Radiographic characteristics and early clinical manifestations of family clustered coronavirus disease 2019 (COVID-19)

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Abstract
Object: To study chest computed tomography (CT) findings in family clusters of coronavirus disease 2019 (COVID-19).
Methods: Twenty-one patients with confirmed COVID-19 were enrolled at the West District Qingdao Municipal Hospital, the Fifth People’s Hospital of Qinghai Province and Jiaozhou Central Hospital. Eleven were family clustered cases and 10 were sporadic cases not associated with family gatherings.
Results: Ten patients were male and 11 were female. The time elapsed onset of fever and cough to diagnosis was 3 to 7 days. The body temperatures of patients fluctuated between 36.7 and 38.9°C. One elderly female patient had no fever. On chest CT, 14 patients with family clustered COVID-19 had bilateral lung lesions. By contrast, 7 patients with no history of familial gatherings showed single lung exudative lesions or consolidation. Seven patients with family clustered COVID-19 had bilateral multiple exudative lesions. Four patients with no history of familial gathering had unilateral lesions.
Conclusion: Not all patients with COVID-19 have direct epidemiological links to an infected case. They may become infected because of poor protection. In patients with family clustered COVID-19, chest CT often showed multiple exudative lesions in both lungs. In some patients, symptoms may be complicated by influenza virus infection.

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Keywords
Coronavirus disease 2019, clinical manifestation, radiographic changes, computed tomography, family clustering, case series

Date received: 22 February 2020; accepted: 7 July 2020

Introduction
Coronaviruses infect several vertebrates, including humans, and primarily cause respiratory and gastrointestinal infections.\(^1\) China has now updated its coronavirus disease 2019 (COVID-19) diagnosis and treatment standards to the fifth edition.\(^2\) In this new edition of diagnosis and treatment norms, it is clearly pointed out that familial clustering and radiographic changes are important bases for diagnosis. Through the study of patients with COVID-19, we have reached a preliminary understanding of the significance of familial clustering and imaging changes in diagnosis.

Patients and methods

Ethics
This study was approved by the Qingdao Municipal Hospital Research Ethics Committee. All patients were fully informed regarding the purpose and procedures of the study and provided written informed consent.

Clinical data
We enrolled COVID-19 cases at the West District Qingdao Municipal Hospital, Jiaozhou Central Hospital and the Fifth People’s Hospital of Qinghai Province from 31 January 2020 to 20 February 2020. All patients were positive by reverse transcription (RT)-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). All patients had mild disease.\(^2\) Blood gas analysis, routine blood tests, D-dimer quantitation, and chest computed tomography (CT) examinations were performed in all patients. We carefully inquired regarding the medical histories of all patients.

Epidemiological history of probable exposure was assessed via the following factors: (i) travel or residence within 14 days prior to onset of COVID-19 in Wuhan and surrounding areas or other communities experiencing outbreaks; (ii) history of exposure to individuals positive for SARS-CoV-2 within 14 days prior to onset of COVID-19; and (iii) exposure to individuals from Wuhan and surrounding areas experiencing fever or respiratory symptoms within 14 days prior to onset of COVID-19.

Laboratory data
Following admission, all patients underwent routine blood tests, arterial blood gas analysis, chest CT examination, and testing for influenza A virus, influenza B virus, and herpesvirus antibody as well as SARS-CoV-2 nucleic acid. The epidemiological histories of the patients were analyzed. Statistics on time from exposure to onset, age and sex distributions, clinical manifestations and imaging examination were tabulated. The 21 patients were divided into a familial clustering group and a non-familial clustering group.

Statistical analysis
All data were analyzed using SPSS version 19.0 software (SPSS Inc, Chicago, IL,
USA). Differences in count data were assessed using the $\chi^2$ test. Differences between two groups or among multiple groups were assessed using the student’s t test or analysis of variance, respectively. Non-normally distributed data were compared using the Kruskal–Wallis test. Values of $P < 0.05$ were considered statistically significant.

## Results

### Analysis of clinical results

We enrolled 21 COVID-19 cases from 31 January 2020 to 20 February 2020 (Table 1). Ten patients were male and 11 were female. Four patients had an epidemiological history of probable exposure (these patients were imported cases from Wuhan).

| Characteristics | Family clustered | Sporadic |
|-----------------|------------------|----------|
| N = 10          | N = 11           |
| Epidemiological exposure | 0 | 4 (36%) |
| No exposure to individuals with respiratory symptoms | 10 (100%) | 7 (64%) |
| Age, years      | 50 (25–75) | 48 (28–68) |
| Sex, male       | 4 (40%) | 6 (55%) |
| Current smoking | 4 (40%) | 6 (55%) |
| Any comorbidity | 1 (10%) | 1 (10%) |
| Diabetes        | 1 (10%) | 0 |
| Chronic obstructive pulmonary disease | 0 | 1 (10%) |

### Signs and symptoms

#### Fever (highest temperature, °C)

- <37.3 | 1 (10%) | 0 |
- 37.3–38.0 | 4 (40%) | 2 (18%) |
- 38.1–38.5 | 5 (50%) | 9 (82%) |

### Cough

- 9 (90%) | 7 (64%) |

- Myalgia or fatigue | 10 (100%) | 11 (100%) |

- Sputum production | 5 (50%) | 6 (55%) |
- Headache | 6 (60%) | 5 (45%) |
- Diarrhea | 3 (30%) | 3 (27%) |
- Dyspnea | 4 (40%) | 3 (27%) |

#### Respiratory rate >24 breaths per minute

- 2 (20%) | 3 (27%) |

### Laboratory examinations

#### White blood cell count, $\times 10^9$/L

- <4 | 1 (10%) | 0 |
- 4–10 | 9 (90%) | 10 (100%) |
- >10 | 0 | 1 (10%) |

#### Lymphocyte count, $\times 10^9$/L

- <1.0 | 5 (50%) | 6 (55%) |
- $\geq$1.0 | 5 (50%) | 6 (55%) |

#### Platelet count, $\times 10^9$/L

- <100 | 2 (20%) | 1 (10%) |
- $\geq$100 | 8 (80%) | 10 (100%) |

#### Influenza A virus antibody

- 0 | 2 (18%) |

Data are shown as n (%) or mean (range).
The remaining patients had no obvious epidemiological link to an infected case. The time elapsed between onset of fever and cough and diagnosis was 3 to 7 days. The patients ranged in age from 28 to 75 years. Their body temperatures fluctuated between 36.7 and 38.9°C. One 75-year-old female patient had no fever. One patient had diabetes mellitus. Eleven cases were associated with familial aggregation and 10 were family sporadic cases.

All patients had mild disease with normal arterial blood gas. Ten male patients had fever. Their body temperatures fluctuated between 37.5 and 38.5°C. All male patients had fatigue. One male patient had chest pain. Three male patients had a dry cough. The remaining male patient only had fever. Two male patients were from Hubei Province and developed COVID-19 after arriving in Qinghai Province. Two male patients were positive for H1N1 antibody. The time elapsed from exposure to symptom onset was 3 to 7 days. The remaining male patients had no clear epidemiological link to an infected case.2 No antibodies to other viruses were detected in male patients with no epidemiological history of exposure.

Eleven female patients had fever. Their body temperatures fluctuated from 36.7 to 38.5°C. One elderly female patient had no fever (36.7°C). All female patients had fatigue. Five female patients had chest pain. Four female patients only had fever (37.8–38.5°C). Two female patients had an epidemiological history of travel to an epidemic area. Two female patients were positive for influenza A virus antibody. The time elapsed from exposure to symptom

Figure 1. A male patient, 47 years old, stated he had returned to Xining from Wuhan. The patient had no history of family gathering. He was in good health. He disclosed he had had a fever for 2 days and was admitted to hospital with a body temperature of 37.8°C. He had a dry cough. His white blood cell and lymphocyte counts were generally normal. He had no nasal congestion or runny nose. His influenza A virus antibody and SARS-CoV-2 nucleic acid tests were positive. Chest CT of the lung showed consolidation and ground-glass opacity.
Figure 2. A female patient, 31 years old, had no epidemiological link to Hubei. The patient had no history of family gathering. She was in good health. The patient disclosed that she had had a fever for 3 days and was admitted to hospital with a body temperature of 38.1°C. She had an unproductive cough. Her white blood cell and lymphocyte counts were generally normal. Her influenza A virus antibody test was negative and her SARS-CoV-2 nucleic acid test was positive. Chest CT showed that the focus of infection was close to the pleural inflammation and distributed along the blood direction of the bronchus. Chest CT revealed ground-glass opacity.

Figure 3. A male patient, 28 years old, had no epidemiological link to Hubei. The patient had a history of family gathering. He was in good health. The patient disclosed that he had had a fever for 1 day and was admitted to hospital with a body temperature of 38.3°C. He had no cough. His white blood cell and lymphocyte counts were generally normal. His influenza A virus antibody test was negative and his SARS-CoV-2 nucleic acid test was positive. Chest CT shows multiple ground-glass opacities in both lungs. Most of the lesions in both lungs were subpleural.
onset was 4 to 7 days. No antibodies to other viruses were detected in female patients with no epidemiological history of exposure.

**Radiographic changes associated with family clustered COVID-19**

Cases of family clustered COVID-19 showed bilateral involvement in chest radiographs, subpleural involvement and ground-glass opacity on chest CT ($P < 0.05$) (Figures 1–4). There were no pleural effusions observed in either family clustered or sporadic COVID-19 cases. Sporadic cases showed solid changes and unilateral involvement on chest CT (Table 2).

**Discussion**

We report here a series of 21 confirmed cases of COVID-19 in provinces and cities. All patients had mild disease in the early stages, and lung lesions occupied less than 30% of total area in all patients. There were no significant differences between the neutrophil and lymphocyte counts of patients with family clustered and sporadic COVID-19.

Chinese diagnosis and treatment guidelines indicate that familial clustering is an important component of COVID-19. Many patients developed cough without fever, which makes it difficult to diagnose the disease. Therefore, it is particularly important to study the early pathogenesis of family clustered outbreaks. Patients in Qinghai

![Figure 4](image-url)
Province represented imported cases and there was no familial clustering. Other patients had no epidemiological history indicating exposure. Patients with no epidemiological history of exposure included patients who might have been exposed to COVID-19 cases during the incubation period.

Based on the results of antibody tests, COVID-19 in two patients was complicated with influenza virus infection. Thus, the symptoms of COVID-19 may be modulated by underlying influenza virus infections. Chest CT has many advantages in the diagnosis of COVID-19. Chest CT may help in early detection of lung abnormalities for screening of patients with suspected disease, especially in those with an initially negative RT-PCR result.

There were many similarities in chest CT between cases of family clustered and sporadic COVID-19. These included the presence of ground-glass opacities and the location of lesions mostly under the pleura. The familial clustering group showed bilateral involvement on chest radiographs, subpleural involvement and ground-glass opacities on chest CT (P < 0.05). There were no pleural effusions in either group. The sporadic group showed solid changes and unilateral involvement on chest CT.

This study enrolled confirmed COVID-19 patients from different regions. Family clustered and sporadic COVID-19 cases showed different changes on chest CT. Our results are significant for the diagnosis of COVID-19. The number of patients included in this study was small, which was a major limitation. Future studies must combine clinical data with radiographic changes to better understand patient prognosis.

**Conclusion**

Not all patients with COVID-19 have a direct epidemiological link to an infected case. They may become infected because of poor protection. In patients with family clustered COVID-19, chest CT often showed multiple exudative lesions in both lungs. In some patients, symptoms may be complicated by influenza virus infection.

**Availability of data and materials**

Anonymized data from the current study are available from the corresponding author on reasonable request. This study was approved by the Qingdao Municipal Hospital Research Ethics Committee. All patients were fully informed regarding the purpose and procedures of the study.

| Characteristics | Familial clustered | Sporadic |
|-----------------|--------------------|----------|
| N               | 10                 | 11       |
| Position        |                    |          |
| Hilum of lung   | 1 (10%)            | 0        |
| Subpleural      | 10 (100%)          | 10 (91%) |
| Bilateral involvement of chest radiographs | 9 (90%) | 6 (55%)* |
| Ground-glass opacity | 9 (90%) | 6 (55%)* |
| Solid change    | 1 (90%)            | 5 (55%)* |
| Nodule          | 2 (20%)            | 1 (10%)  |
| Pleural effusion| 0                  | 0        |
| Lesion area     | <30%               |          |
|                 | 10 (100%)          | 11 (100%)|

*P < 0.05.
Declaration of conflicting interest
The authors declare that there is no conflict of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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