

Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China

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Summary SARS-Coronavirus-2 carriers occurred more often in middle aged people who had close contact with infected family members. Most asymptomatic cases at the time of hospital admission will develop to mild and ordinary COVID-19 during hospitalization.

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Abstract An epidemic caused by SARS-Coronavirus-2 infection has spread unexpectedly in Wuhan, Hubei Province, China since December 2019. It is rarely reported about asymptomatic cases screened from close contacts. We study epidemiological and clinical outcome of 55 asymptomatic carriers who were laboratory-confirmed positive for the SARS-Coronavirus-2 by testing the nucleic acid of the pharyngeal swab samples. The evidence showed that asymptomatic carriers occurred more often in middle aged people who had close contact with infected family members. The majority of the cases developed to be mild and ordinary COVID-19 during hospital.

Key words: SARS-Coronavirus-2; asymptomatic infection; outcome

Introduction

SARS-Coronavirus-2 (SARS-CoV-2) is the focus of global attention which attributed to an outbreak of a febrile respiratory illness since December 2019 in Wuhan, Hubei Provinceⁱ. It was reported that the virus transmitted from human to human^{ii,iii}, especially in family members^{iv}. Prompt public health measures including intensive surveillance, epidemiological investigations have been taken in China. According to the latest recommendation, 2019 novel coronavirus disease (COVID-19) is classified into four types: mild, ordinary, severe and critical cases. Mild and ordinary cases had good prognosis but severe cases, especially those critical cases always presented systematic organic dysfunction and prolonged hospitalization with impaired recovery^{v,vi}. To date, no obvious breakthrough in the treatment of severe coronavirus infection has been identified. Previous report indicated that the onset of symptoms may help physicians identify the patients with poor prognosis and meticulous supportive care was effective^{vii}.

Shenzhen City is located in the southern part of Guangdong, China, and accounts for approximately 70% of migrant people. After the traditional Chinese New Year holidays, massive human movement appeared. Since the first clinical case of COVID-19 was reported on January 11, 2020, Shenzhen has become one of the main epidemic areas of COVID-19. Close contacts are isolated and monitored at home or at designated hotel and more and more asymptomatic cases were found. So we reviewed the asymptomatic cases that were laboratory-confirmed positive for the SARS-CoV-2 by testing the nucleic acid of the

pharyngeal swab samples. A retrospective analysis was carried out about the clinical outcome of 55 asymptomatic cases infected with SARS-CoV-2 admitted in the Third People's Hospital of Shenzhen, China.

Methods

Ethical consideration

This study was approved by the Ethics Committee of the Third People's Hospital of Shenzhen, China, on February 23; 2020. Informed consent was obtained from all the patients or their guardians.

Clinical classification

1. Mild cases: clinical symptoms were mild without pneumonia manifestation through image results; 2. Ordinary cases: having fever and other respiratory symptoms with pneumonia manifestation through image results; 3. Severe cases: meeting any one of the following: respiratory distress, hypoxia ($SpO_2 \leq 93\%$), abnormal blood gas analysis: ($PaO_2 < 60\text{mmHg}$, $PaCO_2 > 50\text{ mmHg}$); 4. Critical cases: meeting any one of the following: Respiratory failure which requires mechanical ventilation, shock, accompanied by other organ failure that needs ICU monitoring and treatment.

Data collection

We obtained data from medical records. All onset symptoms, physical examination, (all study subjects were asymptomatic on admission, when they developed symptoms during hospitalization, these were recorded), laboratory and image data including past and personal history were collected. The asymptomatic case's inclusion criteria were: (1) Asymptomatic cases of laboratory-confirmed positive for the SARS-CoV-2 by testing the nucleic acid of the pharyngeal swab samples^{viii} after their family member's diagnoses of COVID-19. (2) Patients

admitted to the Third People's Hospital of Shenzhen from January 11, 2020 to February 29, 2020. The exclusion criteria were suspected cases of COVID-19 with symptom such as fever, cough, fatigue, bad appetite, diarrhea and headache, etc at admission.

Laboratory data include whole blood count (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), liver and renal function, electrolytes, coagulation test, procalcitonin, interleukin-6, lactate dehydrogenase (LDH) and creatine kinase (CK). Pharyngeal swab samples were collected for the SARS-CoV-2 test on admission day.

The collected samples, stored at 2-8°C, were sent with ice to Center for Disease Control and Prevention (CDC) of Shenzhen. Viral RNAs were extracted from pharyngeal swabs using the QIAamp RNA Viral Kit (Qiagen, Heiden, Germany) and quantitative reverse transcription polymerase chain reaction (qRT-PCR) was performed using the primers and probes targeting the ORF1ab and N genes of SARS-CoV-2 as recommended by China CDC^{ix}. 2 contiguous negative nucleic acid tests (sampling interval of at least 1 day) were considered as virus clearance.

All acquired data were crosschecked by two investigators to ensure that there was no duplicated information. In this study, investigators were trained to use a standardized questionnaire to collect epidemiological information immediately after the patients were admitted, with face-to-face interviews with the patients or their guardians and relevant medical staff.

Statistical analysis

Basic descriptive analyses were performed in all patients. IBM SPSS statistics was used for statistical analyses.

Results

General characteristics of the asymptomatic confirmed cases

55 asymptomatic cases were identified with SARS-CoV-2 infection after their infected family member's illness onset. Of the asymptomatic cases, 22 were male and 33 were female aged from 2 to 69 years old and the median age was 49 years old. The proportion of asymptomatic cases aged from 30 to 49 years old was 30.9% (table 1). More than half of the cases are native population of Hubei Province. 70.9% of the asymptomatic cases developed to be ordinary type of COVID-19 in the end.

Clinical characteristic of the asymptomatic confirmed cases

Of the 55 cases, only 7 cases had mild cough and 7 cases had low fever 3-5 days later (2 cases presenting both cough and fever). A two years old boy was diagnosed as common COVID-19 after testing for three times within two weeks. In spite of being asymptomatic cases, the 55 cases were admitted immediately and medical isolation was carried out. The time from hospitalization to illness onset was 1 to 7 days. On admission, all 55 cases had a chest compute tomography (CT). Initial chest CT showed normal in 16 (29.1%, 16/55) cases and no symptoms occurred during hospitalization. CT showed pneumonia in 37 cases on admission. 2 female cases older than 60 years old with SARS-CoV-2 infection were admitted promptly after their family members. Chest CT showed normal on day 1. During the course of hospitalization, the 2 cases presented mild cough and low fever 5 days later, complicated with hypoxia ($\text{SpO}_2=90\%$) and restlessness. Repeated CT showed pneumonia (figure1).

After informed consent was obtained, Lopinavir/Ritonavir was given to 55 cases as initiated therapy for 7 days. 2 cases with hypoxia received intravenous immunoglobulin 10 g/day and methylprednisolone (1-2 mg/kg/day) therapy for 3 days. Heated humidified high-flow nasal cannula (HHHFNC) was used for 5 days. Eventually, the 2 patients recovered without complication. None of the cases were admitted to ICU.

All the cases recovered and were discharged home. Two contiguous nucleic acid tests of nasopharyngeal swabs (sampling interval of at least 1 day) turned negative for SARS-CoV-2 after 4 to 21 days. 3 samples of sputum from ordinary COVID-19 were negative 3-5 days later after nasopharyngeal swabs' testing. 8 cases had hypertension history. There was 1 case with past history of cholecystitis. Hypothyroidism, Chronic pharyngitis, Hepatitis B and asthma were also presented in 1 patient's past history respectively. Epstein Barr Virus and Mycoplasma pneumonia were diagnosed serology in 1 and 3 cases respectively. Neutropenia occurred in 11 cases and lymphocytes below the normal range were seen in 11 cases. Initial biochemical results showed that elevated CRP, ESR and LDH occurred in 10, 20 and 13 cases respectively (table 2).

Discussion

Over all, of the 55 subjects who presented with asymptomatic SARS-CoV-2 infection in this study group, 14 turned out to be mild, 39 developed ordinary and 2 were severe COVID-19 during hospitalization. Age was significantly associated with asymptomatic occurrence. Asymptomatic cases occurred more often in middle-aged people (30-49 years old). This was

a novel discovery but we should interpret with caution due to a small number of patients with asymptomatic infection.

In this report, we demonstrated 3.6% asymptomatic SARS-CoV-2 infection might take a turn for the worse. Only 2 cases presented typical symptoms^x such as mild cough and fever 3-5 days later during hospitalization. Those family members with fatigue and dry cough especially with fever were observed easily but asymptomatic members were ignored. So large number of asymptomatic cases were actually a source of SARS-CoV-2 infection but considered as “health people” before they were screened out. The risk of virus spread within asymptomatic infection patients, suggest that it is important to timely supervise the family members of COVID-19.

It is evident that family cluster transmission of SARS-CoV-2 was one of the main modes of transmission^{xi}. Previous study indicated that young cases (< 15 years old) were prone to be asymptomatic^{xii} in Nanjing. We found that asymptomatic cases occurred more often in middle aged people in Shenzhen. So nucleic acid testing would be crucial to screen asymptomatic infections in this population.

Previously study indicated that CRP and LDH may be predictors of disease severity^{xiii}. Elevated C-reactive protein (CRP), Lactate dehydrogenase (LDH) and white blood cells (WBC) occurred in 10, 13 and 1 patients respectively. 11 patients (including the 2 severe cases) presented leukopenia. Here we found no relationship between the clinical type and the laboratory results. Further investigation should be carried about the topic.

We discovered 3 cases' sputum turned negative 3-5 days later than nasopharyngeal swabs. Kelvin^{xiv} reported that Serial saliva viral load monitoring generally showed a declining trend. So we recommend that viral load in sputum sample is crucial in late stage of the disease as previous report recommended^{xv}.

Several limitations exist when interpreting the results. First, the data are retrospectively analyzed. So the possibility of recall bias cannot be ruled out. Second, we collected data for most but not all laboratory data. However, Shenzhen is an international city with adequate public health interventions and medications. The enrolled cases were identified from systematic screening of the family members of COVID-19. All asymptomatic cases were admitted to the Third People's Hospital of Shenzhen, the only designated hospital in Shenzhen. So the study population has representativeness of the whole city.

Conclusions

In summary, this report presented the epidemiological and clinical characteristics of cases with asymptomatic SARS-CoV-2 infection in Shenzhen. In this study, asymptomatic infection was more common in middle aged people; the proportion of severe type was low and ordinary type was high. To better minimize the risk of SARS-CoV-2 infection, preventive measures are suggested to focus on high-risk populations. Negative nucleic acid of sputum samples was recommended to the isolation of the infection source.

Notes

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Conflict of interest

The authors declared no conflict of interest.

Contributions

Yanrong Wang and Yingxia Liu searched the literature, conceived the study, Lei Liu designed the study, Xianfeng Wang interpreted the results, and drafted the report. Nijuan Luo and Ling Li collected the data.

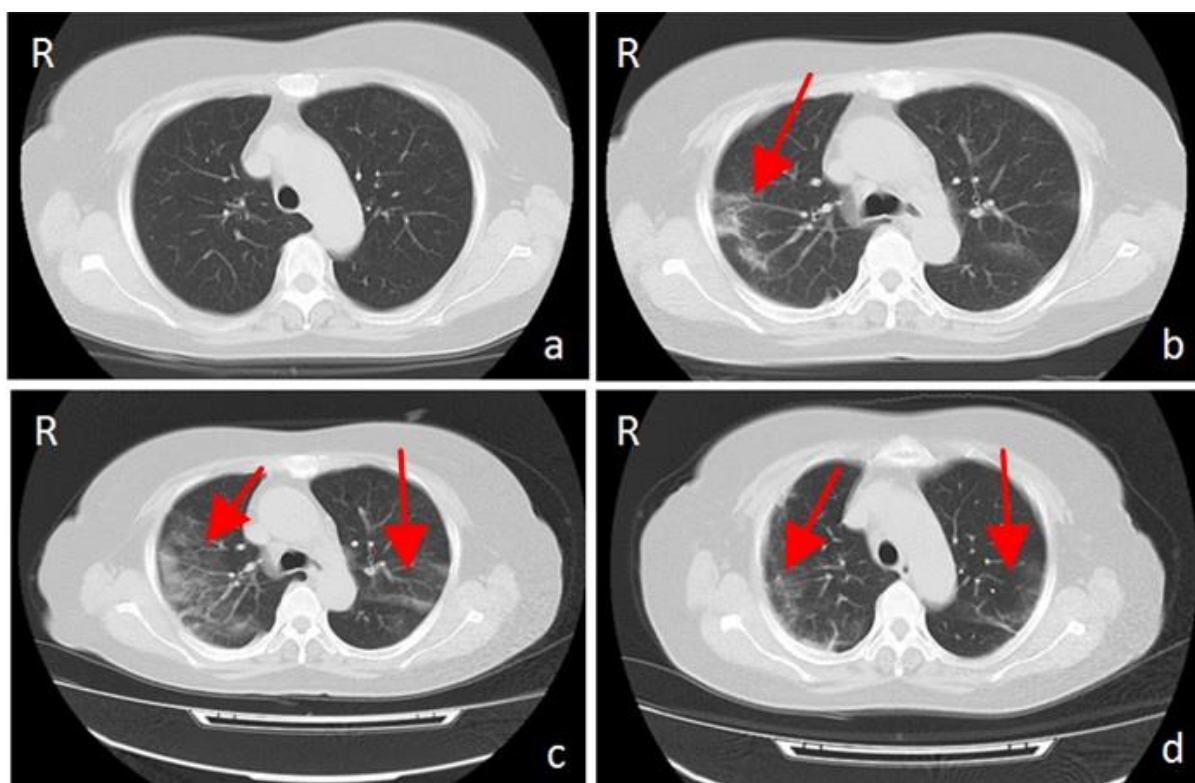
Reference

Table 2 Laboratory and general results of the 55 cases

Data	N
Elevated WBC ($> 1.5 \times 10^9/L$)	1
Decreased WBC ($< 4.0 \times 10^9/L$)	11
Decrease lymphocyte ($< 1.5 \times 10^9/L$)	11
Elevated CRP ($> 8\text{mg/L}$)	10
Elevated ESR ($> 20\text{mm/h}$)	20
Elevated LDH ($> 250\text{U/L}$)	13
<i>Complicated infection</i>	
Epstein Barr Virus*	1
Mycoplasma pneumonia*	3
Time from hospitalization to illness onset** (days)	5(1-7)
Time from positive to negative nucleic acid (days)	10(4-21)

WBC: white blood cell, CRP: C-reaction protein, ESR: erythrocyte sedimentation rate, LDH: Lactate dehydrogenase; *Epstein Barr virus and Mycoplasma pneumonia infections were diagnosed serology; **illness onset: symptoms appeared or abnormal CT

Figure 1



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Figure legends

Figure 1. Representative images of the thoracic CT of severe patient: (a) normal thoracic CT scans on admission day 1; (b) diffuse patchy shadowing on day 5; (c) more diffuse patchy shadowing on day 8; (d) CT of recovery stage on day 15