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Case Report

Treatment of pulmonary fibrosis in one convalescent patient with corona virus disease 2019 by oral traditional Chinese medicine decoction: A case report

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ABSTRACT

After one-month of oral treatment with traditional Chinese medicine decoction, without using other drugs, the lung inflammatory exudate, pulmonary fibrosis and quality of life of a 61-year-old female patient with corona virus disease 2019 (COVID-19) were significantly improved. No recurrence or deterioration of the patient's condition was found within seven weeks of treatment and follow-up, and no adverse events occurred, indicating that oral Chinese medicine decoction was able to improve the pulmonary inflammation and fibrosis in a patient recovering from COVID-19, but further research is still needed.

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1. Introduction

The corona virus disease 2019 (COVID-19) refers to an acute respiratory infectious disease whose main clinical symptoms include fever, dry cough and fatigue, but can also be accompanied by nasal obstruction, runny nose, sore throat, myalgia and diarrhea, following infection with the sudden acute respiratory syndrome coronavirus-2 [1]. After treatment, which may include improving oxygen supply, antiviral therapy, improving body fluid circulation and enhancing body immunity, the symptoms of most patients can be significantly reduced, and the levels of viral nucleic acids in the body will fall below the limit of detection, finally reaching the clinical cure standard. However, even after reaching the standard of clinical cure, some patients continue to suffer from incomplete absorption of pulmonary exudates and pulmonary fibrosis, symptoms that need to be addressed quickly [2,3]. Modern medicine recommends the new anti-fibrosis drugs, pirfenidone

and nidanib, as the main therapeutic agents for pulmonary fibrosis [4]. Considering that both of these drugs have gastrointestinal tract and photosensitive reactions that include nausea, abdominal pain and diarrhea [5,6], and that the spleen and stomach function of convalescent COVID-19 patients are dysregulated, the adverse reactions to pirfenidone and nidanib are poorly tolerated in this population, and there is no safe and reliable specific drug to use in clinical care.

Fitting neatly into the category of “plague” in traditional Chinese medicine (TCM) [7], COVID-19 is a disease that is highly contagious, epidemic-prone, with a sudden onset and critical illness. TCM has a long history of treating diverse diseases that fit the “plague” definition. Relevant studies have shown that TCM can effectively reduce pulmonary exudates and inhibit the release of inflammatory factors [8]; thus it can play a therapeutic role in convalescent patients with COVID-19. At present, the oral administration of decoctions of Chinese medicines has been widely recommended in the rehabilitation treatment of convalescent patients with COVID-19 [9]. Therefore, this case study selected the oral administration of a decoction of Chinese medicine as the primary treatment method for this convalescent COVID-19 patient.

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Due to its ease of transmission, COVID-19 has now spread to many countries in the world, seriously threatening the stability of human society, health of populations and quality of life. In order to provide a reference for effective clinical prevention and treatment of COVID-19, this article reports a clinical case of pulmonary inflammatory exudate and fibrosis in a convalescent COVID-19 patient who was treated through the oral administration of a decoction of Chinese medicine. The study followed the *Case Reporting Guidelines* [10] and “*The COVID-19 Diagnosis and Treatment Plan (trial 7th edition)*” formulated by the National Health Commission of China [11], and obtained the informed consent of the patient and the approval of the Ethics Committee of Guizhou Administration of TCM, China.

Further, the patient has provided written informed consent for the publication of the case and any accompanying images. The publication has also obtained the approval of the Ethics Committee of Guizhou Provincial Administration of TCM (No. KYH2020-003).

2. Case description

A 61-year-old female who had been diagnosed with COVID-19 was placed under inpatient isolation and observation in the designated diagnosis and treatment hospital for COVID-19 in Guizhou Province from February 24, 2020. After initial treatment that included oxygen administration through a nasal catheter, to improve the pulmonary oxygen supply, oral lopinavir, ritonavir and arbidol, inhalation of atomized α -interferon were applied to oppose virus infection, and oral thymosin was applied to enhance the body's immunity. The patient had no typical symptoms of COVID-19 such as fever, dry cough, nasal obstruction, runny nose, fatigue, myalgia and diarrhea. However, when she was kept in the hospital for isolation and observation, she had difficulty in falling asleep and poor appetite, accompanied by hunger and thirst without desire to eat or drink, intermittent dry and loose stools, a dark red tongue with yellowish thick and greasy coating in the middle and posterior part, but smooth and uncoated on both sides and the tip of tongue; her pulse was weak and astringent. Samples for two viral nucleic acid tests were taken at one-day intervals, and returned negative results, meeting the clinical cure standard of “*The COVID-19 Diagnosis and Treatment Plan (trial 7th edition)*”, formulated by the National Health Commission of China. But the chest computed tomography (CT) scan of the patient, performed on February 24, 2020, showed inflammatory exudate and fibrotic lesions in both lungs, accompanied by a small amount of pleural effusion on the right side. The results from routine blood tests, including blood biochemistry, C-reactive protein, troponin and procalcitonin, were all within normal clinical ranges. The patient had a history of type II diabetes, but her blood sugar was stable without abnormal fluctuations during her hospitalization. In order to promote the absorption of pulmonary exudate, reduce the level of pulmonary fibrosis, and prevent the recurrence or aggravation of COVID-19, a consensus was reached, considering the patient's age, spleen and stomach damage, initial recovery after the disease and weakness, the mild nature of Chinese medicine, unobvious gastrointestinal irritation, after discussion at the resident expert group meeting of the designated diagnosis and treatment hospital in COVID-19, Guizhou Province, China. It was decided to keep the patient in hospital for isolation, observation, and oral treatment with a decoction of Chinese medicine as the primary intervention.

Starting February 25, 2020, the patient was administered a dose of Chinese medicine decoction (150 mL) three times a day without other drugs, which is a liquid dosage form made by decocting and extracting water soluble components. Decoctions are prepared according to the patient's clinical symptoms and signs under the guiding principle of TCM syndrome differentiation and treatment;

they have the advantages of simple preparation, quick absorption, and quick effects. During the treatment process, according to the patient's relevant clinical symptoms, tongue coating, pulse condition and other physical examination results, we adjusted the prescription two times after the initial TCM prescription. The specific formulae prepared for this patient are shown in Table 1.

After seven days of treatment with the first TCM decoction (March 3, 2020), the re-examined chest CTs of this patient showed that the bilateral lung exudate and fibrosis were partially absorbed compared to baseline (February 24, 2020), and the right pleural effusion was completely absorbed. The patient reported that the symptoms of difficulty in falling asleep, poor appetite and thirst were relieved, and that her stool was better formed. Further, the dark red of tongue and the yellowness and greasiness of tongue coating were all diminished compared to baseline. The pulse was also a little stronger than before. In order to refine the curative effect considering this second examination, the authors made adjustments to the TCM herbal prescription. After 12 days of oral treatment with this second TCM decoction (March 15, 2020), the chest CT scans were re-examined and showed that the exudate and fibrosis of both lungs were significantly better than at the last check-in (March 3, 2020). The symptoms of difficulty in falling asleep, poor appetite and thirst were better than before, and the stool was normal. Meanwhile, the dark redness of tongue and the color and thickness of tongue coating were again significantly improved compared with March 3, 2020. Further, the pulse was stronger than before, and the slippery and astringent condition was obviously alleviated. In order to achieve better clinical efficacy, the author made a second adjustment to the TCM herbal prescription. After the patient continued to take this new TCM decoction for seven days, another chest CT scan on March 22, 2020 showed

Table 1

The traditional Chinese medicine treatment of the patient from February 25, 2020 to March 24, 2020.

Medication	Phase 1	Phase 2	Phase 3
Prepared aconite tablets (decoct first)	3 g	–	–
Eucommiae Cortex	–	20 g	20 g
Cinnamomi Cortex	3 g	3 g	3 g
Alismatis Rhizoma	10 g	10 g	10 g
Cinnamomi Ramulus	3 g	3 g	3 g
Zingiberis Rhizoma	3 g	3 g	3 g
Zanthoxyli Pericarpium	3 g	3 g	3 g
Chaneomelis Fructus	15 g	15 g	15 g
Paeoniae Radix Rubra	15 g	15 g	15 g
Magnoliae Officinalis Cortex	12 g	12 g	–
Tsaoko Fructus	5 g	5 g	5 g
Arecae Semen	12 g	12 g	12 g
Bupleuri Radix	9 g	9 g	9 g
Scutellariae Radix	10 g	10 g	10 g
Pseudostellariae Radix	–	–	20 g
Pinelliae Rhizoma	–	10 g	10 g
Bambusae Caulis in Taenias	10 g	–	–
Coptidis Rhizoma	6 g	6 g	6 g
Armeniacae Semen Amarum	10 g	10 g	10 g
Amomi Fructus Rotundus (decoct later)	10 g	10 g	10 g
Coicis Semen	30 g	30 g	30 g
Poria	30 g	30 g	30 g
Atractylodis Macrocephalae Rhizoma	30 g	30 g	30 g
Massa Medicata Fermentata	–	15 g	15 g
Asari Radix et Rhizoma	2 g	–	–
Phellodendri Chinensis Cortex	6 g	6 g	6 g
Acori Tatarinowii Rhizoma	–	10 g	–
Curcumae Rhizoma	10 g	–	–
Polygoni Cuspidati Rhizoma	9 g	9 g	9 g
Talcum (wrapped in cooking)	–	–	9 g
Curcumae Radix	–	10 g	10 g
Sojae Semen Praep Aratum	–	20 g	20 g
Tetrapanacis Medulla	–	9 g	–

that the exudate and fibrosis of both lungs were further improved compared to the scan from March 15, 2020. Additionally, the tongue was reddish, the color and thickness of the tongue coating were basically normal, the pulse was soft and strong, and the pathological sense of astringency had disappeared. The chest CT and tongue imaging results for this patient are shown in Figs. 1 and 2, respectively.

On March 23, 2020, it was determined that during the patient's stay in hospital for isolation and observation, no symptoms and signs related to the recurrence of COVID-19 were found. After four evaluations of lab results for novel coronavirus's nucleic acid level, routine blood analysis parameters, blood biochemistry, and the levels of C-reactive protein, troponin and procalcitonin were ameliorated. No abnormalities or adverse reactions were present. Therefore, following her stay in the hospital for observation and isolation, the possibility of recurrence or aggravation of the new coronavirus pneumonia was ruled out, and the patient was determined to have met the discharge standards. Thus, she was released from the hospital on March 23, 2020.

After the patient was discharged from the hospital, she participated in three follow-up consultations on March 30, 2020, April 6, 2020, and April 13, 2020. The follow-ups mainly included asking the patient whether she had fever, dry cough, stuffy nose, runny nose, fatigue, myalgia, diarrhea, and other typical symptoms related to COVID-19 during the period since her last follow-up. The patient told us that her condition did not relapse or worsen after she was discharged from the hospital, nor did she have any

other uncomfortable symptoms. The timeline of this case is shown in Fig. 3.

3. Discussion

COVID-19 belongs to the category of “febrile diseases” in TCM. The long history of TCM's uses against febrile diseases in China has been documented by the published works of celebrated doctors from past dynasties, such as Tianshi Ye's *Treatise on Epidemic Febrile Diseases*, Shengbai Xue's *Paper on Epidemic Febrile Diseases* and Jutong Wu's *Analysis of Heat Disease*. These works still serve as a foundation for the relatively complete diagnosis and treatment system currently used to manage febrile disease in Chinese medicine. As described in this case, the pulmonary exudate and fibrosis present in the convalescent COVID-19 patient have been significantly improved after only one month of oral treatment with a TCM herbal decoction. These results support the use of TCM for effective treatment of febrile diseases. Similar studies have also clearly indicated that oral administration of a TCM decoction can effectively treat the pulmonary fibrosis and inflammatory exudate in convalescing COVID-19 patients, improving dyspnea and helping to restore quality of life [12,13]. Oral Chinese medicine decoctions can play an important role in COVID-19 recovery, but applying them effectively mainly depends on the practitioner's accurate grasp of the progression and transmutation of febrile disease theory and understanding the physical characteristics of convalescent COVID-19 patients.

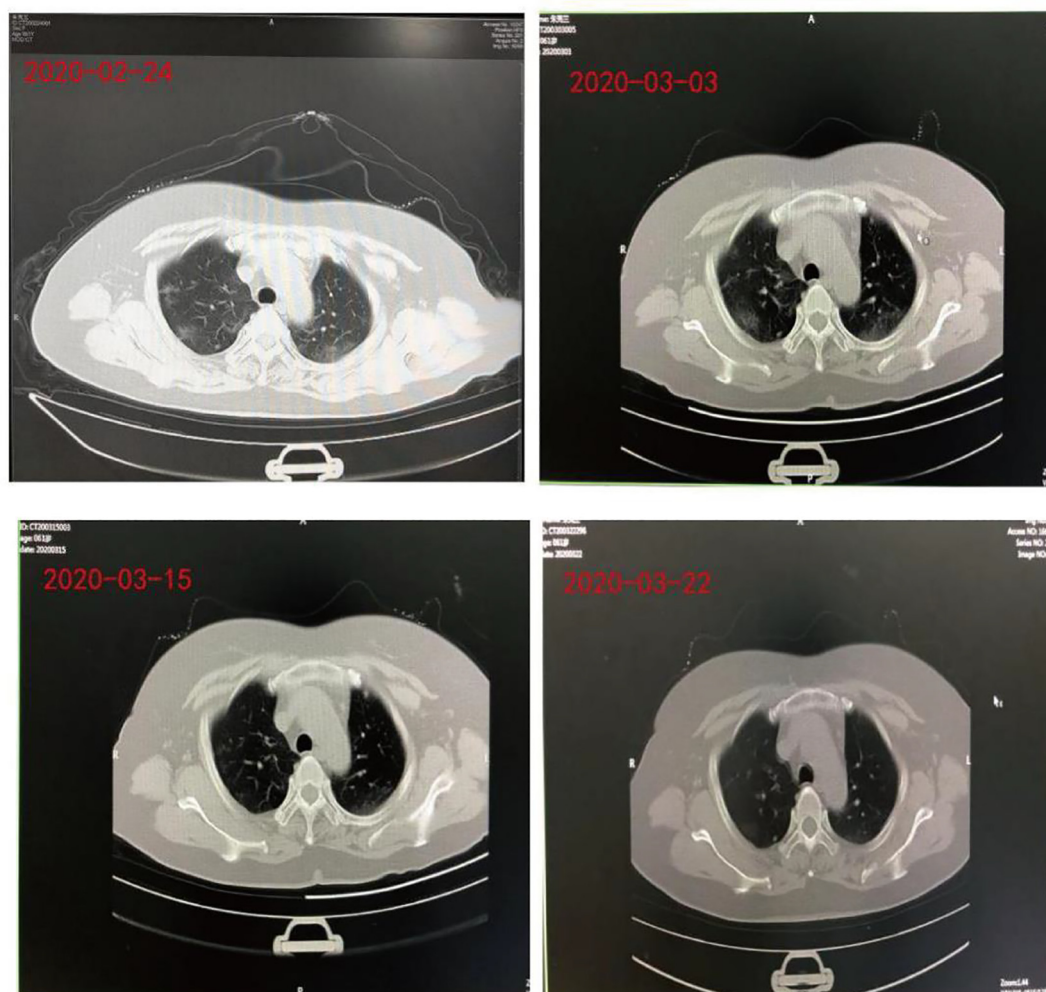


Fig. 1. The results of computed tomography re-examination during the observation period. The use of these pictures has been approved by the patient.



Fig. 2. Changes of the patient's tongue image before and after treatment. The use of these pictures has been approved by the patient.

The author mainly carries out syndrome differentiation and treatment on this patient from three aspects: on the levels of wei, qi, ying and blood, sanjiao or triple burner differentiation, and six meridians differentiation. Common pathological changes from a febrile disease invading the human body can be understood from a thorough analysis of pathomechanisms on the wei, qi, ying and blood levels. Fever, cough, thirst, stomachache, diarrhea, irritability, and insomnia are common symptoms of COVID-19 patients in the early stage; these febrile disease signs and symptoms tend to exhaust the body's qi, blood and fluids. When the course of disease is prolonged, and the patient finally enters the recovery stage, the body is basically in a state of qi and fluid depletion. In TCM, there is a close connection among fluid, qi and blood: qi can produce and move blood, and fluid can produce blood. Due to excessive consumption of qi and fluid, most patients in the convalescent phase of COVID-19 are in a state of blood stasis caused by blood deficiency. Based on the characteristic changes of the patient's dark red tongue, and weak and astringent pulse, it can be understood that the disease has affected the blood, and the patient has suffered from qi and ying injury, and blood stasis and stagnation. Therefore, in this study the practitioner used *Pseudostellariae Radix* for tonifying qi, and *Paeoniae Radix Rubra* in combination with *Curcumae Rhizoma* and *Cinnamomi Ramulus* to promote blood circulation and relieve blood stasis as part of the treatment formula. Secondly, exposure to the damp-heat pathogenic factor is key to the onset of COVID-19 [14]; damp-heat easily stagnates and blocks the middle-jiao in the human body, thus damaging the digestive and absorptive function of the spleen and stomach. Therefore, from the analysis of sanjiao or triple burner pathomechanisms, the inflammatory exudate in the lungs is the external manifestation of the excess dampness stagnating in the middle jiao. The symptoms of poor appetite, or hunger and thirst without desire to eat and drink, indicate spleen and

stomach damage, poor transportation and transformation of food and fluids, and congestion of damp pathogen. In addition, the tongue shows thick and greasy coating in the middle and rear, pointing to damp-heat pathogens mainly stagnant in the middle and lower jiaos. These signs and symptoms prompted the practitioner to use herbs that strengthen the spleen and transform damp, such as *Amomi Fructus Rotundus*, *Coicis Semen* and *Acori Tatarinowii Rhizoma*, to eliminate damp-heat in the middle jiao; the practitioner also selected heat-clearing and diuresis drugs such as *Phellodendri Chinensis Cortex*, *talcum* and *Arecae Semen* to eliminate damp-heat in the lower jiao. Finally, from the analysis of six meridians theory, this patient showed typical signs of both qi and yin deficiency, such as a red tongue, smooth tongue body and tip without coating, and weak and astringent pulse. Regarding yin and yang meridians, yang belongs to excess and yin belongs to deficiency, so the patient is mostly suffering from yin meridian imbalances. Furthermore, in convalescing patients, the pulmonary fibrosis changes into tangible structures, which belongs to the category of "tendon" in the five tissues of TCM and corresponds to liver. The liver meridian of TCM has an internal pathway to the lung, so poor circulation of qi and blood in the liver meridian leads to abnormal physiological function of the lung, which normally has the role of disseminating clear fluids to all meridians. In this case, weakness in lung physiology manifests as incomplete absorption of inflammatory exudate and the development of fibrosis in the lungs. Therefore, liver organ and meridian pathology is one of the causes of disease for this patient. Additional symptoms pointing to liver involvement included the patient's dry and loose stools, which are related to mixed cold and heat and stagnant liver qi. Therefore, the author selected the main prescription "Wume Fructus Pill," and modified its ingredients to offer sour and sweet flavors to nourish yin and blood, regulate cold and heat, and dredge the vessels.

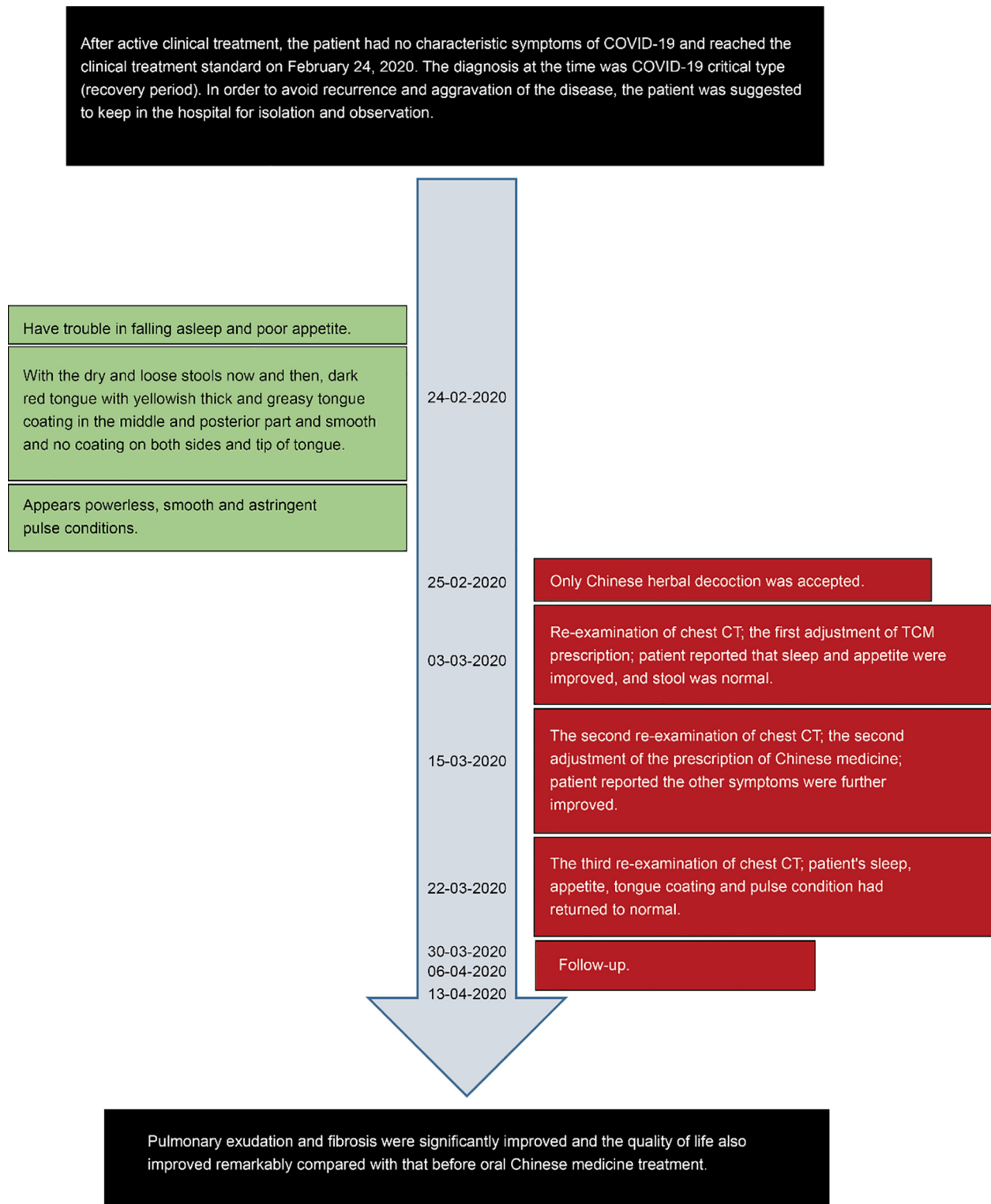


Fig. 3. The timeline of this case. CT: computed tomography; COVID-19: corona virus disease 2019; TCM: traditional Chinese medicine.

From the Western medical perspective, pulmonary fibrosis mainly refers to pulmonary diseases with pathological characteristics, such as alveolar epithelial cell and endothelial cell damage, fibroblast proliferation, excessive collagen deposition, alveolar structure degradation, large accumulation of extracellular matrix and diffuse alveolitis with various causes [15]. Many studies have shown that the pulmonary fibrosis is closely related to some cytokines. Among them, transforming growth factor- β 1 (TGF- β 1) is the key factor that promotes the activation of fibroblasts and causes irreversible lung injury [16]. Tumor necrosis factor- α (TNF- α) is an active marker of alveolar inflammation, which can promote an inflammatory reaction and the differentiation of interstitial cells, and can also interact with other cytokines, such as TGF- β 1, and jointly promote changes in pulmonary fibrosis [17–19]. Therefore, clinically, pulmonary fibrosis is often inhibited or alleviated by reducing the secretion and expression of TGF- β 1 and TNF- α in

patients. Relevant studies have clearly confirmed that most of the TCM drugs taken by the patient in this case study have pharmacological effects on pulmonary fibrosis. Among them, *Poria*, *Alismatis Rhizoma*, *Coicis Semen* and *Polygoni Cuspidati Rhizoma* can inhibit pulmonary inflammatory exudate by down-regulating the expression of TGF- β 1 and TNF- α ; they can also delay and reduce the development of pulmonary interstitial fibrosis [20,21].

To sum up, under the guidance of TCM theory and modern medical research with a long history and rich clinical experience, it is no accident to select oral treatment of TCM decoction as the main intervention method in this case, which can significantly improve the clinical trials of pulmonary insufficiency and fibrosis changes. It has certain reference value for clinical treatment of convalescent patients in COVID-19. However, it is worth noting that an oral treatment with TCM decoction needs to have the formula adjusted to address the overall symptoms and etiological characteristics of each patient. It is necessary for professional Chinese doctors to make reasonable adjustments to the prescriptions of TCM to meet the individualized treatment needs of other COVID-19 convalescent patients.

4. Conclusion

Targeted oral treatment with TCM decoction was able to effectively promote the absorption of pulmonary inflammatory exudate and to reduce pulmonary fibrosis experienced by a convalescing COVID-19 patient. This treatment plays a key role in improving the quality of life of patients and the prognosis of the disease. Compared with clinically recommended anti-pulmonary fibrosis drugs, such as pirfenidone and nidanib, which have more adverse reactions, oral administration of TCM decoction can be used as a reference drug for convalescent patients with novel coronavirus pneumonia, but the insights provided in this case report need further exploration and verification.

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Authors' contributions

NZ, QM and SY contributed to the conception of this research; NZ and QM wrote the original paper; YXQ, HC and ZGW contributed to reviewing and editing the manuscript; CHL and JZ were responsible for guiding the application and contacting the patient; YLL was responsible for preparation of herbal medicines. All authors read and approved the final version of the manuscript accepted for publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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