

Clinical characteristics of non-pneumonia COVID-19 infection adults in Shanghai, China

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Research

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Abstract

Background Adult patients diagnosed as COVID-19 in Shanghai were accepted in Shanghai Public Health Clinical Center. We found around 4.91% of cases showed non-pneumonia on CT imaging when they were confirmed. Understanding the characteristics of non-pneumonia cases is of great significance to guide clinical treatment and improve prevention and control measures.

Methods All dataset of demography, epidemiology, clinical manifestation, laboratory test, diagnosis, classification, condition change, treatment and outcome were obtained by retrospective investigation.

Results 16 cases were confirmed COVID-19 with non-pneumonia with clear epidemiological history. The median age of patients was 37 years old and 81.25% were female. The median incubation period was 15.25 days. 75% patients were familial clusters. These patients were presented with mild clinical manifestations, such as bronchitis, common cold and asymptomatic infection with or without laboratory abnormalities. 4(25%) cases had underlying diseases. 3 of them had mild pneumonia on chest CT imaging during hospitalization. All of the cases were cured and discharged after support treatment.

Conclusions A few of adult patients after COVID-19 infection had non-pneumonia, with mild clinical manifestations and long incubation time. It usually occurred in young women and history of family aggregation. The mild clinical symptom may be caused by the decreasing pathogenicity after multiple generation of virus replication. However, we should be on alert that the virus is still contagious to human. Therefore, an intensive attention should be paid to these patients to avoid misdiagnosis and overlook, because these patients are potential viral source in infection of other people.

Introduction

The novel coronavirus-2019 (2019-nCoV) was discovered in unexplained viral pneumonia cases in Wuhan by the end of 2019, and was initially named as SARS-CoV-2 by Coronaviridae Study Group (CSG) of the International Committee on Taxonomy of Viruses (ICTV) on MAR 2th [1]. By March 5th 2020, according to the government announcement, 80566 cases had been confirmed in China[2] and 14946 cases had been confirmed overseas. There were 338 confirmed cases in Shanghai[3], in which 326 cases were adults and 16 cases had non-pneumonia CT image manifestations when admission. Although the COVID-19 pneumonia Diagnosis and Treatment Program (the fifth edition)[4] was published on February 8, 2020, some patients with mild clinical symptoms and without evidences of pneumonia on CT image, were easily misdiagnosed when admission. More importantly, misdiagnosis of these patients may lead to transmission and increase the difficulties in prevention and control of 2019-nCoV infection and outbreak. The number of patients in China is still high and the international epidemic situation is deteriorating rapidly, it is of great significance to explore the characteristics of such patients towards guidance and implementation of international prevention and control of the disease.

Patients And Methods

This was a retrospective study. A total of 326 cases were confirmed with positive COVID-19 by pharyngeal swab nucleic acid test in Shanghai Public Health Clinical Center from Jan 20 to Mar 5, 2020. 16 cases (4.91%) showed non-pneumonia on CT imaging when confirmed COVID-19 were enrolled in this study.

Statistical analysis

Statistical description and analysis were carried out for the counting data and the relative number was expressed as constituent ratio.

Results

Patient characteristics

On the day of admission, 16 cases (16/326 = 4.91%) showed non-pneumonia on CT image, including 13 females (81.25%) and 3 males (18.75%). The age ranged from 15 to 64 years old (average 37 ± 12.75 years old), including 3 patients over 60 years old, 2 patients between 40–60 years old, 10 patients between 20–40 years old and 1 patient under 20 years old.

a. Epidemiologic features

All of the 16 cases had a clear epidemiological history. 8 (50%) cases came to Shanghai from Hubei, including 7 cases from Wuhan and 1 case from Xianning. Among the patients living outside Hubei, 4 (25%) cases had contacted with Hubei residents, 3 of whom had been to Wuhan. 4 (25%) non-Hubei residents had neither been to Hubei, nor had contacted with Hubei residents, but they had contacted with other confirmed patients. 12 (75%) cases were familial clusters. They all had no close contact with wild animals. Among the patients in this group (Table 1), the average incubation period of 12 cases was clearly 15.25 ± 4.88 days. The incubation period of 8 cases was over 14 days, ranging from 15–23 days, and all of them were familial clusters. Other 4 (25%) cases had no clear contact history.

Table 1

16 patients were admitted for laboratory examination, incubation period and length of stay

project	White blood cell count($10^9/L$)	Lymphocyte count($10^9/L$)	Platelet count($10^9/L$)	Creatine kinase(U/L)	Alanine aminotransferase(U/L)	Aspartate aminotransferase(U/L)	C-reactive protein(mg/L)	D-din
reference	3.50-9.50	1.10-3.20	125-350	29.00-168.00	7.00-40.00	13.00-35.00	0-10.00	0-0
1	9.40	1.59	240	87	23	18	< 3.0	0.1
2	5.12	1.93	207	45	13	15	< 0.499	0.1
3	5.78	2.83	257	38	11	14	< 0.499	0.1
4	7.13	1.42	132	32	9	12	< 0.499	0.2
5	5.53	2.11	243	83	75	49	< 0.499	0.2
6	5.49	2.56	210	42	9	14	< 0.499	0.2
7	4.13	2.25	212	56	9	17	< 3.0	0.6
8	9.24	2.69	322	65	29	17	< 0.499	0.2
9	6.73	2.86	217	48	11	15	< 3.0	0.1
10	5.52	1.83	199	93	21	22	2.51	0.6
11	7.22	2.34	280	73	25	25	< 0.499	0.2
12	5.89	1.40	243	84	17	21	< 0.499	0.3
13	4.58	0.82	182	71	22	29	< 3.0	0.4
14	4.88	1.29	208	57	15	19	< 0.499	0.2
15	4.04	1.49	248	63	17	17	< 0.499	0.2
16	8.50	2.02	187	66	28	26	< 0.499	0.2

b. Underlying diseases

In this group, 4 (25%) cases had definite underlying diseases, including 1 case of hashimoto thyroiditis, 1 case of hypertension and diabetes with a history of percutaneous coronary intervention, 1 case of diabetes with right breast intraductal tumor, and 1 case of chronic renal failure with hypertension.

c. Clinical manifestations

8 (50%) cases began with fever, accompanied by cough, headache, fatigue, and nasal congestion. All of them visited the fever clinic of large hospitals. They met the criteria of suspected cases according to the COVID-19 pneumonia Diagnosis and Treatment Program and were confirmed COVID-19 positive after nucleic acid test. 6 (37.5%) cases had cough and 1 case had dizziness. Their immediate family member was immediately in quarantine after first family member was diagnosed, in which 2 cases (12.5%) were tested positive due to close contact with the confirmed family member, though they were asymptomatic during nucleic acid test.

Laboratory Results (table 1)

On the day of admission, white blood cells, platelets, c-reactive protein and creatine kinase levels of all cases were normal. Some cases had only slight laboratory abnormalities, including 1 (6.25%) case with lymphocytopenia, 1 (6.25%) case with elevation of alanine aminotransferase and aspartate aminotransferase, 2 (12.5%) cases with elevation of D-dimer, 8 (50%) cases with elevated erythrocyte sedimentation rate. Arterial blood gas test were all normal.

Radiological Data

On the day of admission, Chest CT image of 16 cases showed no pneumonia. 8 (50%) cases showed no abnormality. 5 (31.25%) cases had pulmonary nodules. 2 (12.5%) cases had obsolete lung lesions. 1 (6.25%) case had emphysema, bullae and obsolete lung lesions.

Inpatient Changes And Clinical Outcomes

All of the cases in this group were cured and discharged after support treatment. The length of hospitalization was 7–35 days (average 16.44 ± 6.62 days). During the hospitalization, all patients were not treated with oxygen therapy. Small pieces or ground glass pneumonia on chest CT image were observed in 3 cases on the 6th, 7th and 8th day after hospitalization, respectively (Fig. 1). All of the 3 cases (26, 62 and 64 years old respectively) had underlying diseases,

but had no obvious discomfort. All of them were recovered and discharged. One of them had delayed discharge for 30 days because of the sustained positive nucleic acid test of stool sample, even though the lesions in chest CT image were completely absorbed.

Discussion

Analysis of 16 adult cases in Shanghai confirmed that young people infected with COVID-19 was likely asymptomatic and had normal chest CT at the initial stage of the disease, consistent with the basic characteristics of the disease. Most of them were female and accounted for 81.25%, that was inconsistent with the results of previous reports. A retrospective study[5] in 99 patients showed that male(67.7%)and female(32.3%)were infected with COVID-19 in Wuhan Jinyintan hospital from January 1 to January 20. The prevalence of COVID-19 infection between male and female was similar to that of SARS and MERS. It was also reported that females developed milder symptom than males after infection, that was consistent with our finding in this study. We speculate that females has low susceptibility to virus infection and milder symptoms possibly because of the protective role of X chromosome and gonadal hormone, because a body of evidences showed that female hormone has immune regulatory property by suppressing innate and adaptive immunity during immune defense against pathogen infection and pregnancy, etc. It is also possible that females in this group were likely to spend more time at home than males, had more close contact with other family members. As a result, their family member was susceptible to COVID-19 infection, but with milder symptoms. Indeed, we observed 11 female cases, that accounted for 91.67% cases in this study. Thereby, we should pay attention to female patients with mild symptoms after exposure to COVID-19, though COVID-19 was more prevalent in male than female as we observed.

50% of the cases in this group were admitted to fever emergency room due to fever. Chest CT scans showed no pneumonia. All patients had clear epidemiological histories. Considering together with the results of blood tests, COVID-19 infection should not be excluded among these patients. These patients were finally quarantined in single compartment and confirmed positive SARS-CoV-2 after nucleic acid test. We conclude that a comprehensive record of epidemiological history was key to correct diagnosis. After these patients were diagnosed, the close contacts of these patients were subjected to immediate screening by nucleic acid test. Those people with mild clinical symptoms or history of close contacts with the diagnosed patients should be in quarantine immediately. Because we observed 2 asymptomatic patients that were tested positive of SARS-CoV-2 in this group, it was strongly recommended that close contacts were at high risk and should be screened for SARS-CoV-2 by nucleic acid test to avoid misdiagnosis. Non-pneumonia, asymptomatic or mildly symptomatic patients are moving carriers of contagious virus. They should be diagnosed and isolated in time. If not, the virus would rapidly spread to other close contacts, increasing the risk of virus infection outbreak. Therefore, the identification and control of non-pneumonia cases is essential to the early control of COVID-19 infection and outbreak.

The number of cases in this group is not large, but 50% (8 cases) had an incubation period of more than 14 days, which was quite different from recent reports on large samples in China and other countries. The research team led by Zhong Nanshan[6] reported that the median incubation period of 1099 cases in China was 4 days and 13 cases were over 14 days. It was noted by author that only 291 cases had record of medical information and the incubation period was roughly estimated because there was uncertainty of exact date of infection. The recall bias may inevitably affect the estimate accuracy. Some patents may be excluded for statistical analysis, because they experiences mild symptoms and recovered after received treatment at home. In addition, those people exposed to such patients should be not excluded as well. High percent of patients had incubation period over 14 days, that caused a significant problem for early diagnosis, isolate and treatment. In addition, those patients with non-pneumonia, mild symptoms and long incubation period are potential source of infection to other people. The high incidence rate suggests that the virus was highly contagious to their family member. If the prevention and control are inappropriate, it may cause widespread of this disease. Due to clear epidemiological history of these patients in this group, they were immediately isolated and given nucleic acid test for SARS-CoV-2. After infection of SARS-CoV-2 was confirmed, their family members and other close contacts were isolated and closely observed for certain time period, so that transmission to other people was avoided. With the increasing cases with a long incubation period and reoccurrence of positive test of SARS-CoV-2 after discharge from hospital, it become critical to continue to monitor their health status at home for 14 days. These patients should live alone in compartment, always wear face masks, and reduce outdoor activities according to the COVID-19 pneumonia Diagnosis and Treatment Program (the sixth edition)[7].

In the included cases, 4 (25%) cases had underlying diseases, 3 of them developed mild pneumonia after follow-up, 2 of them were over 60 years old. According to our dataset, age was a high risk factor for patients developing COVID-19 pneumonia, consistent with the results reported by other groups[5, 6]. Patients usually developed COVID-19 pneumonia to a peak level 7–10 days after infection according to our observation. During this time period, symptoms and image findings were greatly exacerbated. All of the 3 cases had similar developing courses. However, pneumonia was not developed among 12 patients who had no underlying diseases. According to our experiences, it seems that the pathogenicity of COVID-19 was gradually decreased after multiple generations, because we observed that some patients were asymptomatic or had only a mild clinical symptom after infection. In this case, laboratory results were normal or slightly abnormal. CT examination did not show pneumonia. However, a few of elderly or patients with basic diseases developed slight pneumonia after infection, and they were finally recovered and discharged after COVID-19 nuclei acid testing negative.

Following the deep understanding of this disease, the name of this disease was constantly revised. On February 8, 2020, Chinese health commission temporarily named "pneumonia caused by new coronavirus infection "as" Novel coronavirus pneumonia" (NCP)[8]. On February 11, 2020, WHO named "2019-nCoV diseases" as "Coronavirus Disease 2019 (COVID-19)"[9]. The most common type is COVID-19 pneumonia. Because patients had variable clinical and pathological manifestations after COVID-19 infection, it would be necessary to scientifically classify COVID-19 pneumonia into different categories. For example, in our included patients, 6 cases with only simple bronchitis may be named "COVID-19 bronchitis"; 4 patients with only symptoms of upper respiratory tract infection may be named "COVID-19 cold"; 2 patients without any symptoms may be named "asymptomatic infection of COVID-19". This is in line with the characteristics of respiratory virus infection.

Conclusion

In conclusion, some adult patients had no pneumonia after COVID-19 infection. These patients were characterized with mild clinical manifestation and laboratory abnormalities, prolonged incubation period, familial aggregation and more prevalence in females. We speculate that high passage of virus replication may account for the low pathogenicity of COVID-19, but the virus is still possibly highly contagious. Early screening and diagnosis of non-pneumonia or asymptomatic cases are important measure in prevention and treatment of patients with COVID-19 infection. Not only it benefits patients and prevent the virus outbreak, but also it provides useful information for scientific research in the future. However, due to the limited number of cases in this study, more cases may be required to further confirm our finding in the future. We suggested that the patients without pneumonia should be in quarantine at home or designated place and receive treatment if necessary; the patients with aggravation and pneumonia should be hospitalized for immediate treatment.

Abbreviations

COVID-19, Coronavirus Disease 2019; CSG, Coronaviridae Study Group; ICTV, International Committee on Taxonomy of Viruses; NCP, Novel coronavirus pneumonia; 2019-nCoV, The novel coronavirus-2019.

Declarations

Ethical Approval and Consent to participate

Ethical approval for this study was reviewed and approved by the Ethics Committee of Zhongshan Hospital, Fudan University (Shanghai, China).

Consent for publication

Not applicable

Authors' contributions

LZ and ZLJ conceived the study idea. LZ, TL, LJH and LJG participated in the study design. HYJ, TL and LJG gathered the data and performed the data analyses. All authors interpreted the data analyses. All authors co-wrote and revised the manuscript for intellectual content.

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Conflict of interest

The authors declare no conflict of interest. All the authors listed have approved the manuscript.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

References

1. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, *et al.* **Severe acute respiratory syndrome-related coronavirus: the species and its viruses—a statement of the Coronavirus Study Group.** *bioRxiv.* 2020; published online Feb 11. DOI: 2020.02.07.937862 (preprint).
2. China National Health Commission. update on the novel coronavirus pneumonia outbreak. **Beijing, national health commission of the People's Republic of China** 2020. March 5, 2020. <http://www.nhc.gov.cn/xcs/yqtb/202003/6e02433f7786402d8ea162fb5b80b5a0.shtml>.
3. Shanghai Municipal Health Commission. Update on the novel coronavirus pneumonia outbreak March 5, 2020. **Shanghai, Shanghai Municipal Health Commission** 2020. <http://wsjkw.sh.gov.cn/xwfb/20200305/1f19f60b947345b283e002b307fde069.html>
4. **New coronavirus pneumonia diagnosis and treatment program (5th ed.) (in Chinese).** 2020 <http://www.nhc.gov.cn/yzygj/s7653p/202002/3b09b894ac9b4204a79db5b8912d4440.shtml>
5. Chen N, Zhou M, Dong X, Qu J, Gong F, *et al.* **Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.** *The Lancet.* 2020. 395(10223): p. 507-513.
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, *et al.* **Clinical Characteristics of Coronavirus Disease 2019 in China.** *The New England journal of medicine.* 2020. DOI: 10.1056/NEJMoa2002032.
7. **New coronavirus pneumonia diagnosis and treatment program (6th ed.) (in Chinese).** 2020 <http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2.shtml>
8. China National Health Commission. February 10, 2020 **Notification of the national health commission on the provisional designation of new coronavirus pneumonia.** 2020. <http://www.nhc.gov.cn/yzygj/s7653p/202002/18c1bb43965a4492907957875de02ae7.shtml>

Figures



Figure 2

CT images of pneumonia in 3 cases during hospitalization