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The atypical imaging findings of novel coronavirus pneumonia (COVID-19) and its evolution

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Abstract. – OBJECTIVE: This study aimed to explore the atypical imaging findings of the novel coronavirus pneumonia (COVID-19) and its evolution.

MATERIALS AND METHODS: The atypical imaging data of ten patients in our hospital who tested positive for COVID-19 were analyzed retrospectively, and the distribution, morphology, and image evolution of the lesions were analyzed. High-resolution computed tomography (HRCT) was performed in all cases, and the imaging features were analyzed and summarized by two senior radiologists.

RESULTS: Of these ten patients, three were male, and seven were female. The age of these patients ranged from 21-53 years, with an average age of 36.3 ± 3.6. The first symptom was fever in nine cases and dry cough in one case. A total of 17 lesions were detected in these ten patients. Five patients had a single lesion, and five patients had multiple lesions, for a total of 12 lesions. Ten lesions (58.82%) were located in the inferior lobe of the right lung, four lesions (23.53%) in the left inferior lobe, two lesions (11.76%) in the left upper lobe, and one lesion (5.88%) in the right middle lobe. Among the five single lesions, two were solid lesions, two were mixed ground-glass lesions, and one was a pure ground-glass lesion. Among the 12 multiple lesions, eight were solid lesions, two were mixed ground-glass lesions, and two were pure ground-glass lesions. Atypical manifestations in image signs: five lesions (29.41%) had single solid and sub-solid nodules, and four lesions (23.53%) had cavitary nodules. Typical manifestation (the presence of "white lung"): three lesions (17.65%) had an air bronchogram, two lesions (11.76%) had crazy-paving signs, two lesions (11.76%) had vascular thickening, and one lesion (5.88%) had halo signs. At reexamination 2-6 days later, 15 lesions (88.24%) had enlarged or increased, and two lesions (11.76%) had decreased or absorbed.

CONCLUSIONS: Patients with COVID-19 may have atypical imaging findings. Radiologists should improve their understanding of the novel coronavirus pneumonia to avoid any missed diagnoses.

Key Words:

Novel coronavirus pneumonia, COVID-19, Computed tomography, Atypical manifestations in the CT features, Misdiagnosis.

Introduction

The novel coronavirus pneumonia is an epidemic infectious disease that was first found in Wuhan, Hubei, in December 2019. In late January, the epidemic spread throughout China. On February 8, 2020, the National Health Commission of the People's Republic of China temporarily named the new pneumonia "novel coronavirus pneumonia" (NCP). On February 11, the World Health Organization (WHO) named this new disease "coronavirus disease 2019" (COVID-19)[1]. NCP is characterized by fever, fatigue, cough, dyspnea, etc. Some studies confirmed that COVID-19 could cause family[2] and community[3] transmission through respiration and contact. It is highly infectious[2]. The epidemic has a high prevalence and mortality in China and other countries[4]. Therefore, early detection, early diagnosis, and early isolation are the most critical links in the disease prevention and control system. Although the positive result of novel coronavirus Reverse Transcription-Polymerase Chain Reaction (RT-PCR) nucleic acid test is the gold standard[5], it takes too long to carry out. Computed tomog-

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raphy (CT), as a convenient examination method, plays an important role in early diagnosis. Diagnoses based on typical imaging manifestations[6] are relatively straightforward, but atypical manifestations are easy to misdiagnose or fail to diagnose altogether. This increases the difficulty of prevention and control of the disease. Therefore, the atypical manifestations of COVID-19 were analyzed in this study to provide more clues for clinical diagnosis.

Data and Methods

General Information

Clinical data of 63 patients with COVID-19 who were diagnosed in the First Affiliated Hospital of Nanchang University from January 23, 2020, to February 4, 2020, were analyzed retrospectively. Patients with atypical imaging findings were screened. Inclusion criteria: (1) patients with a positive epidemic history; (2) patients with a positive novel coronavirus nucleic acid test; (3) patients with atypical imaging findings; and (4) patients who underwent CT reexamination within 2–5 days after the first CT examination.

Detection Methods

All patients were scanned with Philips Brilliance iCT (the Netherlands) and Siemens Somatom Emotion 16-slice CT (Berlin, Germany). Scan parameters: the tube voltage was 120 kV, the tube current was 50-100 mAs, the slice thickness was 0.5 mm, the interslice gap was 5 mm, and the pitch was 0.5 mm. Conventional reconstruction of a 1-mm thin layer image was performed. The scanning range was from the apex to the base of the lung.

Image Analysis and Data Statistics

A chief physician and a senior attending physician in the Imaging Department interpreted the HRCT images. The contents included the sites of the lesions (left upper/lower lung, right upper/middle/lower lung, yes/no located under the pleura), the number of lesions (single/multiple lesions), and the image characteristics of the lesions (single nodule/patch, cavitary node, air bronchogram, crazy-paving sign, vascular thickening, halo sign). The changes in lesions before and after reexamination were compared. SPSS 20.0 (IBM Corp., Armonk, NY, USA) was used for the descriptive analysis of the data.

Results

Ten patients with COVID-19 who had atypical imaging findings were included. Of these, three were male, and seven were female. These patients' age ranged from 21-53, with an average age of 36.3 ± 3.6. The first symptom was fever in nine cases and dry cough in one case.

Location of the Lesions

A total of 17 lesions were located. Five patients had a single lesion, three patients had two lesions, and two patients had three lesions. Of these lesions, 12 (70.59%) were located under the pleura, and five (29.41%) were in the intrapulmonary zone. Ten lesions (58.82%) were located in the inferior lobe of the right lung, four lesions (23.53%) in the left inferior lobe, two lesions (11.76%) in the left upper lobe, and one lesion (5.88%) in the right middle lobe. The specific results are shown in Table I.

Characteristics and Nature of the Lesions

Five patients had a single lesion. Two were solid lesions, two were mixed ground-glass lesions, and one was a pure ground-glass lesion. Five patients had multiple lesions, for a total of 12 lesions. Of these, eight were solid lesions, two were mixed ground-glass lesions, and two were pure ground-glass lesions. Detailed results are shown in Table II.

Imaging Features of the Lesions

Atypical manifestations: five lesions (29.41%) had single solid and sub-solid nodules (Figures 1, 2, 3), and four lesions (23.53%) had cavitary nodules (Figures 3, 4, 5). Typical manifestations: three lesions (17.65%) had an air bronchogram (Figures 6, 7), two lesions (11.76%) had cra-

Table I. Site characteristics of 17 lesions in novel coronavirus pneumonia patients with atypical imaging.

Characteristics	N	%
Location of the lesions		
Under the pleura	12	70.59
Intrapulmonary zone	5	29.41
Location of the lesions (by lobes)		
Right inferior lobe	10	58.82
Left inferior lobe	4	23.53
Left upper lobe	2	11.76
Right middle lobe	1	5.88

Table II. Characteristics and natures of 17 lesions in novel coronavirus pneumonia patients with atypical imaging n (%).

Nature of the lesions	Single lesion	Multiple lesions	Total
Solid lesions	2 (40.0)	8 (66.6)	10 (58.9)
Mixed ground-glass lesions	2 (40.0)	2 (16.7)	4 (23.5)
Pure ground-glass lesion	1 (20.0)	2 (16.7)	3 (17.6)
Total	5	12	17

zy-paving sign (Figure 6), two lesions (11.76%) had vascular thickening (Figure 1-b), and one lesion (5.88%) had halo signs.

Dynamic Observation of the Lesions

Ten patients underwent two or more CT examinations. At reexamination 2-6 days later, 15 lesions (88.24%) had enlarged or increased, and two lesions (11.76%) had decreased or been absorbed. The lesions were detected in eight patients in the initial examination. In one case, on reexamination, the lesion in the left upper lung had been absorbed, and the lesion in the right lower lung had decreased. In another case, the lesion in the right lower lung changed from solid to mixed ground-glass shadow and crazy-paving sign. All lesions in the other cases were enlarged or increased at reexamination. In one case, no abnormality was found at the initial CT, but a reexamination four days later found cavitary nodules.

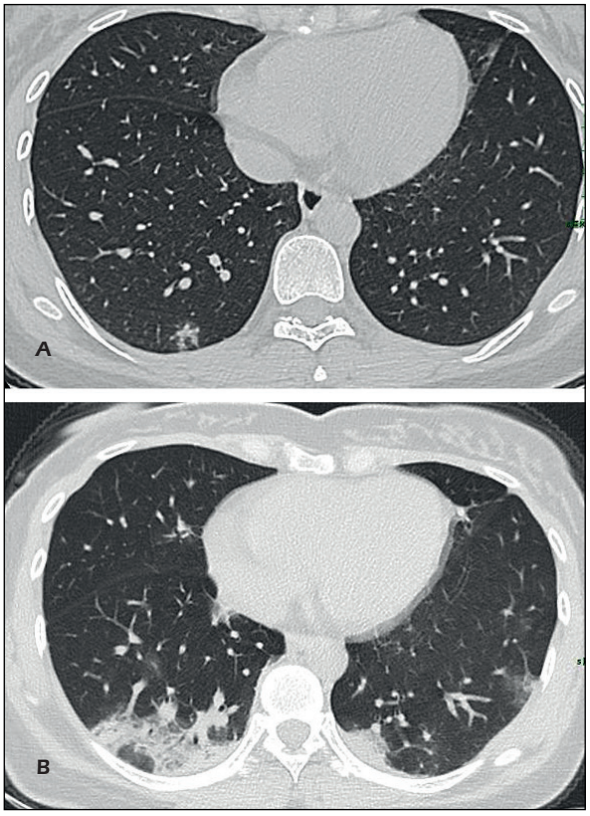

Figure 1. A female, 31 years old, fever for two days. **A,** A single patchy dense shadow was found in the subpleural of the inferior lobe of the right lung. The edge was fuzzy, and a few exudations were found. Reexamination was performed five days later. **B,** The scope of the lesion had increased significantly. It showed a mixed ground-glass shadow and vascular thickening. Fine grid-like changes could be seen. A lesion was found in the left lung.

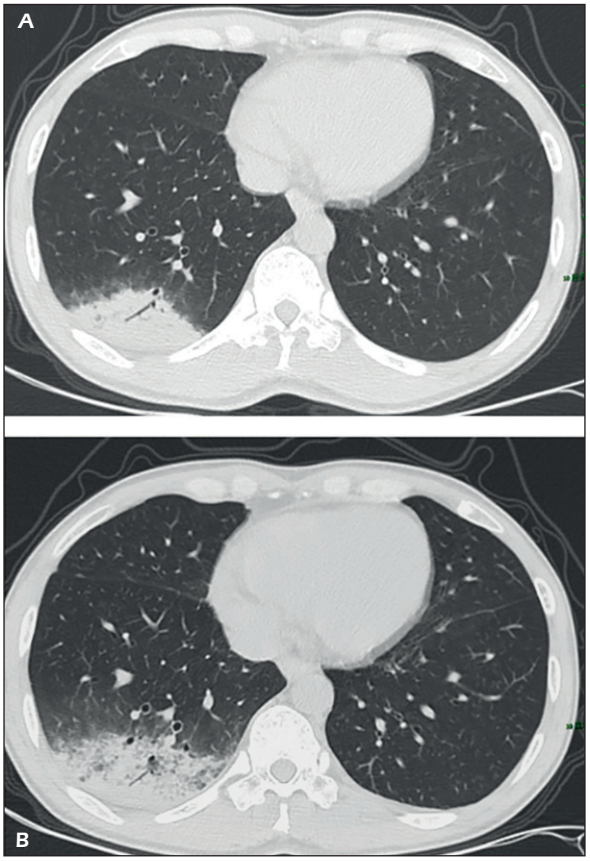

Figure 2. A female, 42 years old, fever for three days. **A,** A solid nodular shadow with a clear boundary was found in the inferior lobe of the right lung. **B,** Reexamination was performed five days later. The lesion was partially absorbed, and the edge was fuzzy.

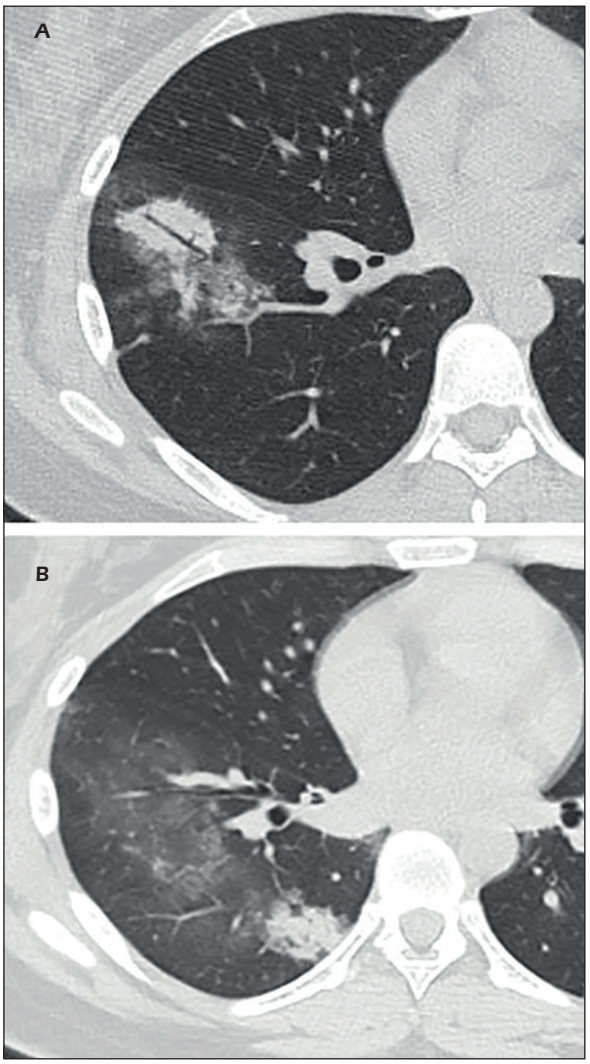

Figure 3. A female, 53 years old, fever for one day. Multiple nodules were found in the inferior lobe of the right lung. Cavitary shadows were seen in the subpleural nodule, and the edge was smooth. The CT result taken less than four days later was negative for the patient.

In another case, the initial direct digital flat X-ray examination found no abnormality. However, six days later, a few faint and fuzzy shadows were found near the heart border with the right lower lung.

Discussion

The typical clinical manifestations of COVID-19 are fever, fatigue, and dry cough[7]. In the present study, all patients visited our hospital because of the first symptoms of fever and dry cough. According to "The Novel Coronavirus Pneumonia Diagnosis and Treatment Plan" (Trial Version Fifth) issued by the National Health Commission of the People's Republic of China[8], chest imaging has an important value in the diagnosis of COVID-19. Chest CT, especially high-resolution computed tomography (HRCT), is the first choice of image examination for patients because of advantages in its high spatial resolution and various post-processing imaging. The typical CT manifestations of COVID-19 are pure ground-glass shadows or a few solid components. These

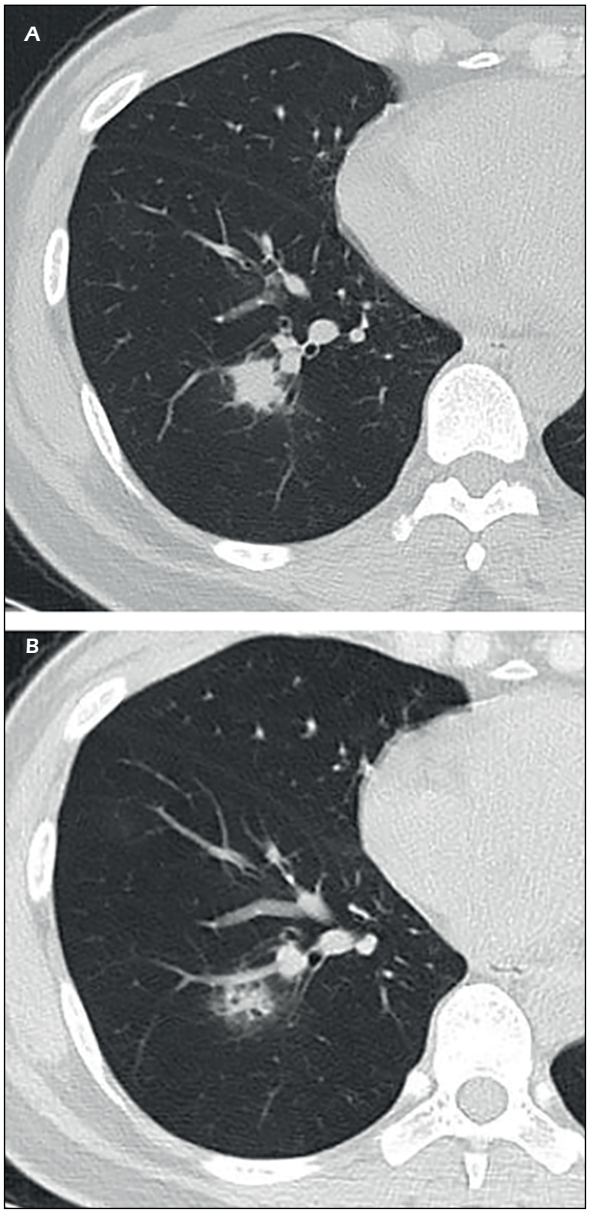

Figure 4. A female, 53 years old, fever for seven days. A cavitary nodule was found in the inferior lobe of the right lung, and the edge was smooth.

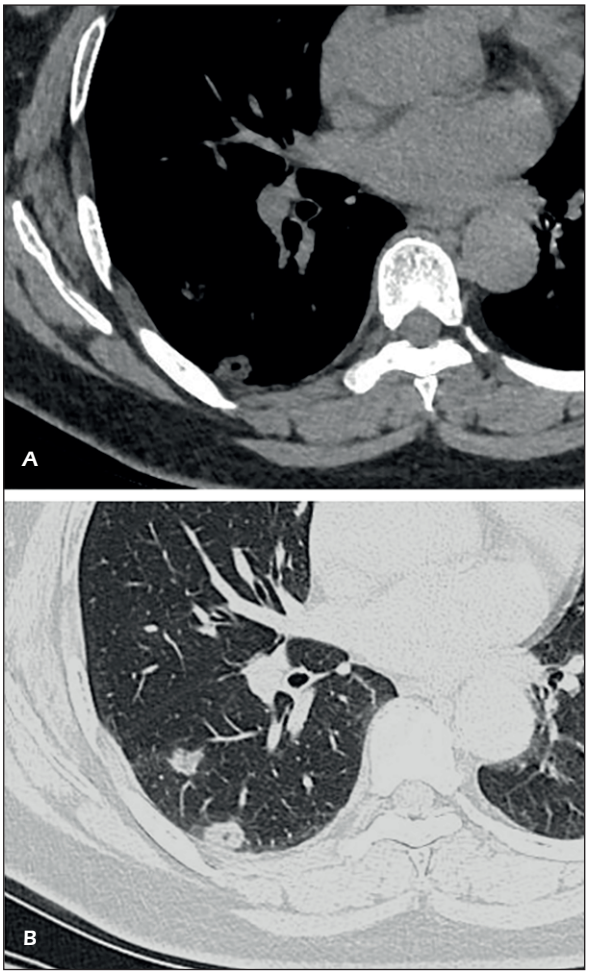

Figure 5. A male, 46 years old, cough for five days. **A,** A dense nodular shadow was found in the subpleural of the inferior lobe of the right lung, and a cavity was found in it. **B,** Reexamination was performed two days later. The scope of the lesion had increased, the cavity shadow disappeared, and multiple lesions were found in both lungs.

are mainly distributed in the subpleural areas. No lymphadenectasis and pleural effusion are found, and it often has interstitial thickening, crazy-paving sign, and air bronchograms[9]. Different clinical types have different imaging features. The main manifestations of chest CT images are solid patchy shadow with halo signs in patients with common type, stripe shadow and ground-glass shadow in patients who are severely ill, and consolidation shadow in patients who are critical[10].

Images are the embodiment of pathology, and pathology is the basis of images. As COVID-19 is the latest infectious disease mainly transmitted by the respiratory tract, there are only two cases of autopsy pathology for the disease at present[11]. There was edema, protein exudate, globules, and focal hyperplasia of lung cells in both cases. Only patchy inflammatory cell infiltration and multinucleated giant cells were observed, and the transparent membrane was not significant. These changes may represent the early stage of pulmonary pathology in patients with COVID-19.

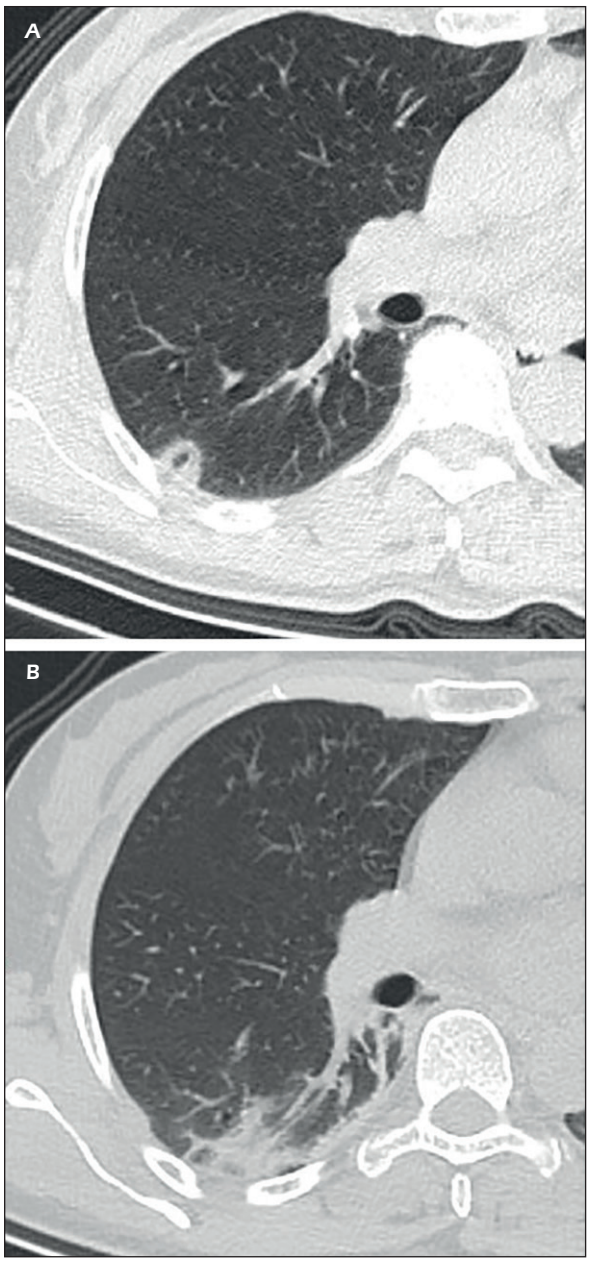

Figure 6. A male, 46 years old, fever for three days. A patchy consolidation shadow was found in the subpleural of the inferior lobe of the right lung. An air bronchogram was also found. Reexamination was performed five days later. The scope of the lesion had increased. The density had decreased, showing a mixed ground-glass shadow, an air bronchogram, and crazy-paving sign.

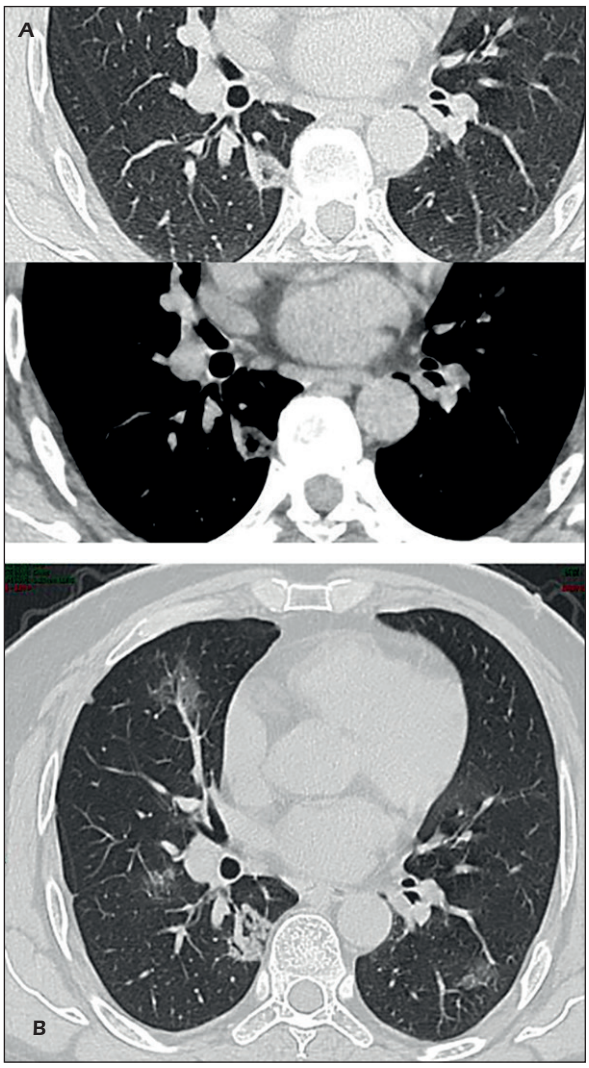

Figure 7. A female, 24 years old, fever for six days. **A,** A patchy consolidation shadow with fuzzy margins was found in the right lower lung, and an air bronchogram could be seen. Reexamination was performed five days later. **B,** The original solid variable shadow was absorbed. It showed a large flaky, thin, and fuzzy shadow, and new solid subpleural nodules of the right lower lung were found.

Some studies[12-16] revealed that, like most respiratory viruses, novel coronavirus first invades the epithelial cells of bronchioles. It then causes interstitial changes in and around the lobules to form ground-glass density shadows, interlobular septal thickening, interstitial thickening, and edema around the bronchial vessel, forming a fine grid shadow. Progression of the lesions can extensively affect pulmonary alveoli, inducing alveolar exudation, congestion, and consolidation to form patchy density, increasing shadow, and consolidation shadow. If lesions develop further, "white lung" almost always emerges in the severe stage. If the lesion is absorbed, a fiber strip shadow can be found. Therefore, the typical image findings of COVID-19 are multiple ground-glass shadows in the cortex area of the peripheral lung under the subpleural area or along the shape of the bronchovascular bundle. In the lesions, vascular thickening can be seen, and fine grid shadows and mosaic signs can also be found.

In the present study, the sites of the lesions were atypical for these ten patients. Most were in the right lower lung, with the rest in the intrapulmonary zone. The imaging findings were atypical. Four lesions were single irregular solid nodules or mixed ground-glass nodules, which needed to be differentiated from early lung cancer. One lesion was a single patchy shadow with a little surrounding exudation, which needed to be differentiated from bacterial infection. Chung et al[6] revealed that no cavitary shadow was found in CT images of patients with COVID-19. In the present study, four lesions were characterized by nodules and cavity shadows. The cavity was a bright area formed by necrosis and liquefaction of lung lesions drainage through bronchi, and then, gas entry. It needed to be differentiated from tuberculosis. One lesion was a large flaky consolidation shadow of the right lower lung. An air bronchogram was found in it, and this needed to be differentiated from lobar pneumonia. Some lesions were multiple patchy shadows with fuzzy edges, which needed to be differentiated from bronchopneumonia.

Although the lesions were atypical, in the present study, fever was the first symptom of most cases, and the epidemic history of all patients was positive. However, CT reexamination and nucleic acid tests were still recommended. Reexamination was performed 2-5 days later. The result suggests that the degree of changes of the lesions was larger, and atypical lesions were found in patients with negative images, such as cavitary nodules and single patchy fuzzy shadows. The original atypical image findings were converted into typical findings. For example, patients with consolidation and air bronchial shadow exhibited mixed ground-glass shadows and crazy-paving changes in the reexamination. Conversely, patients with single irregular solid nodules or mixed ground-glass nodules exhibited a significantly enlarged scope of the lesions at reexamination, and air bronchograms and crazy-paving sign could be seen. Some of the lesions were migratory, the original atypical lesions had decreased, and other

lesions had enlarged or increased. These showed multiple ground-glass shadows and fine grid-like changes.

The present study revealed that the cases with atypical imaging findings were mainly young and middle-aged people. This may be due to the strong resistance and atypical pathological changes in young and middle-aged people. Because the number of such cases was small, it was necessary to increase the sample size for further demonstration.

In summary, image diagnosis plays an important role in the diagnosis of COVID-19. We need to be highly alert to its atypical image findings when we are familiar with its typical image findings, and the image findings may change greatly in a short time. Depending on the clinical manifestations and epidemic history, an atypical imaging finding should be taken as a suspected case for further reexamination or nucleic acid test. This is important to avoid missed diagnoses that increase the difficulty of prevention and control.

Conclusions

Patients with COVID-19 may have atypical imaging findings. Radiologists should improve their understanding of the novel coronavirus pneumonia to avoid any missed diagnoses.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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