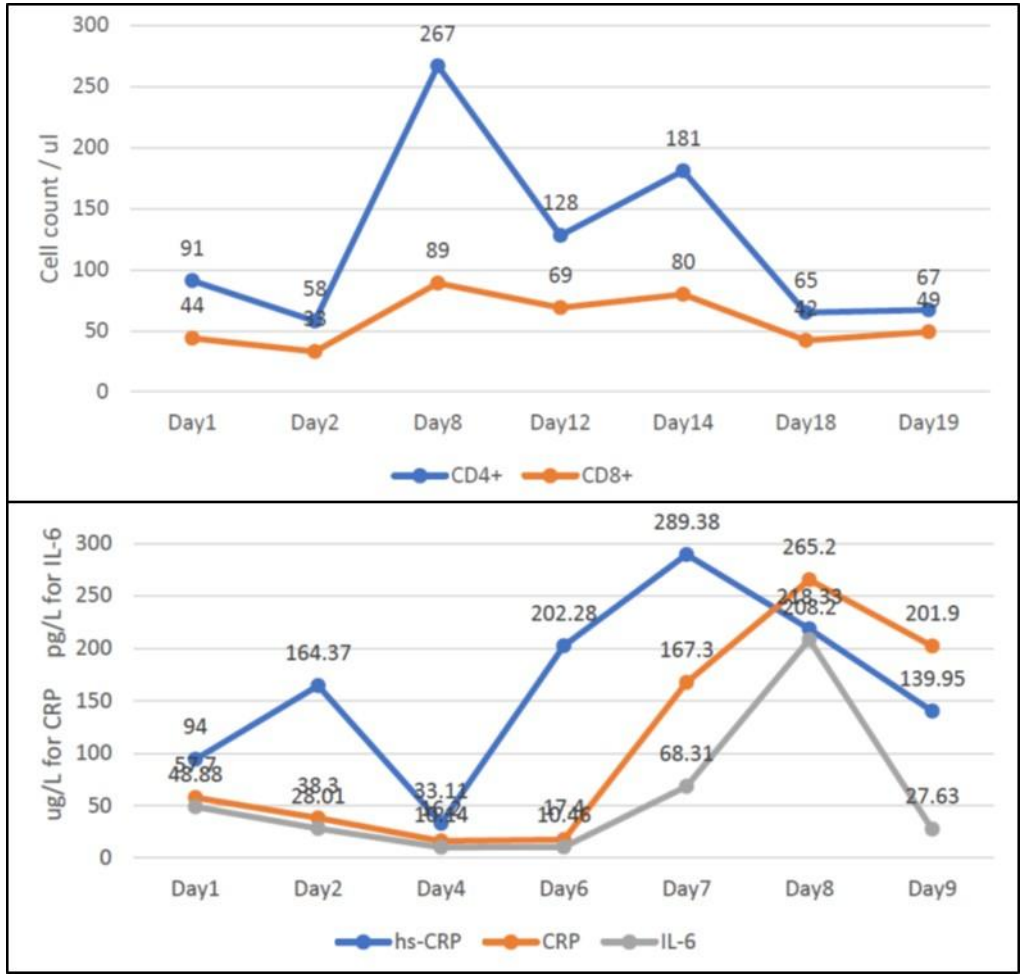

Figure 4: (A) Counts of CD4+ and CD8+ T lymphocyte cells in blood. (B) Trends of hs-CRP, CRP and cytokine of IL-6.

Apart from severe Acute Respiratory Distress Syndrome (ARDS), the patient fell into Multiple Organ Dysfunction Syndrome (MODS), including acute hepatic insufficiency

(an elevated alanine aminotransferase, Gamma-glutamyl Transferase and bilirubin), acute renal injury (Phase III, KDIGO) and acute myocarditis (an elevated creatine kinase, CK-MB and cardiac troponin I). Unfortunately, the patient died on day 30 of admission.

Discussion

Our report of the first confirmed severe case of COVID-19 under ECMO in Shenzhen, China illustrates several aspects of the emerging outbreak that are not yet fully understood. The patient had traveled to Wuhan, China, but not visited the Huanan seafood market or health care facilities or any sick contacts during his stay in Wuhan. That means, his source of SARS-CoV-2 infection is unknown and he should be infected by 2019-nCoV carrier(s) **[9,10].** The patient was in mild symptom at the first illness week but broke out in severe condition on day 6 of illness. Wang et al. **[11]** also reported that the median durations from first symptoms to dyspnea and ARDS were 5 to 8 days respectively. In addition, most mild cases of confirmed COVID-19 with approximate one-week hospital stay had inflammatory cascade reactions in the third People's Hospital of Shenzhen (data not demonstrated). The present patient fell into MODS on day 6 of illness without any distinct omens, which indicates the episode for duplication of SARS-CoV-2 to plateau may be around one week. Detection of SARS-CoV-2 RNA in specimens from respiratory tract with low Ct values suggests high viral loads and potential for spread. RT-PCR is the golden standard to confirmed SARS-CoV-2 RNA infection. However, it may present false-negative occasionally, as Ct value of oropharyngeal swab revealed negative on days 8 and 12 of illness. Moreover, CT presented the representative viral pneumonia on day 15 of illness which was strong recommended to diagnosis COVID-19 by Jin et al. **[12]**.

There have not been any miracle antagonism drugs to treat COVID-19 till now, though remdesivir for compassionate use was based on the first case patient's worsening clinical status in the United States **[13]** and may be the best potential drug for the treatment of COVID-19 **[14],** randomized controlled trials are needed to determine the safety and efficacy of remdesivir and any other investigational agents for treatment of patients with SARS-CoV-2 infection **[15].** Ribavirin, interferon, and lopinavir and ritonavir solution were administered for the present case. Fortunately, SARS-CoV-2 RNA in nasopharyngeal swab and BALF specimen collected on days 24 and 25 of the patient's illness is negative. As in Severe Acute Respiratory Syndrome (SARS) treatment, patients treated with lopinavir/ritonavir and ribavirin had lower risk of ARDS or

death [16]. An enigma was hypercarbia. The patient was under mechanical assist ventilation in prone position on day 6 of illness and even with tracheotomy on day 20 of illness, however, PCO_2 remained higher than 45 mmHg in arterial blood on admission before ECMO day. Bronchoscope was applied to examine lung branches which demonstrated plenty of jelly like discharges accumulated in terminal bronchiole. To the best of our knowledge, we are the first to report the gelatin at the end of airway in severe COVID-19 case. However, there has not been any therapeutic agents to resolve this problem yet.

Currently, our understanding of the clinical spectrum of COVID-19 is very limited. Complications such as severe pneumonia, respiratory failure, ARDS, and cardiac injury have been reported [4,17], but seldomly reported hepatic insufficiency as we presented in the present case. However, it is important to note that these cases were identified on the basis of their diagnosis of pneumonia and thus may bias reporting toward more severe outcomes.

Conclusions

We report the clinical features of the first severe case of COVID-19 under ECMO in Shenzhen, China. Key aspects of this case included symptoms of the patient deteriorated approximate at the end of the first week of the illness days. As the symptoms extended into severe condition, the patient fell into MODS and hard to recover. A large quantity gelatin was found at the end of airway under bronchoscope, which may impede recovery, even with negative SARS-CoV-2 detection. It warrants further strength to beat COVID-19 back.

Ethics Approval and Consent to Participate

Our study was approved by the Institutional Ethical Committee for the Third People's Hospital of Shenzhen (Guangdong, China). Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Author Contributions

PF Chen, YH Zhang and FX Wang contributed to the clinical case report. JH Jiang and L Chen collected and analyzed the image findings. X Shi and ZQ Wang collected and provided blood test result data. L Liu provided ECMO data. All authors contributed to drafting the manuscript. BJ Hu directed the study and had final responsibility for the manuscript.

Competing Interests

All authors declare no conflict of interest here.

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