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Case Report

Integrated Chinese and Western Medicine in Treatment of Critical Coronavirus Disease (COVID-19) Patient with Endotracheal Intubation: A Case Report

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Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The disease has spread globally, resulting in the coronavirus pandemic.[2,3] Common symptoms include fever, cough, and shortness of breath. Muscle pain, sputum production and sore throat are less common.[4,5] While the majority of cases result in mild symptoms,[6,7] some progress to severe or critical pneumonia and multi-organ failure. Worldwide, there is a high mortality rate in severe or critical patients of COVID-19.[8,9] Here we report a critical case of COVID-19 patient with endotracheal intubation successfully treated with integrated Chinese and Western medicine (ICWM).

Case Presentation

A 37-year old male patient was admitted to the Xiangtan Central Hospital on Jan 28, 2020 with complaint of aggravating cough for 2 months (admission No. 831991). He had a history of chronic cough. He has been coughing for at least 3 months every winter and spring for the past 10 years. The present cough was caused by a cold 2 months ago. He said that he had right chest pain when coughing, but was mostly free of phlegm, occasionally coughing up small amounts of yellowish-white thick phlegm.

On Jan 28, results of reverse transcription polymerase chain reaction (rRT-PCR) to SARS-CoV-2 from nasopharyngeal swab were positive. The test results of influenza A and influenza B virus antigens were negative. The patient denied the history of hypertension, diabetes, coronary heart disease and other chronic diseases. He had lived locally for a long time and denied that he had a recent travel or living history in Hubei province, or that he had close contact with people who had fever and respiratory symptoms. So he was diagnosed as COVID-19 (suspected) and chronic bronchitis. The main treatments and examination results of the patient are shown in Appendixes 1–8 for details.

On Feb 3, the patient's condition worsened and the diagnosis was adjusted to severe COVID-19. The main symptoms and signs of the patients were fever, fatigue, poor appetite, cough, expectoration, slight shortness of breath. The tests indicated that the patient had severe acute respiratory distress syndrome (ARDS). On Feb 4, the patient's condition worsened further and the diagnosis was adjusted to critical COVID-19. Endotracheal intubation was carried out. On Feb 10, critical value reported indicated that gram-positive *Cocci* grew in aerobic blood culture bottle of the patient's catheter blood. Physicians removed central venous catheter. On Feb 11, the patient's tracheal intubation was removed due to infection. On Feb 12, *Staphylococcus haemolyticus* was detected in the central venous catheter blood culture, which was resistant to penicillin G, ciprofloxacin, oxacillin, compound sulfamethoxazole, moxifloxacin, levofloxacin and rifampin, and sensitive to tetracycline, tegacyclin, clindamycin, vancomycin and linezolid. On Feb 14, *Escherichia coli* was detected in two consecutive sputum cultures, with a bacterial count of 3+. It was resistant to cefuroxime, cefepime, amoxicillin, clavulanic acid, levofloxacin, cefoxitin, ceftriaxone, ceftazidime, compound sulfamethoxazole.

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It was sensitive to gentamicin, yaanpeinan, meropenem, amikacin, tegacyclin and cefepime ketsulbactam and piperacillin tazobactam. Extended-spectrum β-lactamases (ESBL) was also positive.

On Feb 16, the physicians in Xiangtan Central Hospital contacted the Chinese medicine (CM) master LIU Zhi-ming's team for consultation. The patient did not have chest tightness and shortness of breath, no cough or expectoration, and no nausea. He had a good appetite, normal stool and urination. The team decided to use a modified prescription for the first 3 days, which is a combination of Shashen Maidong Decoction (沙参麦冬汤) and Zhuye Shigao Decoction (竹叶石膏汤), including *Radix Adenophorae* 15 g, *Radix Pseudostellariae* 30 g, *Radix Glycyrrhizae* 6 g, *Semen Armeniacae Amarum* 10 g, *Bulbus fritillariae Thunbergii* 10 g, *Fructus Trichosanthis* 15 g, *Folium Eriobotryae* 15 g, *Radix Salviae Miltiorrhizae* 15 g, *Caulis Bombusae in Taeniam* 10 g, *Pericarpium Citri Reticulatae* 10 g, *Poria* 15 g, *Herba Dendrobii* 15 g. The CM decoction made by Xiangtan Central Hospital were administered to the patient on the next day, 200 mL once, twice a day.

On Feb 19, the main symptom was dry cough, but the frequency of coughing decreased significantly. There were no chest tightness, shortness of breath, fatigue, abdominal distention and muscle soreness. His sleep and appetite were normal, and he defecated once a day. The sputum culture indicated that there were *Escherichia coli* with ESBL positive and multidrug-resistant but sensitive to acepenem. The team decided to use a modified prescription based on the previous one for the next 3 days. New herbs were administered to the patient on the next day, including *Radix Adenophorae* 15 g, *Radix Ophiopogonis* 15 g, *Radix Panacis quinquefolium* 10 g, *Fructus Schisandrae* 6 g, *Gypsum Fibrosum* 15 g, *Folium Phyllostachydis henonis* 15 g, *Folium Mori* 10 g, *Rhizoma Phragmitis* 15 g, *Radix Salviae Miltiorrhizae* 15 g, *Radix Glycyrrhizae* 6 g, *Pheretima* 10 g, *Semen Lepidii seu Descurainiae* 15 g. The mode and time of taking CM prescription was same as the first time.

On Feb 23, the patient occasionally had low fever and paroxysmal dry cough without any other discomfort after taking the last prescription. The last prescription was effective, so there was no change. Finally, the patient was discharged from hospital on Feb 25. On Mar 13, we conducted a follow-up visit to the patient. He tested negative for SARS-CoV-2.

DISCUSSION

The World Health Organization (WHO) declared the coronavirus outbreak in 2019–2020 as a pandemic[2] and a Public Health Emergency of International Concern (PHEIC).[10] Confirmed cases were reported from at least 213 countries, areas, or territories.[11] The outbreak has caused at least 12,322,395 confirmed infections and 556,335 deaths as of July 11, 2020.[12]

The severity of COVID-19 varies. The disease may take a mild course with few or no symptom, resembling other common upper respiratory diseases such as the common cold.[5] Mild cases typically recover within 2 weeks, while those with severe or critical disease may take 3 to 6 weeks to recover. Among those died cases, the time from symptom onset to death has ranged from 2 to 8 weeks.[13]

The lungs are the organs most affected by COVID-19 due to the virus accesses host cells via the angiotensin Ⅰ converting enzyme 2 (ACE2), which is abundant in the type Ⅱ alveolar cells of the lungs. The virus uses a special surface glycoprotein, called "spike", to connect to ACE2 and enter the host cell.[14] As the alveolar disease progresses, respiratory failure might develop and death may follow.[15] In those severely affected, COVID-19 may rapidly progress to ARDS causing respiratory failure, septic shock, or multi-organ failure.[16] Many who died of COVID-19 had pre-existing medical conditions, including hypertension, diabetes mellitus, cancer and cardiovascular disease.[5,17]

In this case report, the patient's total admission time was 4 weeks, which can be divided into 4 stages. From Jan 28 to Feb 3, it was the first stage of rapid deterioration. The patient showed only mild symptoms, but the disease progressed rapidly. In the second stage, which was from Feb 4 to Feb 11, physicians carried out a series of rescue measures. It had been proved that these measures have a significant effect, but accompanied by serious drug-resistant bacteria infection. Therefore, the venous catheter and endotracheal intubation had to be removed, and only non-invasive ventilator could be used to maintain life. The third stage was from Feb 12 to Feb 16. Owing to endotracheal intubation is only a maintenance measure, the patient's pathological changes have not been significantly cured. So the condition worsened rapidly for the second time. Considering the side

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effects, the treatment measures were basically stopped, only anti-coagulant and anti-infective drugs were kept. The fourth stage started from Feb 17 and ended on Feb 24. This stage was essentially a recovery phase. In the absence of additional Western medicine treatment measures, the patient took CM. The overall condition continued to improve.

At the first consultation of the CM team, the patient's symptoms and signs seemed to be no obvious abnormality. These were an illusion caused by the hormones. Judging from the tests, the patient's condition was actually critical, and the external performance was not the same as the internal situation. So constitution and past disease information were crucial. Constitution was an important concept of CM, which is formed by congenital heredity and acquired. The inherent and relatively stable characteristics of human individual in morphological structure and functional activities are related to psychological character. The difference of individual constitution shows some differences in response and adaptation to external stimulation in physiological state, as well as the susceptibility to some pathogenic factors and the tendency of disease development in the process of onset.[18]

The patient had a history of dry cough for more than 10 years. The main symptom of this disease was dry cough. In addition, the patient was consistent with the common manifestations of yin deficiency constitution, as well as physical and psychological characteristics. Therefore, it is more likely that his constitution was yin-deficiency, which is just an emergency judgment. The patient was hospitalized in a critical condition and in a poor mental state. He is too ill to cooperate with the questionnaire. So the CM Constitution Scale for quantitative assessment was not carried out. However, the patient's condition improved significantly with the use of the CM of nourishing yin and clearing heat, which indicates that this judgment is basically correct.

Yin and yang are akin to water and fire. They can be regarded as two mutually restricted systems. Yin-deficiency is akin to the lack of water in the body, so it is prone to have dry symptoms or signs, such as dry cough, thirst, dry skin, dry stool and so on. On the other hand, the lack of water can not restrict the fire, so the human body is prone to fever. In the theory of CM, the COVID-19 belongs to the plague with heavy dampness. Dampness is a sort of abnormal yin, which belongs to perverse qi. One of the most obvious signs of heavy dampness is thick and greasy tongue coating.

So the general CM treatment is to nourish yin,[19] clear away heat (fever), remove dampness and regulate Fei (Lung) function. Yin-deficiency is related to some extent with the disturbances in the hypothalamus-pituitary-adrenal axis, hypothalamus-pituitary-thyroid axis, cyclic nucleoside system and immune function.[20] Therefore, the mechanism of treating yin-deficiency may be to restore the immune system and circulatory system function. Dampness is a description set of the unique effects and manifestations of a particular virus on the human body, such as decreased respiratory function, fatigue, muscle soreness, thick tongue coating. Therefore, the tongue moss of the patients obviously thinned and decreased, and the symptoms, signs and examination results all improved after the treatment of CM.

If CM was used early in treatment, it is likely that tracheal intubation and the use of invasive ventilators can be avoided, reducing complication rates and the risk of death. The primary purpose of tracheal intubation and invasive ventilators is to keep the patient's airway open and oxygenated for life. It can be seen that CM treatment can have the same effect, besides CM can also have antibacterial and antiviral effects. If treated promptly in the early mild stages, it may even prevent the disease from progressing to critical illness, essentially eliminating the need for tracheal intubation or invasive ventilators. This is also an idea that CM has emphasized since ancient times, 'diseases that have already occurred need to be prevented from spreading or aggravating'.

In conclusion, ICWM in the treatment of critical patient with COVID-19 is likely to significantly improve the symptoms and signs of the patient, alleviate the patient's pain. It also significantly improved the results of respiratory function tests such as oxygen index, oxygen partial pressure and carbon dioxide partial pressure, and also improved the state of leukocytes and lymphocytes to some extent. All of these suggest that the treatment of ICWM can improve the respiratory and immune function of patients and the overall situation of the body. In the current situation of the world COVID-19 epidemic, it is worth to further promote and carry out more clinical and experimental

research to reduce mortality and save more lives.

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Clinical data materials were provided by Lei CQ and Liao X. Data analysis and collation was done by Yao SY, Lei CQ, Chang X, and Liu RX. Paper writing and revision was done by Yao SY, Liu RX, and Liu ZM.

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