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Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19

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ARTICLE INFO

Keywords: COVID-19, family aggregation, CD4+ counts, RT-PCR-CT values, Neutrophil-lymphocyte ratio

ABSTRACT

Background: Since December 2019, a new outbreak of the coronavirus disease 2019 (COVID-19) in Wuhan (Hubei, China) and rapidly spread throughout China, however, confirmed cases are still increasing worldwide.

Objectives: To investigate the epidemiological history and initial clinical characteristics of 10 patients with family aggregation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Western Chongqing, China.

Study design: Ten patients positive for SARS-CoV-2 nucleic acid detection by real time Reverse Transcription-Polymerase Chain Reaction (RT-PCR), were collected from The People’s Hospital of Dazu District, Chongqing. Epidemiological data and laboratory and imaging results were collected on the first day of admission, and analyzed based on the Diagnosis and Treatment Guideline for COVID-19 (5th edition, China).

Results: Of the 10 cases, case A had a history of a temporary stay in Wuhan and transmitted the virus to the others through family gathering, living together, and sharing vehicles. The average age was 56.5 years (± 11.16), six patients were males, and the incubation period was 2–14 days. Dry cough was the main symptom, followed by fever and fatigue. Most patients were clinically classified as ordinary-type, with three cases being severe-type. Chest computed tomography results were nonspecific, mainly with ground-glass attenuation and/or shadow images. Extensive lesion distribution was seen in severe cases. CD4+ lymphocyte counts were 61, 180, and 348 cells/uL in severe-type patients, respectively. Notably, viral nucleic acid values in nasopharyngeal swabs were lower (19, 25, and 26) than those of ordinary-type patients, suggesting a higher viral load. Neutrophil-lymphocyte ratio (NLR) was also higher in severe-type patients.

Conclusions: Initial examination results of lower CD4+ lymphocyte counts and RT-PCR-CT values coupled with higher NLR may indicate the severity of COVID-19 infection for these family clusters.

1. Background

The outbreak of the new emerging disease COVID-19 coincided with the Chinese Lunar New Year holiday, and the large movement of people has expanded and spread this outbreak rapidly, from Hubei province to the other areas of China. The continuous rising number of infected people is causing a serious threat to public health and a great loss to the social economy. As of February 18, 2020, a cumulative report confirmed that the number of cases had risen to 74185 [1], based on 31 provinces (autonomous regions and municipalities directly under the central government) and Xinjiang Production and Construction Corps, confirmed cases are still increasing worldwide.

2. Objectives

To provide the information for public health strategies for rapid and appropriate assessment and corresponding initial management, we investigated the epidemiological and clinical features of these SARS-CoV-2-infected family clustering patients between January 23 and February 18, 2020.

3. Study design

3.1. Patients

Our hospital serves as one of the designated hospitals for the initial...
diagnosis and assessment of suspected SARS-CoV-2-infected patients in Western Chongqing, China. Diagnoses were made with reference to The Diagnosis and Treatment Guideline for COVID-19 (5th edition, China) from The National Health Commission of China [2]. Suspected cases were isolated using air borne precautions in the designated hospital. Patients positive for nasopharyngeal-swabs SARS-CoV-2 nucleic acid detection by real time RT-PCR were identified as confirmed cases. Of the 80 suspected cases were admitted into our hospital, 14 patients were confirmed to be infected with SARS-CoV2 mong which 10 patients with family aggregation of COVID-19 were identified. This study was approved by the Ethics Commission of The People's Hospital of Dazu District. Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

3.2. Information collection

3.2.1. Epidemiological data

Patient data were acquired in detail regarding any travel history in Wuhan and its surrounding areas, contact with local community confirmed cases within 14 days before disease onset, contact with febrile patients with respiratory syndrome from Wuhan and its surrounding areas, any possible contact with pathogenic nucleic acid-positive patients within 14 days before onset, or any chance of family aggregation, among others. The criteria used for determination of close contacts was from the Reference to Prevention and Control Guideline for COVID-19 (4th edition, China) from The National Health Commission of China [3]. The number of close contacts of the first confirmed case was provided by the Center of Disease Prevention and Control (CDC) of Dazu District, Chongqing.

3.2.2. Clinical data

Clinical data of the 10 patients positive for nasopharyngeal-swab SARS-CoV-2 nucleic acid detection by RT-PCR, were collected from The People's Hospital of Dazu District. SARS-CoV2 open reading frame 1ab (ORF1ab) and nucleoprotein (N) gene were detected with the use of real-time quantitative fluorescence quantitative. Cycling threshold (CT) values of both ORF 1ab and N gene that both less than 35 were considered as confirmed case was provided by the designated hospital for emerging infectious diseases.

4. Results

4.1. Close contacts

According to the investigation of Dazu District CDC, case A had a total of 75 close contacts, including 15 relatives and 60 non-relatives. Among the relatives, 9 patients were positive for SARS-CoV-2 nucleic acid detection except for his wife, daughter, son, sister, sister-in-law and niece. Family relationships are shown in Fig. 1.

4.2. Epidemiology

Case A was born in Dazu District, and lived in Foshan, Guangdong, China for a long time. On December 18, 2020, he returned to Chongqing West railway station by high-speed rail, and then to Dazu District by coach. On January 1, 2020, he went to Hunan province for a commercial meeting, returned home 4 days later via high-speed rail, went to Guangzhou thereafter via the same vehicle on January 15, and returned to Dazu by car on January 17 (passing through Wuhan). He had dinner with his father (case B), younger aunt (case C), younger brother (case D), cousin (case E), uncle (case F), and older aunt (case G) several times between January 19, 2020 and January 24, 2020. Since January 24, case F lived in case G's house, and case G lived with her husband (case H) and son (case J). On January 28, case A had dinner with case I, the mother of case E, and they stayed together. On January 19, case A had a cough and felt fatigue, then consulted the doctor that day; a chest CT scan showed scattered multiple ground-glass shadows in the bilateral lung periphery, and final confirmation was verified by positive novel coronavirus nucleic acid detection based on two nasopharyngeal swabs. Cases B, C, D, E, F, G, H, I and J were confirmed by contact-tracing and screening with typical symptoms of fever, cough, and fatigue, and the incubation period was 2–14 days, the average incubation period was 7 (SD 2.59) days. The chronology of symptom onset and identification of positive SARS-CoV-2 findings on RT-PCR and CT among the family cluster are shown in Fig. 2.

4.3. Demographics and Clinical manifestations

The 10 individuals infected with SARS-CoV-2 were of clustering onset; the average age was 56.5 years (SD 11.16), including six men and four women; two of the patients had underlying diseases. Patients showed clinical manifestations of dry cough (70%, 7/10), fever (70, 7/10), fatigue (30%, 3/10), diarrhea (10%, 1/10), shortness of breath, nausea, itchy throat, and chills. According to the clinical classification criteria, one patient was mild-type (10, 1/10), six were ordinary-type (60%, 6/10), and three were severe type (30%, 3/10) infection (Table 1).

4.4. Laboratory examinations

Only one case had reduced WBC and platelet counts owing to complications of liver cirrhosis, whereas the rest had normal counts for both. Except for one case with normal absolute value of lymphocytes, the rest had lower values. Eight cases had increased CRP values up to varied extents. Four patients had reduced partial pressure of oxygen (PO2), out of which, three were severe cases; The CT values of nasopharyngeal-swab RT-PCR for the three severe cases were lower than those of other patients, and CD4+ lymphocyte counts were reduced to different extents, with a minimum of 61 cells/μL (reference value: 355-1213 cells/μL). NLR was higher than 10 in these three severe cases, the others being between 1.29 and 6.14. All cases had normal PCT, creatinine, coagulation function, influenza A/B virus antigen, and respiratory virus antigen (Table 2).

4.5. Chest CT

Chest CT showed ground-glass shadow, fuzzy shadow, or nodular shadows, mainly in the lung periphery. Eight cases (80%, 8/10) involved the bilateral lungs and two cases involved the unilateral lung; subpleural lesions were seen in two cases and interstitial pulmonary diseases were involved in 2 cases. The severe cases of A, G, and I had extensive lesion distribution, as shown in Fig. 3.

5. Discussion

According to previous investigations [4], the initial confirmed cases
of COVID-19 shared a history of exposure to seafood markets in Wuhan. However, with the development of the epidemic, studies in several provinces and cities in China have identified the phenomenon of family aggregation in this outbreak, which accounts for 50 to 80% of all confirmed cases [5]. In this area, 14 cases were confirmed with 10 of whom sharing the same family relationship. Characteristics of the 10 familial clusters were as follows: the initial case, Case A, had a history of Wuhan stay; Case B, C, D, E, F, G, and I were infected during family
meals, among which, Case E and F took the same transportation means.

Table 2
Baseline characteristics and clinical manifestations of the 10 COVID-19 cases.

| Case  | Gender | Age  | Underlying diseases | First symptom  | Concomitant symptom | Clinical classification  |
|-------|--------|------|---------------------|----------------|---------------------|------------------------|
| Case A| male   | 48 y | no                  | cough and fever| fatigue             | severe                 |
| Case B| male   | 70 y | no                  | fever          | no                  | ordinary               |
| Case C| female | 51 y | no                  | fever          | no                  | ordinary               |
| Case D| male   | 43 y | no                  | diarrhea       | no                  | ordinary               |
| Case E| female | 47 y | no                  | fatigue        | chill and dry cough| ordinary               |
| Case F| female | 54 y | no                  | dry cough and fever| itchy throat    | ordinary               |
| Case G| female | 66 y | no                  | cough and fever| fatigue, nausea, and shortness of breath | severe |
| Case H| male   | 71 y | Liver cirrhosis     | cough          | fever               | mild                   |
| Case I| female | 71 y | no                  | cough          | fever               | severe                 |
| Case J| male   | 44 y | hypertension        | cough          | no                  | ordinary               |

Table 2
Laboratory indicators of the 10 COVID-19 cases.

| Case  | WBC $10^9$/L | Lymphocyte $10^9$/L | CRP mg/L | NLR | CD4 cells/µL | RT-PCR-CT values 1ab N gene | PO2 mmHg | PCT ng/mL |
|-------|--------------|---------------------|----------|-----|--------------|-------------------------------|----------|----------|
| CaseA | 7.62         | 0.59                | 55.78    | 10.47 | 61           | 19.19                         | 19.85    | 63.20     |
| Case B| 6.12         | 0.43                | 7.01     | 4.58 | 452          | 27.62                         | 27.60    | 83.40     |
| Case C| 5.50         | 0.78                | 48.54    | 5.45 | 418          | 32.19                         | 32.75    | 100.23    |
| Case D| 6.44         | 0.77                | 12.75    | 6.14 | 618          | 33.42                         | 32.04    | 88.61     |
| Case E| 4.22         | 0.65                | 13.51    | 4.82 | 399          | 33.58                         | 34.54    | 89.20     |
| Case F| 4.26         | 0.96                | 48.51    | 2.93 | 402          | 27.60                         | 27.73    | 78.14     |
| Case G| 4.49         | 0.46                | 33.47    | 10.13 | 180          | 25.01                         | 25.61    | 70.11     |
| Case H| 2.77         | 0.99                | 1.66     | 1.29 | 425          | 27.02                         | 27.60    | 96.18     |
| Case I| 7.96         | 0.60                | 35.84    | 11.35 | 348          | 26.29                         | 26.73    | 72.34     |
| Case J| 6.44         | 1.48                | 2.67     | 2.80 | 688          | 27.93                         | 27.90    | 125.05    |

WBC = white blood cells, Lymphocyte = lymphocyte absolute values; CRP = C-reactive protein; NLR = neutrophil-lymphocyte ratio; CT = cycling threshold; ORF1ab = open reading frame 1ab; N gene = ucleo protein; PO2 = partial pressure of oxygen; PCT = procalcitonin;
of these cases. Previous studies [14,15] showed that PCT is normal during virus infection and that the specificity of predicting bacterial infection is higher than that of CRP. Therefore, the routine use of antibiotics is not recommended for COVID-19 patients in the absence of PCT elevation.

As is well known, viral infection is closely related to the human immune system [16,17]; good immune function can help the body to eliminate foreign microorganisms, control infection, and eventually restore health. Wang [17] analyzed the correlation between changes in the immune system and the disease itself and reported that CD3, CD4, and CD8 T cells are significantly diminished in the first week of the infection. The patients’ conditions improved as CD4 T lymphocytes became normal; in contrast, it indicates the deterioration of diseases related to cellular immunity damage. Recently, Guo et al. [18] analyzed the clinical data of patients with viral pneumonia and found that the absolute counts of CD3 + T cells, CD3+CD4 + T cells, and CD3 +CD8 +T cells in the group that died was significantly lower than those in the surviving group, indicating the impairment of cellular immunity as well. In the severe-type in our study, the CD4 count for Case A was 61 cells/μL, for Case G was 180 cells/μL, and for Case I was 348 cells/μL, whereas the CD4 counts were all above 399 cells/μL for other patients, with both ordinary- and mild-types, suggesting decreased cellular immunity at the onset of disease in severe patients.

Currently, the fluorescence-based real-time RT-PCR method is widely used to detect SARS-CoV-2 nucleic acids [19–22]. Although at present the nucleic acids of SARS-CoV-2 cannot be quantified, it is known that the lower the RT-PCR-CT value during amplification, the higher the virus load in the specimen being examined [23] and vice versa. With recovery of the patient’s condition, the CT values can change from low to high, and therefore, the communicability of the patient as an infectious source also decreases [24]. In this study, the RT-PCR-CT values in three patients with severe-type infection were lower than those in the rest; specifically, in case A, the RT-PCR-CT was 19.19, implicating a high viral load and the strong infectivity of this patient.

Based on these data, we consider a higher NLR, lower CD4 counts, and lower RT-PCR-CT values likely to predict severity of the disease at the early stage. Lower RT-PCR-CT values also indicate the infectivity of the patient. Therefore, the three parameters can be used to predict the prognoses of patients. Certainly, the clinical significance of NLR, CD4 counts, and RT-PCR-CT values need to be verified further using larger sample sets.

Ethical Approval

This study was approved by the Ethics Commission of The People’s Hospital of Dazu District. Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Fig. 3. Chest CT images of the 10 COVID-19 cases.

**Authors’ contributions**

XYX conceived the study. XYX, JW and HLL collected the data. XYX and HLL analyzed the data. XYX and JW wrote this article. BJ and WXH revised it. HX supervised study conduct. All the authors have read and approved the final version of this manuscript.

**Funding**

The study was supported by the Key Funding for COVID-19 Clinical Investigation (Special and Urgent item) by Chongqing Medical University and also supported by the Medical Research Project of Science and Health Union from Chongqing, China (2019ZDMX042)

**Declaration of Competing Interest**

The authors declare that there are no competing interests.

**CRediT authorship contribution statement**

**Xiao-ying Xia:** Conceptualization, Methodology, Investigation, Formal analysis, Writing - original draft. **Jing Wu:** Investigation, Writing - original draft. **He-lei Liu:** Investigation, Formal analysis. **Hong Xia:** Supervision, Funding acquisition. **Bei Jia:** Writing - review & editing, Supervision, Funding acquisition. **Wen-xiang Huang:** Writing - review & editing.

**Acknowledgments**

We acknowledge all health-care workers involved in the diagnosis and treatment of patients in Dazu Chongqing. We thank the clinical laboratory department from The People’s Hospital of Dazu District and Dazu Center for Disease Control and infection (CDC) for providing data for patients with SARS-CoV-2.

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