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Case Report
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Clinical and Pathological Features of the Cured Severe COVID-19 Patient Who Received Successful Lung Transplantation

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Abstract

Background: During the pandemic of COVID-19, lots of features of this disease have been discovered. However, the morphology and the correlated clinical changes of the patients recovered from the severe state of COVID-19 are still largely unknown. Especially for those who underwent Diffuse Alveolar Damage (DAD), morphological data were obtained from the autopsy specimens. In the present report, the pathologic changes in the lungs of a patient who had successfully received lung transplantation at the recovery stage of severe COVID-19 were described.

Methods: The male patient aged 65 years underwent severe COVID-19 and received ECMO treatment in Wuhan, 2020. After evaluating his condition, lung transplantation was performed. The morphology of his lungs was inspected.

Results: Diffuse alveolar damage, hyperplasia of interstitial fibroblast and alveolar type II epithelial cells, and the filling of macrophages in alveoli were observed. Hyperemia and thickening of blood vessels and interstitial lymphocytic inflammation were also prominent. SARS-CoV-2 nuclear capsid was detected spotty in the alveolar epithelial after several times' negative nucleic acid taking from his pharyngeal swab. Evidence of combined virus infection, such as *Cytomegalovirus*, could also be found. A few eosinophils were found in the parenchymal of the lung, which combined with the elevated eosinophils in the blood, might indicate a recovery of this patient.

Conclusion: This rare case provides a chance for us to observe the pathological changes in the diffuse fibrosis stage of severe COVID-19, which might help us to further understand how pulmonary fibrosis formation after severe pathogen infection.

Keywords: COVID-19; Lung transplantation; Diffuse pulmonary fibrosis; Lymphocytes

Abbreviations

COVID-19: Coronavirus Disease; DAD: Diffuse Alveolar Damage; ECMO: Extracorporeal Membrane Oxygenation; CT: Computerized Tomography; ICU: Intensive Care Unit; V-V ECMO: Venovenous Extracorporeal Membrane Oxygenation; MRSA: Methicillin-Resistant *Staphylococcus aureus*; EBV: Epstein-Barr Virus; CMV: *Cytomegalovirus*; CRAB: Carbapenem-Resistant *Acinetobacter baumannii*; TIA-1: a Cytotoxic Granule- Associated RNA-Binding Protein; CK: Cytokeratin; CRP: C Reaction Protein; APTT: Activated Partial Thromboplastin Time; AT II: Alveolar Type II; SMA: Smooth Muscle Actin; TTF-1: Thyroid Transcription Factor 1

Importance

Data of pathology and clinical features in the late phase of diffuse alveolar damage in lived COVID-19 patients are mostly based on autopsy. In this observation, the patient who adopted Extracorporeal Membrane Oxygenation (ECMO) during severe COVID-19 and received lung transplantation presented diffuse pulmonary damage and fibrosis. Although there were several

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similarities, diffuse pulmonary fibrosis after SARS-CoV-2 infection was different from the previous knowledgeable pulmonary fibrosis, for example, the sac-like honeycomb sign was not found in this case. There was still heavy inflammatory infiltration in the host lungs even though the immune cells in the peripheral blood were approaching the normal level at the sixth month after infection. The virus and the combination infection of other pathogens, the reactions of the immune system, and the treatments may synergistically cause the pathological processes of the lung fibrosis and related clinical presentations. To observe how the long-term pathological changes of lungs after the severe SARS-CoV-2 infection help us to understand the host reacts to the severe damage in the diffuse fibrosis stage, and to give us a hint of the mechanisms that underline the lung fibrosis after severe infection.

Background

Coronavirus disease 2019 (COVID-19) has caused massive mortality globally. Although plenty of researches have been published about the source of the pathogen, the transmission, and the clinical features of this novel infectious disease [1-3], much is still unknown about the pathogenesis, development, and long-term prognosis. Several studies reported the systemic pathological description of the severe cases in the early phase [4,5]. However, there was no report about pathological features of advanced lung fibrosis in lived patients to the best of our knowledge. In the present study, we report the clinical and pathological features of a severe case of a patient who recovered from COVID-19 after successful lung transplantation. The duration of the illness was over 180 days.

Case Presentation

Patient's clinical features

A 65-year-old male patient, who lived in Wuhan city, presented with a high fever and was admitted to the hospital on January 23rd, 2020. The highest temperature was 39.6 centigrade. He had no previous medical history of hypertension, chronic obstructive pulmonary disease, or allergic diseases. Ground-glass opacities in his lungs were later detected through a Computerized Tomography (CT). On 16th, February, he was admitted to a hospital and was transferred to the Intensive Care Unit (ICU) because of the worsening clinical indicators. On 17th, February, he received intubation and mechanical ventilation. From 18th, February, Venovenous Extracorporeal Membrane Oxygenation (V-V ECMO) was used to provide the adjunct support. During his hospitalization, he underwent multiple tests for SARS-CoV-2 nucleic acid using his throat swab specimen, anal swab specimen, and bronchoalveolar lavage. The results were all negative. However, his serum and swab specimens were tested positive for SARS-CoV-2 IgG antibodies. On 6th, February, he was tested positive for Methicillin-Resistant *Staphylococcus aureus* (MRSA) in his blood culture. Specific IgG for Epstein-Barr (EB) virus and *Cytomegalovirus* (CMV) were also found in his serum specimen. He was given a comprehensive treatment that included antibacterial, anti-fungal, antiviral, and supportive treatment. On 20th, March, he was tested as coinfection with Carbapenem-Resistant *Acinetobacter baumannii* (CRAB). On 20th, April, he was evaluated for the clinical indices and received double lung transplantation. After 92 days of rehabilitation, he made a complete recovery by 21st, July and was discharged from the hospital.

Pathological inspection

Fresh samples of both lungs of the patient were inspected immediately after resection by the Wuhan Institute of Virology, Chinese Academy of Sciences. The outcome of the test was negative for the SARS-CoV-2 live virus and nucleic acid (data not shown). For pathologic inspection, each lung lobe was sampled for 4 to 6 blocks after fixing with 10% neutral formalin for at least 72 h. Routine hematoxylin-eosin staining and immunohistochemistry were performed. The antibodies against CD3, CD4, CD8, CD20, CD56, CD68, CD163, TIA-1, Granzyme B, TTF-1, CK, and P40 were purchased from Zhongshan golden bridge Biotechnology, Beijing. Antibodies against PD-1, PD-L1 (Dako 22c3), *Cytomegalovirus*, and EBER RNA CISH Probe were purchased from Agilent Technologies, Inc. Antibody against SARS-CoV-2 nucleocapsid protein was purchased from Abcam Public Limited Company, MA, USA. Immunohistochemistry was performed with the Bond-max automated Immunohistochemistry instrument (Leika Biosystems, U.S.) following the manufacturer's instruction.

Laboratory findings

The dynamic laboratory results prior to and post lung transplantation are listed in Table 1. Before transplantation, his peripheral white blood cells were elevated. Detailed analysis showed an increase in neutrophils and eosinophils, while the lymphocyte count was close to the lower limit of the normal reference in the peripheral blood. Amongst the subsets of lymphocytes, the T lymphocyte value was close to the lower limit of the normal range before transplantation. After transplantation and long-term treatment, the number of neutrophils dropped to the normal range, while the eosinophils were slightly higher than normal. He presented with lymphocytopenia before discharging from the hospital, while the counts of subgroups of T lymphocytes were even lower than those before the transplantation. At the same time, the values of C Reaction Protein (CRP) and hypersensitivity CRP were significantly higher than normal before and after the transplantation. In the humoral immunity, only complement C3 had a lower value than the normal range before and after transplantation, while other biochemical parameters showed at normal ranges. The coagulation function was also evaluated. Prothrombin time was slightly longer than the normal

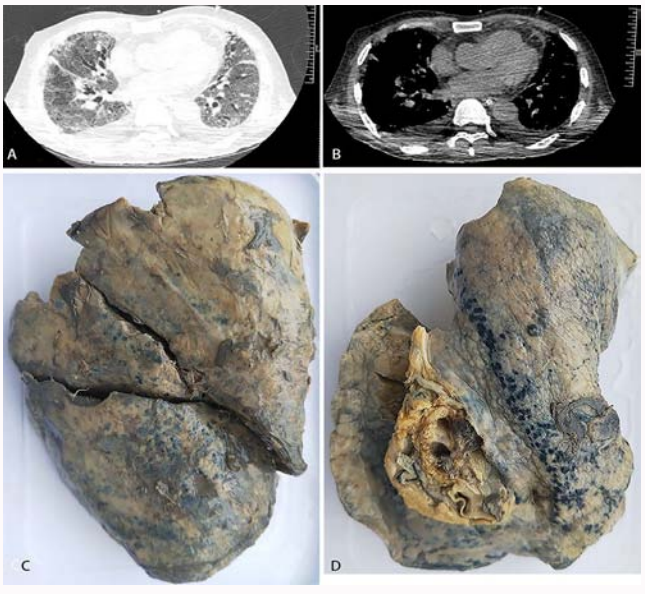

Figure 1: A&B. The lung window (A) and mediastinal window (B) of CT showed diffused fibrosis of both lungs. C&D showed decreased size of right (C) and left (D) lungs.

Table 1: Laboratory findings prior and post lung transplantation.

Date	04/17/20	04/22/20	04/24/20	06/16/20	07/11/20	07/20/20
White blood cell (3.5-9.5 × 10^9/L)	12.8	24.58	36.87	20.4	4.9	5.2
Neutrophils (1.8-6.3 × 10^9/L)	8.52	23.21	34.14	17.08	4.17	3.55
Eosinophils (0.02-0.52 × 10^9/L)	2.15	0.02	1.37	0.01	0.28	0.87
Lymphocytes (1.1-3.2 × 10^9/L)	1.16	0.52	0.98	0.44	0.27	0.57
Hypersensitivity CRP (0-3 mg/L)	>5	>5	>5	>5	N/A	N/A
C reaction protein (0-5 mg/L)	49.5	26	68.8	27.9	24.4	37
Prothrombin time (9-13 S)	13.9	15	13.7	13.9	18.4	13.9
APTT (S) (25-31.3s)	78.1	32.9	35.8	37.2	39.8	41.6
FIBRIN (2-4 g/L)	2.98	1.51	1.91	1.85	0.63	1.63
AT III (80-120%)	44.10%	44.40%	40.10%	50.20%	50.20%	48.30%
D-dimer (0-0.55 mg/L)	11.76	5.35	7.22	3.57	8.2	10.91
Evidence for infection						
Nucleic acid for SARS-CoV-2	negative	negative	negative	negative	negative	negative
Tissue culture for other pathogens	N/A	N/A	N/A	ABA	negative	negative
Subgroups of lymphocytes						
CD3 (727-2737 count/uL)	806	378	613	283	243	334
CD4 (404-1612 count/uL)	510	256	429	153	129	124
CD8 (220-1129 count/uL)	310	122	196	136	112	212
CD4/CD8 (0.9-2.0)	1.65	2.09	2.19	1.13	1.16	0.58
CD19 (80-616 count/uL)	49	37	77	36	8	12
CD56 (84-724 count/uL)	180	47	69	66	94	88
Humoral immunity						
IgG (8-16 g/L)	7.35	7.95	12.8	15.5	7.45	11
IgM (0.4-3.45 g/L)	0.561	0.646	0.849	0.593	0.774	0.895
IgA (0.76-3.9 g/L)	0.975	1.34	1.44	0.803	0.96	0.8
IgE (<100 IU/mL)	55.6	88.7	132	21.2	32.4	18.8
Complement C3 (0.81-1.6 g/L)	0.667	0.286	0.418	0.454	0.621	0.55
Complement C4 (0.1-0.4 g/L)	0.207	<0.067	0.091	0.169	0.184	0.163

Abbreviations: ABA: *Acinetobacter baumannii*, APTT: Activated Partial Thromboplastin Time, CRP: C-Reaction Protein

reference, while Activated Partial Thromboplastin Time (APTT), fibrin, and D-dimer showed higher values than normal.

Pathological findings and ancillary tests

CT images of the lungs showed ground-glass opacities, septal thickening, and traction bronchiectasis which indicated diffuse fibrosis in both lungs (Figure 1A, 1B). The gross inspection showed shrunken lungs with characteristic stiffness and a tinge of yellow color (Figure 1C, 1D). Microscopically, the lungs exhibited Diffuse Alveolar Damage (DAD) and a fibrotic nonspecific interstitial pneumonia pattern, i.e., diffuse involvement of the alveolar walls with thickening, fusion, and simplification [6]. Dense collagen and fibers were diffusely distributed in the septa of alveoli (Figure 2A, 2B). Some alveoli collapsed and massive inflammatory cells were observed in the interstitium. Prominent empyema in small bronchia was detected but not much purulent exudate was collected in the alveolar space. In the regions near the pleura, there was hyperplasia of fibroblasts and small blood vessels, while the newly formed fibers constituted the fascicles and divided the lung parenchyma into several small lobules (Figure 2A). In some regions, hyperemia and intra-alveolar bleeding were evident (Figure 2B). In this case, neither was the fibrinoid exudate in the alveoli nor was the hyaline membrane identified, unlike the previously reported cases in the acute phase. Only a few intra-alveolar fibroblast nodules were found (Figure 2C). The epithelial cells are desquamated from the alveolar wall. Hyperplasia of alveolar type II (ATII) epithelial cells and metaplasia of the bronchial epithelial cells were also noted. Some alveolar spaces were filled with mucous plugs (Figure 2D). The walls of small blood vessels were significantly thickened. The expanded intima of small blood vessels could be identified by elastic staining (Figure 2E). Not only were the clusters of alveolar epithelia that underwent atypical hyperplasia seen (Figure 2F), but pulmonary bulla at the margin of the lungs was also observed (Figure 2G). Various amounts of lymphocytes, eosinophils, and histiocytes infiltrated the interstitial tissue. Most of the inflammatory cells were surrounding small blood vessels. There were a few lymphoid follicles formed near the bronchia. Some of the remaining alveoli were filled with macrophages along with the desquamated alveolar epithelium. A few intranuclear inclusions were identified and proven by the immunohistochemistry staining for *Cytomegalovirus* (CMV) (Figure 2H, 2I). The SARS-CoV-2 nucleocapsid protein was detected positive in the epithelial cells of a few alveoli and bronchia (Figure 2J). Immunohistochemistry staining showed that SMA was expressed in the interstitium of the lungs (Figure 3A, 3B), which indicated the hyperplasia of fibroblasts. CD163+ macrophages were distributed in both the interstitium and in some alveolar spaces (Figure 3C). The

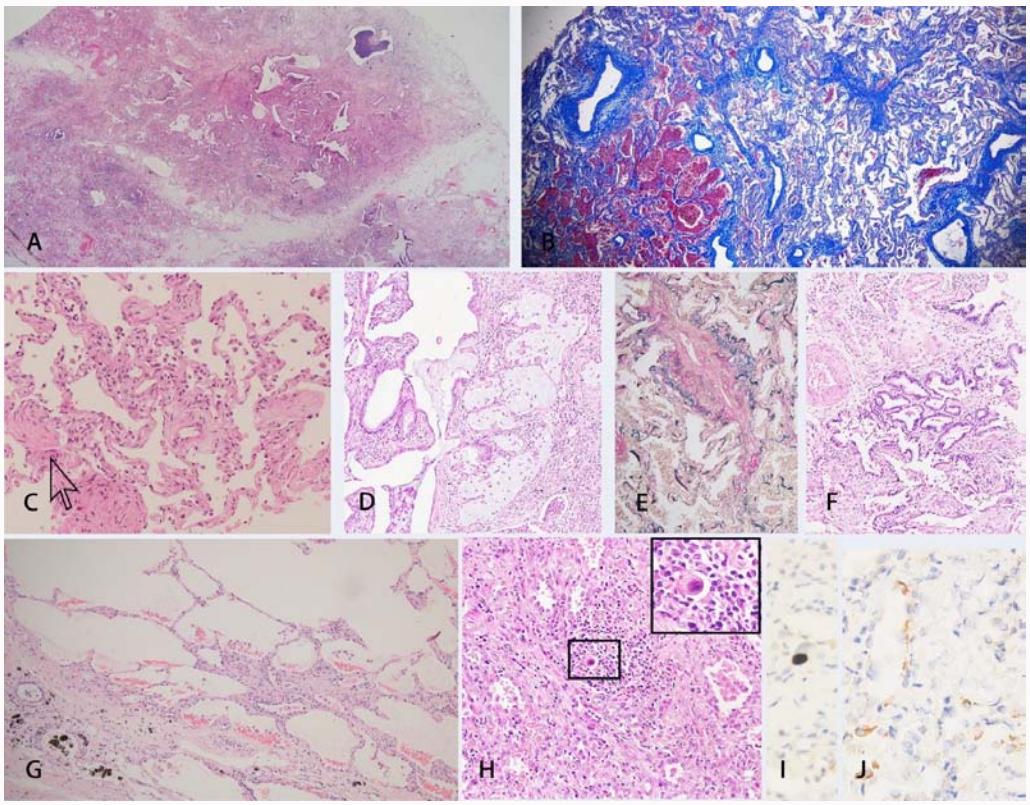

Figure 2: H&E staining of the lungs showed diffused damage and inflammation. A. Collagens extended from the pleura to the parenchyma of the lung, which separated lung parenchyma into several lobules. B. Masson trichrome staining showed the diffusely distributed fibers in the mesenchyme. C. Intra-alveolar fibroblast nodules could be scarcely found (indicated by the arrow). D. Intra-alveolar mucus plug could be found. E. Elastic fibers staining showed the thickened intima of the blood vessel wall. F. There was a cluster of alveolar epithelia undergoing atypical intra-epithelial hyperplasia (AIH). G. Bullae of the lung was shown under the pleura. H. An intranuclear inclusion body was showed in the background of diffuse inflammation and was amplified in the inserted right upper rectangle. I. Immunohistochemistry showed a cell-infected *Cytomegalovirus* (CMV). J. The SARS-CoV-2 nucleocapsid protein was detected in the epithelial of a few alveoli by immunohistochemistry staining.

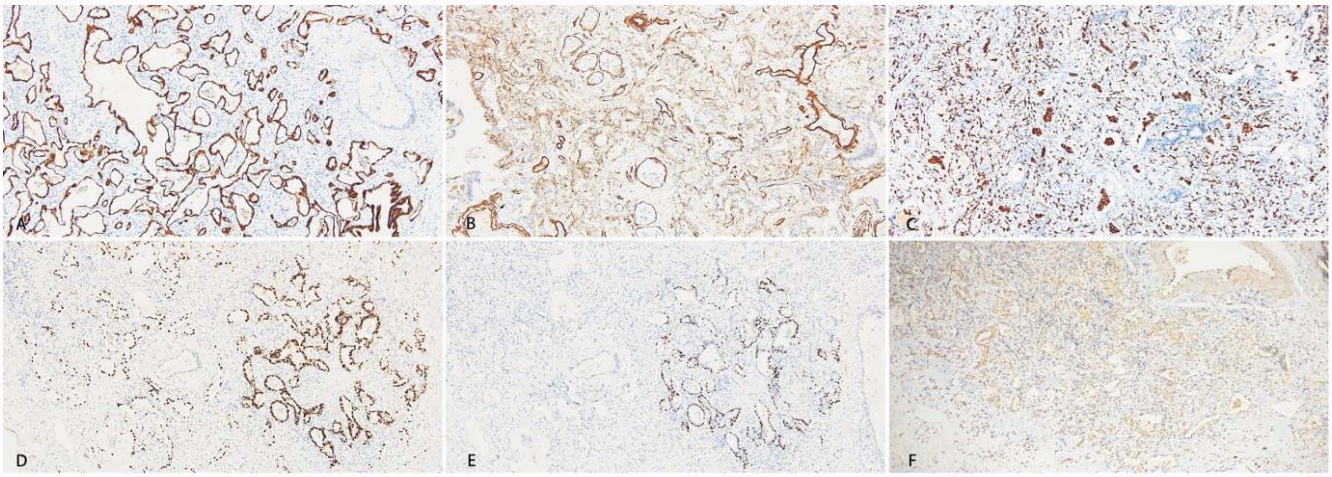

Figure 3: A. Immunohistochemistry staining of Cytokeratin (CK) depicted the epithelial of alveoli and bronchus. B. Smooth Muscle Actin (SMA) showed hyperplasia of interstitial fibroblasts. C. Intra-alveoli and interstitial distribution of CD163 positive macrophages. D. Thyroid Transcription Factor-1 (TTF-1) showed the hyperplasia of Alveolar Epithelial II (AT-II). E. The staining of the squamous epithelial marker, P40, showed a cluster of alveoli that underwent squamous metaplasia. F. Diffuse expression of IL-6 indicated a heavy inflammation.

co-expression of P40, which is the marker of squamous epithelia, and ATII epithelial marker TTF-1, proved the metaplasia of squamous epithelium in several alveoli (Figure 3D, 3E). Inflammatory cytokines such as IL-6 (Figure 3F), IFN-γ, and IL-17 (data not shown) showed diffused distribution in the parenchyma of the lungs. Additional immunohistochemistry staining was performed to further delineate the infiltrated inflammatory cells. Most of the lymphocytes that infiltrated the septa of alveoli were CD3+ T lymphocytes (Figure 4A), and a few CD20+ B lymphocytes were scattered in the lymphoid follicles (Figure 4D). The ratio of CD4+ T lymphocytes to CD8+ T

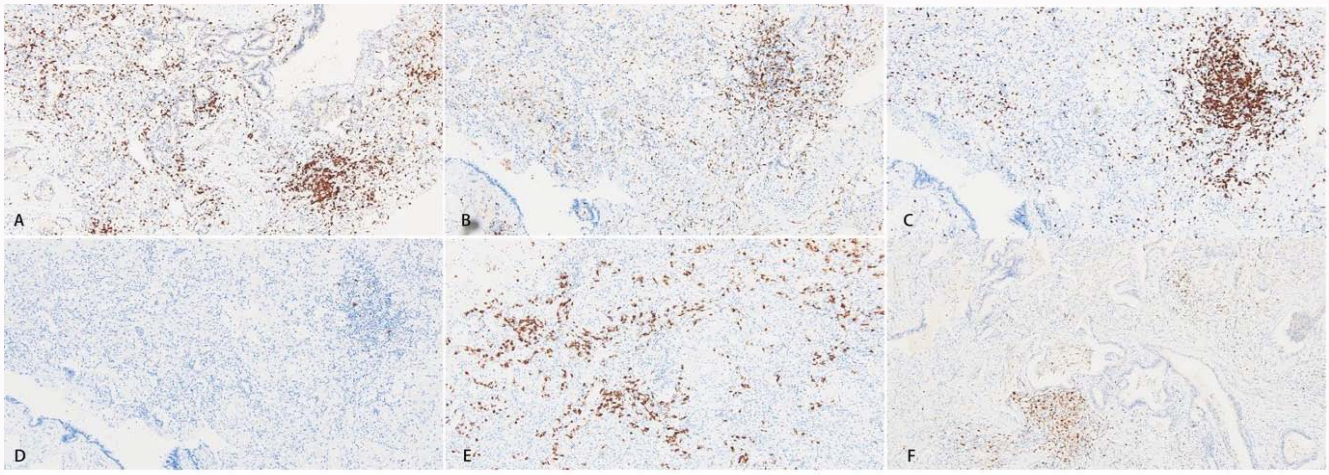

Figure 4: Immunohistochemistry staining for the inflammatory cells in the lungs. A. Diffusely distributed CD3+ T lymphocytes were identified. B&C. CD4+ T lymphocytes (B) were lesser than CD8+ T lymphocytes (C) in the interstitium of the lung. D. CD20+ B lymphocytes were hardly found in the lung. E. CD38+ plasma cells were scattered in the interstitium of the lung. F. Cytotoxic cytokine, granzyme B, was identified in the region near small bronchia.

lymphocytes was between 1:1 to 1:2 (Figure 4B, 4C). There were also CD38+ plasma cells distributed along with parts of the interstitium of the alveoli (Figure 4E). Other inflammatory cells that were scarcely observed in the interstitium were CD56+ NK/T cell, and CD25+ regulatory T cells (data not shown). Cytotoxic molecules, such as Granzyme B was majorly distributed adjacent to the bronchia and alveoli (Figure 4F). While T cell Intracytoplasmic Antigen -1 (TIA-1) was sparsely expressed in the interstitial immune cells. The Programmed cell Death-1 (PD-1) and PD-L1 were sparsely expressed on lymphocytes and epithelial cells of the alveoli (data not shown).

Discussion and Conclusion

Previous reports about pulmonary pathology of SARS-CoV-2 infection encompasses congestion in small blood vessels, hyaline degeneration, fibrinous exudation in the alveoli, as well as the infiltration of T lymphocytes, neutrophils, and eosinophils in the interstitium [5,7-10]. Most of these reports were obtained from the autopsies conducted on the patients who died in the acute phase. Reports regarding the pathological and clinical features of the diffuse fibrosis stage after the SARS-CoV-2 infection were scarce. Although a transplanted case in severe COVID-19 was reported, the major morphology of that case also showed diffuse alveolar damage and early fibrosis but not late-stage fibrosis [11]. In Severe Acute Respiratory Syndrome (SARS), a long-term follow-up showed that a minority of the patients reported lung fibrosis [12], while in the Middle East Respiratory Syndrome (MERS), 33% of the patients reported lung fibrosis [13]. However, this coronavirus-related lung fibrosis was investigated in patients with mild presentations during the infection since most of the severe patients died through the acute pulmonary injury caused by the viruses. To check whether mild cases of COVID-19 develop into lung fibrosis in the long run still requires a long-term follow-up and large-scale investigation. In the present case, the patient lived through DAD and diffused fibrosis since the application of ECMO and successful lung transplantation. This case provided us an opportunity to discover the pathology of whole lungs that underwent persistent responses after coronavirus infection, which provided us precious data on lung repair in severe damage, and its correlation with the patient's clinical presentations. In the present case, we observed dense diffuse fibrosis, hyperplasia of AT-II cells, and metaplasia of squamous epithelium in the alveolar epithelial, thickening of blood vessel walls, and a massive inflammation in the interstitium of the lungs. Histologically, the pattern of fibrosis in the present COVID-19 case was similar to Idiopathic Pulmonary Fibrosis (IPF). However, IPF is a chronic disease that presents with fibroblast foci, patches of interstitial fibrosis, and cystic spaces with bronchial metaplasia (honeycomb fibrosis). It appears in patches initially, and then the lesions fuse in decades [6]. In the present case, the formation of diffuse lung fibrosis came up in only several months, which progressed significantly faster than IPF. The interstitial inflammation and diffused fibrosis were prominent, while there were no findings of typical honeycomb fibrosis in the present case. Coronavirus infection and the correlated DAD could be at least one of the reasons that caused the excessive inflammation and fibrous repair [5,14]. It was also reported that several reasons correlated with lung fibrosis, such as the nature of lung injuries, immune regulations, and genetic abnormalities, etc. [15]. In this case, the inflammation and necrosis caused by co-infection of bacteria could not be ignored because bacterial sepsis might not only destroy the structure of alveolar walls but also the cause of fibrotic repair [17]. Furthermore, the application of mechanical ventilation, ECMO [18], and the usage of some medications such as corticosteroids and immune regulators should also be considered as the factors that accelerate lung fibrosis. The fibrosis after coronavirus infection is most probably post-inflammatory fibrosis, which is different from IPF [16]. Even after 6 months, the inflammatory infiltration throughout the lung was still prominent, corresponded to his elevated peripheral white blood cells, and indicated a general mobilization of the immune system to cope with the virus and to promote lung reparation and fibrosis. According to the humoral and cellular immunity reports in COVID-19 patients [19], the sepsis caused by the virus might cause an imbalance of immune cells, especially the decrease of lymphocytes in peripheral blood [20]. The most popular hypothesis for hypolymphemia in COVID-19 patients was the redistribution of lymphocytes to the infected areas or the destruction of lymphocytes. Indeed, we observed that the infiltrated inflammatory cells were majorly lymphocytes, eosinophils, and monocyte- macrophages. There were a few lymph follicles which consisted of dominantly CD3+ T cells and a small portion of CD20+ B lymphocytes. Actually, there were scarce CD20+ B cells in his whole lungs, which indicated that in the repair stage after coronavirus infection, CD3+ T lymphocytes played a more important

role. Previous reports stated the absence or scarce presence of CD4+ T lymphocytes in the early stages of COVID-19 [21]. However, in the present case, we found that although the ratio of CD4/CD8 T lymphocytes was lower than 1:1, it was close to the ratio in the blood. This seemed to indicate a recovery of the immune system. In the acute phase, the expression of the chronic exhausting marker PD-1 in peripheral lymphocytes was prominent [22]. However, in the present case, it was scarcely detected in the inflammatory cells, which might be another indicator of immune system recovery. The plasma cells were antibody-producing resources, as well as an indicator of chronic inflammation. Whether the diffuse distribution of plasma cells indicated the possibility of SARS-CoV-2 neutralizing antibody secretion in the lung still needs further investigation. Since the patient was also infected with CRAB at the time of transplantation, the inflammation in his lung could be also part of a result of the CRAB septicopyemia. Although there were reports about neutrophils causing lung fibrosis [21], however, we didn't find prominent abscess formation and the neutrophil infiltration was poorly presented in his lung. This patient neither had any history of allergies nor did he report any previous history of chronic inflammatory diseases or auto-immune diseases. An enormous rise in eosinophils was observed in his peripheral blood and lung parenchyma. Since he was in a state of CRAB septicopyemia during lung transplantation, the myeloid cells might have been largely recruited and mobilized from the bone marrow and the abnormal infiltration of eosinophils might still play a role in the virus-induced hyperimmune responses. Indeed, we also found an abnormal increase of IgE and hyperimmune C Response Protein (CRP) in his peripheral blood. Both of these indicators along with eosinophil elevation was also seen in patients with allergies. In CRAB bacterial infection, we did not find such an increment in eosinophil count to the best of our knowledge. During the onset and early phase in the COVID-19 patients, the eosinophil count in the peripheral blood dipped lower than the lowest threshold of the normal range [23-25]. A study reported that a decrease in the eosinophil count in the peripheral blood was accompanied by the SARS-CoV-2 infection, however, a rise in eosinophil count was observed in the recovery stage [26]. Eosinophils were detected in the lungs of the autopsy specimens in both acute and recovered patients [10]. In the present case, after the transplantation, the eosinophil counts gradually tended to become normal. Taken together, the eosinophil count was thought to act as an indicator and a prognostic predictor of COVID-19. The detailed mechanism still requires more investigation. It was reported that the lung repair caused by SARS-CoV-2 infection and damages presented as a proliferation of blood vessels, vascular congestion, and thickening of the blood vessel walls. In the autopsy reports of COVID-19 patients, diffuse thrombi and endothelialitis were detected in the lungs [27]. However, in this case, the thrombi and endothelialitis were not discovered, and this is corresponding to the changing process of his prothrombin time (Table 1). Instead, diffused thickened blood vessel walls were prominent, which was agreed with the previous reports [28]. These changes indicated that the injured blood vessels underwent repair after the virus clearance, which in turn might cause pulmonary hypertension and may contribute to the endothelial transition to mesenchymal in the long run. Both thickened blood vessels and pulmonary hypertension could also be found in IPF [28]. The present patient was on his fourth-month clinical cause when he accepted the lung transplantation. Repeated nucleic acid detections showed negative results in his different specimens. However, the SARS-CoV-2 nucleocapsid protein was still spot stained in the epithelium of alveoli. In general, the duration of the existence of the virus nucleic acid in nasopharyngeal/oropharyngeal swabs is 14 to 63 days according to a clinical investigation [29]. There were also isolated reports about positive virus nucleic acid in recovered patients who were tested negative several times [29-33]. Whether the "re-positive" in the previous reports was caused by the second infection or the relapse of the remaining virus, is still unclear. Since there was no more new local infection of SARS-CoV-2 in the city of Wuhan when the patient was undergone lung transplantation, our result might serve as evidence for the long-term existence of the virus or protein of the virus *in vivo*. Although this patient was treated for over three months, there can still be a presence of a few viruses. There is no specific medicine for eliminating SARS-CoV-2 *in vivo* up till now. However, the presence of the virus protein might be evidence of the sustained viral infection. Several specimen detections for the virus nucleic acid turned out to be negative, which meant the least chance for the existence of any active replicating virus. On the other hand, IHC should be explained with caution to exclude the over-reactivity of the antibodies with other antigens or the random nonspecific signals. However, in this case, the spot expression of the virus capsid protein was found only on a few epithelial cells of alveoli and bronchus, which was the specific site of infection for the virus and was unlikely an unspecific signal. The IHC result might also be speculated as a viral protein capsule but no live virus. This speculation explained the reason for the negative result for nucleic acid but a positive result for IHC. However, no matter what the status was for this patient, he had a clinical virus clearance when he accepted the lung transplantation. SARS-CoV-2 causes DAD in severe cases of COVID-19, which is lethal to most patients. We cannot conclude that this patient showed the typical lung pathology of late-stage COVID-19, but the features of this case, together with other reports will help us to understand more clear nature of lung repair after severe infection of SARS-CoV-2 and might shed a light on the researching of mechanisms of lung fibrosis after organism infection.

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