

CT imaging findings and clinical correlation analysis of different clinical types of novel coronavirus pneumonia

G. Wang¹, X. Zheng¹, Y. Zou^{1*}, H. Xie¹, H. Wen¹, F. Yu¹, H. Yuan¹, H. Du¹, Y. Liao²

¹Department of Radiology, Affiliated Dongguan People's Hospital, Southern Medical University, Dongguan 523059, China

²GE Healthcare, Guangzhou 510623, China

ABSTRACT

► Original article

***Corresponding author:**

Yujian Zou, Ph.D.,

E-mail: zouyujian@sohu.com

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Background: To deepen the understanding of COVID-19 and provide a theoretical basis for clinical diagnosis and treatment, the clinical manifestations, laboratory test findings and chest computed tomography (CT) signs of this disease and the correlations among them were explored in this study. **Materials and Methods:** A total of 85 patients with confirmed cases of COVID-19 were included, and their disease courses, symptoms and laboratory test results were recorded. **Results:** The main characteristics of COVID-19 infection were fever (56 cases), respiratory symptoms (47 cases), normal or decreased white blood cell count (84 cases), decreased lymphocyte count (43 cases), and increased C-reactive protein (CRP) level (37 cases). There was a positive correlation between fever and each of white blood cell count, lymphocyte count, and CRP level ($P < 0.05$). Age, disease course, fever, lymphocyte count, CRP level and CT findings were statistically correlated. In the CT-positive group, the lesions were often multiple (57 cases) and peripherally distributed (53 cases). The main manifestations included ground-glass density shadows (61 cases), grid-like changes (47 cases), abnormal pleural changes (53 cases), abnormal blood vessels (52 cases) and bronchial abnormalities (40 cases). **Conclusion:** Mild and common COVID-19 cases have certain characteristics, clinical manifestations and laboratory parameters are correlated with CT manifestations. The comprehensive diagnosis according to clinical manifestations, laboratory and CT characteristics can minimize the missed diagnosis rate.

INTRODUCTION

Novel coronavirus pneumonia, a newly discovered highly infectious disease, was named "COVID-19" by the World Health Organization (WHO) on February 11, 2020. From December 2019 to February 2020, in just over 3 months, an outbreak of COVID-19 occurred in many countries and regions around the world. It is essential to fully recognize the severity of the epidemic and study the disease. The outbreak period of COVID-19 is short, the virus mutates quickly, and the spread of some mutant viruses has increased. Due to the short outbreak time of this disease, the understanding of the disease is still continuously expanding⁽¹⁻⁴⁾.

According to the literature, the novel coronavirus belongs to the *Beta coronavirus* (β -CoV) genus of coronaviruses, has an envelope and has a diameter of 60~140 nm⁽¹⁻⁴⁾. The spike protein (S), one of the five essential genes, enters the host cell by binding to the angiotensin-converting-enzyme 2 (ACE2) receptor, causing local and systemic inflammation, oxidative stress and other reactions⁽⁵⁻⁷⁾. ACE2 is widely expressed in all tissues of the human body and is

most abundant in alveolar epithelium, small intestinal epithelium and vascular endothelium⁽⁵⁻⁷⁾. Therefore, the disease mainly affects the respiratory system, but multiple systems, such as the digestive system, cardiovascular system, and central nervous system, can be affected⁽⁵⁻⁷⁾. Although there are typical clinical symptoms and laboratory and CT signs of this disease, many atypical cases with complex manifestations occur⁽⁸⁻¹¹⁾. The main clinical symptoms are respiratory symptoms, such as fever, dry cough, and sore throat; other symptoms include fatigue, decreased or lost sense of smell (taste), nasal congestion, runny nose, conjunctivitis, myalgia, and diarrhea⁽⁴⁻⁷⁾. Children's symptoms are mild and may be more atypical; children may show only show shortness of breath or poor response⁽⁴⁻⁷⁾.

In the COVID-19-confirmed population, some asymptomatic infections exist; individuals may have abnormal CT findings but no clinical manifestations⁽⁸⁻¹⁰⁾. Therefore, epidemiological history combined with CT examination is particularly important for identifying asymptomatic infections⁽¹¹⁻¹³⁾. Practice has shown that the CT screening response is fast and convenient. CT screening is an important measure for

epidemic prevention and control, and it has high screening value for viral pneumonia⁽¹⁴⁻¹⁵⁾. Furthermore, some patients have clinical symptoms but show no obvious abnormalities on laboratory or CT examination. These mismatches between clinical or laboratory examinations and imaging results have hindered the early diagnosis and treatment of the disease, disease classification, the evaluation of treatment efficacy and follow-up, and decisions release from quarantine.

Are there correlations among the clinical manifestations of COVID-19 patients, laboratory examinations, and chest CT findings? It is important to identify the associations. Therefore, in the present study, data from 85 confirmed cases of COVID-19 were collected, and a retrospective analysis was performed, summarizing the clinical manifestations, laboratory examination results, and chest CT characteristics of the patients. The purpose was to deepen the understanding of the disease and explore the correlations among the clinical, laboratory examination and chest CT manifestations of the disease. The results are expected to help guide clinical disease diagnosis, the evaluation of treatment efficacy, and follow-up and provide a theoretical basis for clinical diagnosis and treatment. This is also the innovative point of this article.

MATERIALS AND METHODS

Patients

Ethical approval from the institutional review boards was obtained for this retrospective study, and the need to obtain informed consent was waived (KYKT2020-019, March 1, 2020). A total of 85 patients admitted to hospitals between January 1 and March 1, 2020, with COVID-19 confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) were enrolled. Routine blood tests, CRP measurements and chest CT scans were performed. All cases were traceable to a clear source of infection and divided into mild and common types. According to the CT findings, the patients were divided into two groups: a CT-negative group with no pneumonia and a CT-positive group with pneumonia⁽¹⁻²⁾.

CT examination

Non-contrast-enhanced chest CT imaging was performed with a 16-slice CT scanner (GE Optima 520, GE Healthcare, USA) in a designated computer room with personnel protection and equipment and environment disinfection⁽⁴⁻⁵⁾. The patient was positioned in a supine position and held his or her breath during acquisition, which ranged from the thoracic inlet to the diaphragmatic level. The main scanning parameters were as follows: tube voltage =120 kVp, automatic tube current modulation (50-

350 mAs), slice thickness =1.25 mm, and slice pitch =1.25 mm.

Clinical and laboratory data

The time of onset and symptoms were recorded at the time of admission to hospital, and hematology laboratory examination and CT examination were performed within 24 hours after treatment. We recorded the onset time (disease course) and symptoms (including fever, respiratory symptoms and other symptoms) of each patient. According to the normal/increase/decrease classification, the counts of white blood cells, neutrophils, and lymphocytes and the CRP level of each patient were recorded.

CT image characteristics

We recorded the number (single / multiple), distribution (peripheral / nonperipheral / mixed), boundary status (clear/blurred/partially clear), and density (uniform/heterogeneous) of lesions. The following signs were recorded: ground-glass opacity, reticular changes, subpleural line, interlobular septal thickening, honeycomb changes, bronchial abnormalities, vascular abnormalities, blurring, acinar nodules, dendritic signs, consolidation, striping, pleural abnormalities, and pleural effusion. The specific morphologies of abnormal bronchial, vascular and pleural structures were recorded.

The completed images were uploaded to a picture and archiving communication system (PACS). All images were viewed on both lung (width, 1250 HU; level, -600 HU) and mediastinal (width, 250 HU; level, 40 HU) settings. Image evaluation was performed by two senior CT diagnosticians. Discrepancies in their evaluations were resolved through joint discussion with a third senior doctor.

Statistical analysis

Statistical analysis was performed using R software (version: 3.6.0, <http://r-project.org/>). Continuous variables are presented as the mean \pm standard deviation, and categorical variables are reported as counts and percentages. To evaluate the differences in characteristics between the CT-positive group and the CT-negative group, a t-test was used for continuous variables, and a chi square test or corrected chi-square test was used for categorical variables. Kendall's tau-b correlation analysis was used to analyze the correlations between clinical characteristics and laboratory test parameters. $P < 0.05$ was considered statistically significant.

RESULTS

Statistics of characteristics

Eighty-five patients with confirmed cases of COVID-19, aged 3~79 years and an average age of

37.89 ± 18.31 years, were included (table 1). There were 48 males, accounting for 56.5% of the patients, and 37 females, accounting for 43.5%. The mean disease course was 3.28 ± 2.25 days. Of the 85 patients, 56 patients (65.88%) had fever symptoms, 47 patients (55.29%) had respiratory symptoms, 33 patients (38.82%) had both fever and respiratory symptoms, 19 patients (22.35%) had other symptoms, and 11 patients (12.94%) had no symptoms.

Among the patients, 64 and 21 patients were in the CT-positive group and CT-negative group, respectively. Patients in the CT-positive group had a higher age ($P < 0.001$) and longer disease course ($p=0.004$) than those in the CT-negative group. The percentages of patients with fever ($P<0.001$) and both fever and respiratory symptoms ($p=0.008$) were higher in the CT-positive group than in the CT-negative group. There was no significant difference in the other factors, including sex ($P=0.563$), presence of respiratory symptoms ($P=0.844$), presence of other symptoms ($P=0.627$) and presence of no symptoms ($P=0.182$).

Table 1. Statistics on the clinical characteristics of CT-positive and CT-negative patients.

Characteristic	All patients (N=85)	CT-positive patients (N = 64)	CT-negative patients (N = 21)	Statistic value	P value
Age (years)	37.89±18.31	42.55 ± 16.28	23.71 ± 17.11	-4.54 ^a	<0.001
Disease course (days)	3.28±2.25	3.61 ± 2.37	2.29 ± 1.49	-3.01 ^a	0.004
Gender (N)				0.34 ^b	0.563
Male	48 (56.47%)	35 (54.69%)	13 (61.90%)		
Female	37 (43.53%)	29 (45.31%)	8 (38.10%)		
Fever (N)	56 (65.88%)	52 (81.25%)	4 (19.05%)	27.22 ^b	<0.001
Respiratory symptoms (N)	47 (55.29%)	35 (54.69%)	12 (57.14%)	0.04 ^b	0.844
Fever and respiratory symptoms (N)	33 (38.82%)	30 (46.88%)	3 (14.29%)	7.07 ^b	0.008
Other symptoms (N)	19 (22.35%)	13 (20.31%)	6 (28.57%)	0.24 ^c	0.627
No symptoms (N)	11 (12.94%)	6 (9.38%)	5 (23.81%)	1.78 ^b	0.182

N: number; ^a: t-test; ^b: chi-square test; ^c: corrected chi-square test; $p<0.05$ was considered statistically significant.

There were 56 (65.88%), 71 (83.53%), 41 (48.24%) and 48 (56.47%) patients with normal values of white blood cell count, neutrophil count, lymphocyte count and CRP level, respectively. There were 28 (32.94%), 10 (11.76%), and 43 (50.59%) patients with decreased white blood cell count, neutrophil count, and lymphocyte count, respectively, and 37 (43.53%) patients with increased CRP level. The combination of a decreased or normal white blood cell count and a decreased lymphocyte count was designated Combination 1. The combination of a

decreased or normal white blood cell count, decreased lymphocyte count and increased CRP level was designated Combination 2. There were 42 (49.41%) and 32 (37.65%) patients with Combination 1 and Combination 2, respectively. Lymphocyte count, CRP level, the number of patients with Combination 1 and the number of patients with Combination 2 were significantly different between the CT-positive group and the CT-negative group ($P=0.001$, $P=0.001$, $P<0.001$ and $P=0.002$, respectively).

Table 2. Statistics on the laboratory test characteristics of CT-positive and CT-negative patients.

Characteristic	All patients (N = 85)	CT-positive patients (N = 64)	CT-negative patients (N = 21)	Statistic value	P value
White blood cell count				0.749	0.454
Normal	56 (65.88%)	40 (62.50%)	16 (76.19%)		
Decreased	28 (32.94%)	23 (35.94%)	5 (23.81%)		
Increased	1 (1.18%)	1 (1.56%)	0 (0.00%)		
Neutrophil count				-1.009	0.313
Normal	71 (83.53%)	54 (84.38%)	17 (80.95%)		
Decreased	10 (11.76%)	6 (9.38%)	4 (19.05%)		
Increased	4 (4.71%)	4 (6.25%)	0 (0.00%)		
Lymphocyte count				3.424	0.001
Normal	41 (48.24%)	24 (37.50%)	17 (80.95%)		
Decreased	43 (50.59%)	40 (62.50%)	3 (14.29%)		
Increased	1 (1.18%)	0 (0.00%)	1 (4.76%)		
CRP level				-3.092	0.001
Normal	48 (56.47%)	29 (45.31%)	19 (90.48%)		
Decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)		
Increased	37 (43.53%)	35 (54.69%)	2 (9.52%)		
Combination 1				14.705	<0.001
With	43 (50.59%)	40 (62.50%)	3 (14.29%)		
Without	42 (49.41%)	24 (37.50%)	18 (85.71%)		
Combination 2				9.397	0.002
With	32 (37.65%)	30 (46.88%)	2 (9.52%)		
Without	53 (62.35%)	34 (53.12%)	19 (90.48%)		

N: number; CRP: C-reactive protein.
Combination 1: Decreased or normal white blood cell count plus decreased lymphocyte count. Combination 2: Decreased or normal white blood cell count, decreased lymphocyte count and increased CRP level. All test *statistic* values and *p* values were obtained by chi-square test or corrected chi-square test; $p<0.05$ was considered statistically significant.

Correlation analysis

Figure 1 shows the correlations between clinical characteristics and laboratory test characteristics. Lymphocyte count, CRP level, Combination 1 and Combination 2 had weak correlations with age

(tau-b=-0.29, 0.28, 0.27 and 0.2, respectively; all P<0.05). There was a weak negative correlation between Combination 1 and sex (tau-b=-0.22, P<0.05). All laboratory test characteristics except neutrophil count had strong correlations with the presence of fever and the presence of both fever and respiratory symptoms. Neutrophil count, CRP level and Combination 2 had weak positive correlations with the presence of respiratory symptoms. Neither the laboratory test characteristics nor the other symptoms was correlated with disease course.

Regarding clinical characteristics, disease course and the presence of both fever and respiratory symptoms were weakly negatively correlated with the CT group (tau-b=0.25 and 0.29, respectively; all P<0.05). Both age and fever were strongly correlated with the CT group (tau-b = 0.37 and 0.57, respectively; all P<0.05).

All of the laboratory test characteristics except white blood cell count and neutrophil count had strong correlations with membership in the CT group.

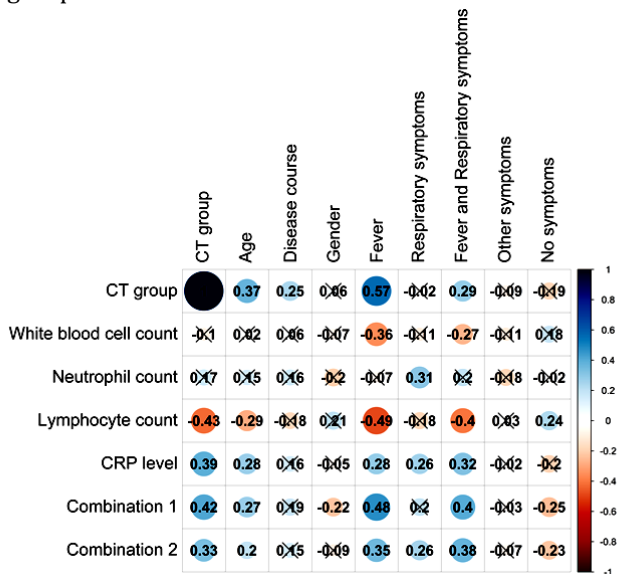


Figure 1. Correlations among CT group membership, clinical characteristics and laboratory test characteristics. The numbers on the circles are correlation coefficient values (tau-b values), and the size and color of each circle indicate the absolute value and valence of the tau-b value. A black x on a circle indicates that the corresponding p-value > 0.05. CRP: C-reactive protein. Combination 1: Decreased or normal white blood cell count and decreased lymphocyte count. Combination 2: Decreased or normal white blood cell count, decreased lymphocyte count and increased CRP level. CRP: C-reactive protein.

Imaging characteristics and signs in the CT-positive group

In the CT-positive group, there were 64 patients, among whom 57 patients (89.06%) had multiple lesions. Fifty-three patients (82.81%) had lesions with a peripheral distribution. Forty-five patients (70.31%) had blurred lesion boundaries, and 41 patients (64.06%) had a nonuniform lesion density (table 3).

Table 3. CT imaging characteristics in the CT-positive group.

Characteristic	Category	Patients (N)	Percentage
Quantity	Single	7	10.94
	Multiple	57	89.06
Distribution	Peripheral	53	82.81
	Nonperipheral	3	4.69
	Mixed	8	12.50
Borderline	Clear	1	1.56
	Partially clear	18	28.13
	Blurred	45	70.31
Density	Uniform	23	35.94
	Nonuniform	41	64.06
N: number			

The CT signs appearing in CT-positive patients in descending order of prevalence were as follows: ground-glass opacity (95.31%, 61/64), abnormal pleural changes (82.81%, 53/64), vascular abnormalities (81.25%, 52/64), reticular changes (73.43%, 47/64), and bronchial abnormalities (62.50%, 40/64). There were 8 patients with acinar nodules (12.50%), 5 patients with tree-in-bud signs (7.81%), 3 patients with honeycombing (4.69%) and 3 patients with pleural effusions (4.69%) (table 4). Three typical CT images are shown in figures 2-4.

Table 4. The CT signs in the CT-positive group.

CT sign	Patients (N)	Percentage
Ground-glass opacity	61	95.31
Pleural disorder	53	82.81
Vascular abnormalities	52	81.25
Mesh-like change	47	73.44
Interlobular septal thickening	41	64.06
Bronchial abnormalities	40	62.50
Consolidation	33	51.56
Blurring	31	48.44
Subpleural line	30	46.88
Striping	29	45.31
Acinar nodule	8	12.50
Tree-in-bud sign	5	7.81
Honeycombing	3	4.69
Pleural effusion	3	4.69
N: number		

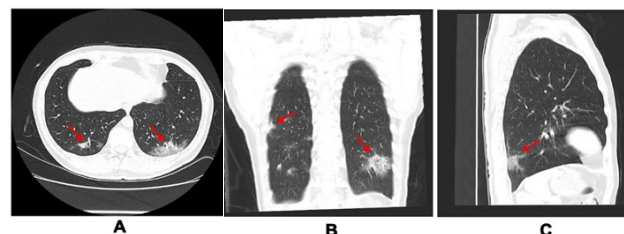


Figure 2. CT scans of a 35-year-old male presenting with fever, cough, headache, reduced lymphocyte count, and normal white blood cell count, neutrophil count and CRP level. A-C: Scans showing multiple lung lesions with a peripheral distribution, visible ground-glass density shadow, grid-like changes, subpleural signs, and thickening and deformation of bronchial and vascular branches. CRP: C-reactive protein.

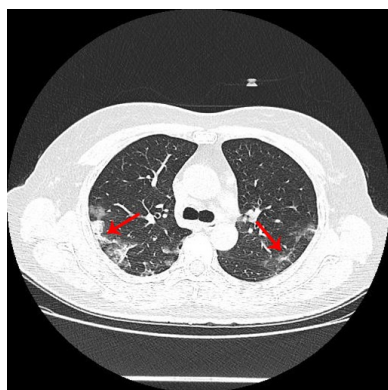


Figure 3. CT scan of a 57-year-old female presenting with fever, cough, dry throat, reduced lymphocyte count, increased CRP level, and normal white blood cell and neutrophil counts. The lesions of the two lungs are mixed, and the peripheral distribution is mainly within the central part of the lung in the lower lobe of the right lung. Ground-glass density shadows, consolidations, patches, striping, and other coexisting lesions of various densities and morphologies adjacent to pleural thickening and stretching are visible. CRP: C-reactive protein.

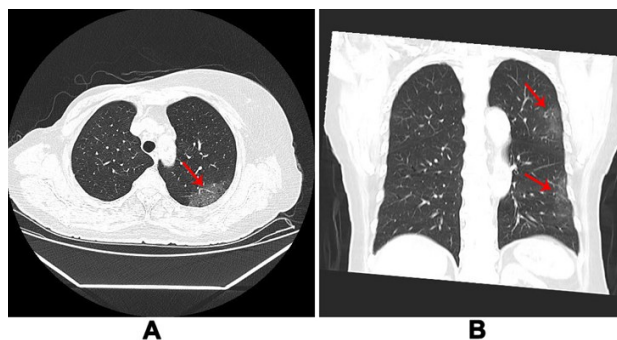


Figure 4. CT scan of a 70-year-old asymptomatic female presenting with increased CRP level and normal white blood cell, lymphocyte and neutrophil counts. **A-B:** Scans showing multiple ground-glass density foci in both lungs; blurred borders; and thickened, rough, and deformed internal blood vessel branches. CRP: C-reactive protein.

DISCUSSION

Novel coronavirus particles are round or oval shaped and often pleomorphic, and the genetic characteristics of this virus are significantly different from those of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) ⁽¹⁻²⁾. The target organ of virus attack is mainly the lung. When the virus pathogenesis and immune response reach certain degrees, various clinical and imaging manifestations begin to appear ^(1-2,17-19). As COVID-19 is an acute respiratory infectious disease, identifying the clinical and imaging characteristics of this disease and their correlations can help achieve early detection, reporting, isolation and treatment and reduce mortality.

According to the findings of previous studies and this paper ^(3,8-15,17), the clinical manifestations and CT imaging features of COVID-19 have certain characteristics and correlations.

The clinical manifestations mainly include diverse respiratory symptoms, such as fever, cough and sore throat. In the present study, a small number of patients had nonspecific symptoms, such as diarrhea and headache, but fever and respiratory symptoms were the main symptoms. The main laboratory findings were normal or decreased peripheral white blood cell counts, decreased lymphocyte counts, and elevated CRP levels, suggesting that the hematological characteristics of bacterial infection are different from those of viral infection. The above results all suggest that COVID-19 is an acute viral infectious disease with respiratory system involvement as the main manifestation. Among patients with fever symptoms, white blood cell and lymphocyte counts are sometimes reduced, and the CRP level is often increased. Similar manifestations and correlations between the clinical symptoms of COVID-19 and laboratory parameters have been reported in many other studies, and these characteristics are significantly different from those of other common pathogen infectious diseases, which is helpful for initial clinical identification ^(1-3,20-21).

The patients in the CT-positive group were older than those in the CT-negative group, and age was positively correlated with CT findings. With increasing age, the possibility of CT pneumonia findings increases. These observations suggest that age cannot be ignored in clinical treatment follow-up and disease evaluation of COVID-19 patients. Fever and respiratory symptoms were the main clinical manifestations of our patients, and there were significant positive correlations between the presence of fever and CT findings. These results suggest that in diagnosis with lung CT, patients with fever are more likely to show pneumonia than are patients with other symptoms, once again showing the importance of fever for the diagnosis of COVID-19 ^(1-2,4-7,11,19,22). In addition, the authors analyzed combinations of clinical manifestations and laboratory observation indicators. The results indicated that when the clinically positive results of the above indicators are obtained, CT may already show pneumonia and that clinical treatment and follow-up should be closely monitored.

However, we found that some patients with normal clinical and laboratory findings had viral pneumonia manifestations on CT and that some with normal CT examinations had abnormal clinical and laboratory findings. During follow-up, 5 patients showed viral pneumonia manifestations. These observations suggest dynamic changes and diverse manifestations of this disease. During follow-up, both the clinical and CT manifestations may change, and CT plays an important role in monitoring the evolution of the disease ^(1-3,8-15,17). According to correlation analysis, if a certain test is not implemented or does not indicate the presence of a condition, the patient's condition can be evaluated according to other tests to guide treatment.

The current histopathological features indicate that the novel coronavirus mainly causes an inflammatory response characterized by deep airway and alveolar injury. After inhalation, due to their very small size (60~140 nm) and large number, the virions are randomly deposited or distributed in the lung tissues of different regions. Then, the virus spreads to the periphery along the alveolar pores, not in the form of acinus, leaflets or leaf segments. At the same time, it causes lesions in the alveolar wall and interstitium of different regions. Lesions appear in the alveolar cavity, alveolar epithelium and alveolar septum. Focal hemorrhage and necrosis of the lung tissue, exudate production and pulmonary interstitial fibrosis can be seen (23-24). Based on the pathological changes in multiple sites, the main manifestations on imaging are the peripheral distribution and coexistence of multiple morphological lesions.

In the patients, "ground-glass density" was the most prominent chest CT finding. Several factors might be related to this result, such as the formation of serous fluid, fibrinous exudates and hyaline membrane in the alveolar space; incomplete filling of the alveolar cavity; significant proliferation of alveolar epithelial cells; swelling of the alveolar wall; involvement of type II alveolar epithelium; alveolar collapse; and alveolar septal hyperemia (11,18-19,23-24). The alveolar cavity was completely filled, the lung tissue was hemorrhagic and necrotic, hemorrhagic infarction occurred, and halo signs and consolidation were observed on CT. Alveolar exudate mechanization and pulmonary interstitial fibrosis produce fibrous traction, which causes abnormal changes in bronchial vessels inside the lesion and abnormal signs of pleural traction and displacement, while fibrous slivers are seen on CT (11,18-19,23-24). A few alveoli are hyperinflated, alveolar septa are broken, and cysts may form, which can produce honeycombing.

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