Report of a COVID-19 Case Combined with HIV Infection

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Case Report

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Abstract

Background: Confirmed as a familial clustered case, a COVID-19 patient displaying established symptoms was simultaneously diagnosed with an HIV infection, and treated with several antiviral and compassionate drugs.

Case presentation: The upper respiratory tract Nucleic Acid Testing (NAT) for the novel coronavirus continued to be positive for consecutive 49 days. During the course of treatment, it was observed that the other six cases in the family were non-HIV infected and displaying common Covid-19 symptoms, the familial cluster received parallel treatment along with the aforementioned patient, and the median time for the NAT to present as negative was 29 days.

Conclusions: The results of this research indicate that the novel coronavirus attacks T lymphocyte subsets, andfurther studies with larger sample sizes are required to verify how the immune escape mechanism of the new coronavirus interacts with HIV infection.

Background

As of December, 2019, an outbreak of a novel coronavirus disease (COVID-19)(1, 2) was reported in Wuhan, China,(2)which has subsequently affected virtually all nations worldwide. Following May27, about 2,897,985 cases have been confirmed and reports have corroborated over 347,397 deaths. This research investigates the clinical features of a patient infected with concurrent severe acute respiratory syndrome coronavirus (3) (SARS-CoV-2) and HIV. These findings will facilitate understanding of the immunology and its implications for therapy of COVID-19 complicated with HIV.

Case Presentation

As a suspected case of COVID-19, a 51-year-old female patient admitted to the hospital presented with the symptoms of a “cough, runny nose, and a fever for 2 days” and a maximum body temperature of 37.8℃. The family cluster included seven family members; the patient’s husband, daughter, son-in-law, son, two grandchildren. Within this group the oldest was 65 years old and the youngest was 2 years old. The history reported close contact between the members within the past 10 days. Their upper respiratory tract viral RNA tests were positive for SARS-CoV-2 RNA.

SARS-CoV-2 RNAdetection method: Duplex Real-Time PCR Diagnostic Kit for Rapid Detection of 2019-nCoV ORF1ab/ Ngene.HIV antibodies detection method: the Abbott chemiluminescence method, ZhongxiaoKeju colloidal gold method, Meieril colloidal selenium method, etc. Serum Ab-IgM, Ab-lgGdetection method:colloidal gold method.

Examination of the positive SARS-CoV-2 and HIV case on the day of admission: T 37.2 ℃, P 86 times / min, R 20 times / min, BP 118 / 81mmHg. Conscious, no skin rashes or subcutaneous bleeding points on the whole body, superficial lymph nodes in the whole body did not display swelling upon clinical touch

examination, the breath sounds of both lungs were thick, and no moist rales or rhonchi were heard in the lungs. An abdominal examination revealed no abnormalities. Blood routine test: White blood cells 4.02 10×9/L, lymphocyte count 1.03 10×9/L, CRP0.3 mg/L. Calcitonin < 0.05 ng/mL, and erythrocyte sedimentation rate 14 mm/h. The arterial blood gas analysis was normal. A chest CT (Image A) showed multiple ground-glass nodular-like shadows (GGO) under the left lower lobe pleura. HIV antibodies tested positive. The WB band gp160 gp120 p66 p55 / 51gp41p31p24p17 indicated that the HIV-1 antibody was positive and HIV-RNA 27544cp/ml.HIV-1 resistance measurement shows sensitivity to tenofovir (TDF), lamivudine (3TC), lopinavir / ritonavir (LPV/r), and 16 other drugs. IL-6, IL-10 and TNF-α were not tested. The patient had been separated from her husband for an approximate 2 years and confirmed HIV transmission from her male partner.

The six family members were tested for HIV antibodies, her husband received testing twice, and all presented negative results. All patients provided written informed consent before enrolment in this study. All cases receive ECG examination before receiving drug treatment, particular attention was given to the ECG monitoring of the patient receiving Hydroxychloroquine Sulfate.

On January 22, 2020, the patient's daughter came into proximity with her, arriving from a residence in Hubei, China, after a family gathering. A cluster of infections was reported in Hubei, while other family members had no history of stay in other places.

According to the Treatment Program issued by the National Health and Health Commission of China, the cases in this cluster clearly has only one inducing case; no other potential sources of infection are plausible. This conclusion is based on the history of the first case imported from the Wuhan epidemic area in Hubei, China, one day before the onset of illness. Along with a close contact history, it is clear that six family members had fever, imaging evidence of pneumonia, low or normal white blood cell count or low lymphocyte count, and SARS-CoV-2 RNA positive detection by upper respiratory tract samples. In light of the above diagnostic criteria, the case was diagnosed as COVID-19 common type and an asymptomatic period of HIV infection; her husband was diagnosed with COVID-19 common type, type 2 diabetes; the other 5 cases were diagnosed as COVID-19 common type (Fig. 1).

In accordance with the Treatment Program of China, compassionate drug use was given to seven family members 3based on in vitro evidence of SARS-CoV-2 inhibition. Table 1 lists the detailed treatment of this case. Table 2 lists the results of the SARS-CoV-2 RNA test, which continued to be positive, and serum Ab-IgM, Ab-IgG test which continued to be negative. Table 3 lists the comparison reports of $CD4^+$, $CD8^+$, and lymphocytes during the treatment. The chest CT lesions increased slightly 5 days after admission (Image B), a small amount was gradually absorbed 14 days after admission, and the chest CT lesions still existed 35 days after admission (Image C). A combined highly effective antiretroviral therapy (HAART) on the 37th day after onset, the following drugs was administered: TDF 300mg once / day, 3TC 300mg once / day, and LPV/r 200 / 50mg twice / Day, etc. On the 50th and 51st days after onset, SARS-CoV-2 RNA test was negative, twice in succession, and chest CT lesions were completely absorbed at 51 days after admission (Image D).

In this case, a follow-up review was conducted on the 2nd and 4th weeks after discharge. Chest CT (Image E) showed no abnormalities, and SARS-CoV-2 RNA, Ab-IgM, and Ab-IgG testing were negative, and COVID-19 has been cured.

Discussion And Conclusions

In this case, the clustered incidence of COVID-19 among this family is clear. It can be inferred that the infected virus strains are the same, and the seven patients received parallel treatment in the same hospital. With an approximate gestation period of 6 days, this case is typical, originating during close contact with the source case progressing to the onset of symptoms. This is similar to the communication dynamics reported from Wuhan, China, (4) and the onset time was 5.2 (95% CI 4.3-7.5) days; the time from onset to negative NAT was 49 days for the patient, which was significantly longer than the rest of the 6 members in the family cluster who received negative NAT after a median time of 29 days. One report from Wuhan, China, (5) declared an average time from onset to negative NAT in the infected population was 24.7 days (95% CI 22.9–28.1), with a coefficient of variation of 0.35. In another report from Wuhan, China, (6) the time from onset to negative NAT was 20.0 days (IQR 17.0–24.0). From this it can be understood that the median positive to negative time for NAT of other members of the family is similar to that in domestic reports. Under the consistent conditions of strain virulence, latent infection to onset time, and treatment compared with other family members, it is speculated that a HIV complicated SARS-CoV-2 infection is the main relevant factor for the patient's prolonged virus clearance.

After infection, $CD4^+$ and $CD8^+$ show a protracted and tortuous decline. The rate of decline from $CD4^+$ is relatively large, gradually increasing in distance from $CD8^+$, which eventually leads to the inversion of the ratio of $CD4^+$ / $CD8^+$. Recent studies in China have found that the activity of $CD4^+$ and $CD8^+$ simultaneously inhibited by SARS-CoV-2. In the early stages of infection, $CD4^+$ and $CD8^+$ decreased significantly, but the ratio of $CD4^+$ / $CD8^+$ was not inverted. About 4 weeks after infection, once the symptoms of COVID-19 showed signs of improvement, $CD4^+$ and $CD8^+$ gradually increased, and the ratio of $CD4^+$ / $CD8^+$ also increased in direct proportion. In this case, $CD4^+$ and $CD8^+$ decreased rapidly from day 1 to day 12, which is similar to the report, the difference is that $CD4^+$ and $CD8^+$ reached a plateau period, and in this instance there was no gradual increase in $CD4^+$ and $CD8^+$ from the 2nd to the 4th week of onset. The plateau period may be the result of double infection of SARS-CoV-2 and HIV, resulting in a cumulative suppression of the body's immune function, however, there are no domestic or international publications on whether they are additive or synergistic.

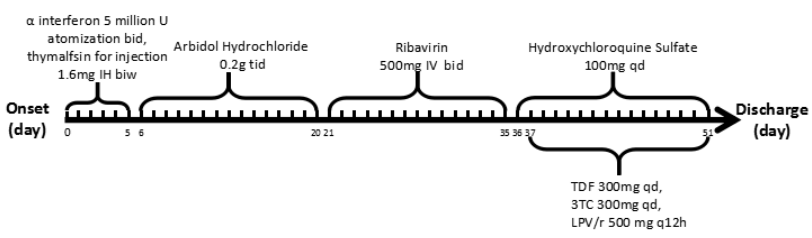
In this case, we also observed significant changes in lymphocytes. Interestingly, the lymphocytes did not show a gradual decline. After treatment with antiviral drugs, the early lymphocytes increased slightly to form a plateau, this coincides with the time at which $CD4^+$ and $CD8^+$ form a plateau. Therefore, we speculate that novel coronavirus attacks not only $CD4^+$ and $CD8^+$, but also T lymphocyte subsets.

This case which is combined with an HIV infection is the most important reason for our meticulous selection of HAART. Based on the following considerations: At present, there are no relevant guidelines or clinical experience to recommend a systematic timing and program for AIDS combined with COVID-19 in accordance to the ideal methodology for initiating HAART. In the early stage of this COVID-19 case, that is, when the immune baseline was close to normal, and regardless of HAART's potential to rebuild or improve immune function, it is unclear whether immune reconstitution inflammatory syndrome (IRIS) and the cytokine storm of COVID-19 in HIV-infected people may be hampered because of the lack of immune inflammatory factors. Two studies reported that patients with frequent severe disease had increased IgG response and higher plasma levels of total antibodies, which was associated with a worse outcome. (7, 8) In this case, with an HIV infection which is being newly treated the baseline of cellular immunity is $CD4^+$ 421 / microliter, $CD4^+$ / $CD8^+$ 0.67. The mildly reduced cellular immunity resulted in adaptive immunity, which may impede the generation of cytokine storms. Insufficient cytokine production may be confirmed by low levels of CRP (0.3ng/L) in the early stages of onset. However, excessive suppression of cellular immunity may also reduce the immune system's ability to eliminate viruses, resulting in a continual positive for SARS-CoV-2 RNA testing. In this case, HAART was chosen to be given on the 37th day after onset, based on a chest CT suggesting that lung lesions had been gradually absorbed and $CD4^+$ decreased to 328 / microliter. It is probable that the pros and cons of immune escape are worthy of further study for COVID-19 complicated with HIV infection.

In this case, use of multiple compassionate drugs for more than 30 days and COVID-19 NAT continued as negative, further confirming that the current drugs used are actually not effective.[9]Fourteen days after starting HAART, HIV-RNA decreased to 1723 cp / ml, $CD4^+$ rose to 454 / microliter, and SARS-CoV-2 RNA was negative two consecutive times, taken at intervals of more than 24 hours. It is suggested that the removal of SARS-CoV-2 in this case is still based on the body's immune clearance. The investigation of the immune mechanism of COVID-19 combined with HIV infection and the timing and optimum schedule of initiation of HAART will require further study with a larger sample size.

Tables

Table 1: Detailed treatment of this case*



*Above the time axis is the medication and time, dosage, and usage of sympathetic treatment for this case, and below the time axis is the medication and time of HAART1).

Table 2: Detection of SARS-CoV-2 RNA, Ab-IgM and Ab-IgG in this case

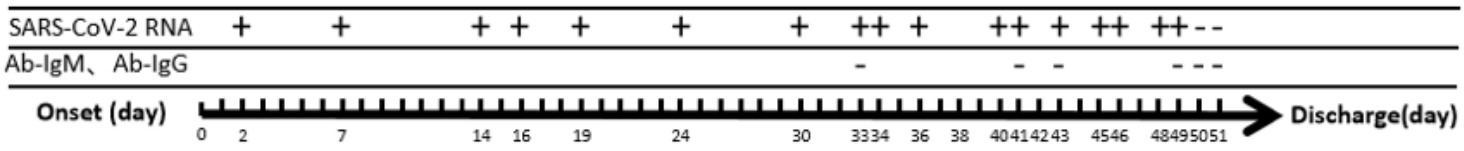
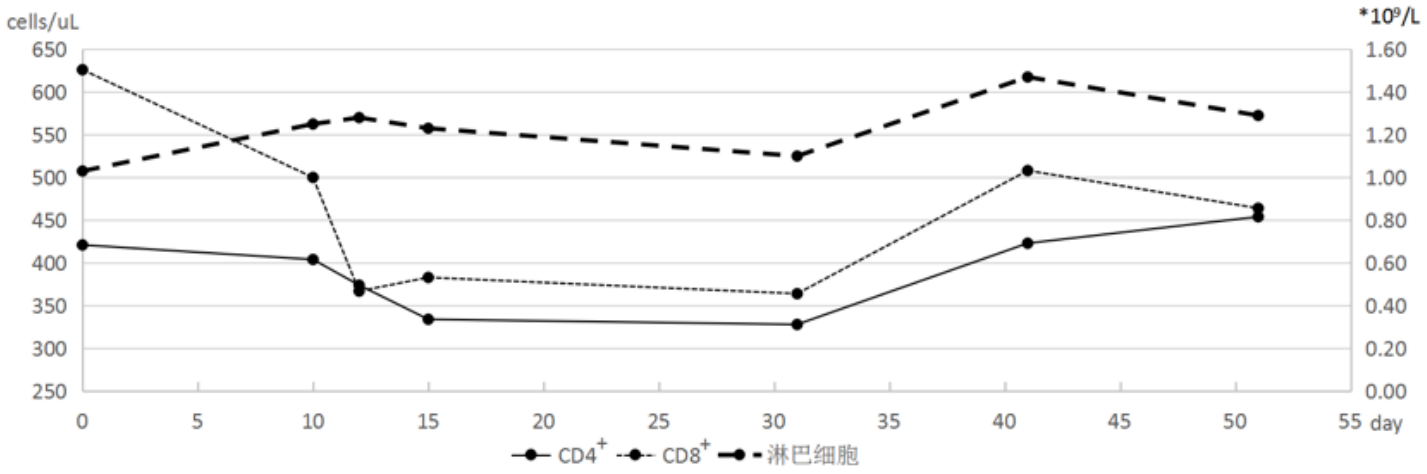


Table 3: Monitoring of T lymphocytes in this case



Abbreviations

Nucleic Acid Testing (NAT), novel coronavirus disease (COVID-19), severe acute respiratory syndrome coronavirus (SARS-CoV-2), ground-glass nodular-like shadows (GGO), tenofovir (TDF), lamivudine (3TC), lopinavir / ritonavir (LPV/r), highly effective antiretroviral therapy (HAART).

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the ethics committee of Longtan Hospital of Guangxi Zhuang Autonomous Region (Guangxi Province, China). All participants, or legal guardians of participants if necessary, provided written informed consent.

Consent for publication

All authors agreed to publish.

Availability of data and materials

All relevant data are within the paper.

Competing interests

None to declare.

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Authors' contributions

A-ML and JW,Y-LX conceived the study. A-ML designed the study. JW collected clinical data. G-WW collected the x-ray images. A-ML analysed and interpreted the data.D-YH and K-YL,Z-HM,A-ML formulated the treatment regimen and analysed the x-ray images. J-LH made the tables and figures. L-LH searched the literature. JW wrote the manuscript. A-ML critically revised the manuscript.

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Figures

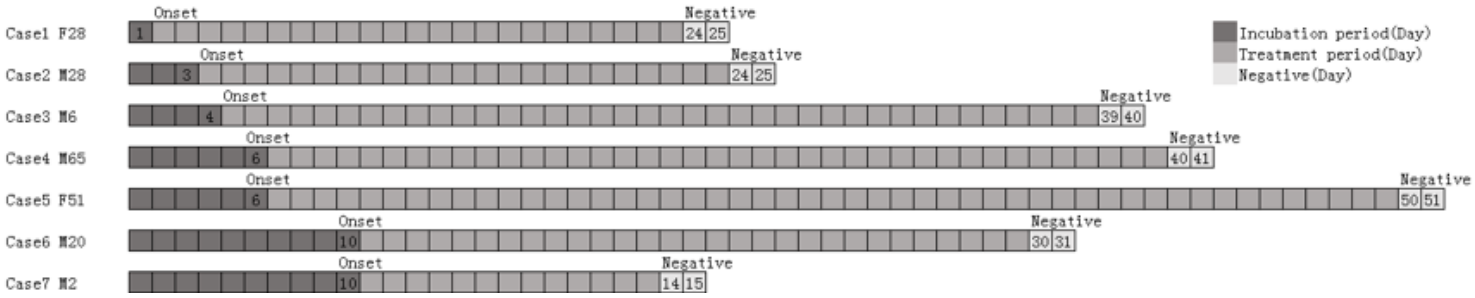

Figure 1

Detailed Information on Exposures and Dates of Illness Onset in Cluster Including 7 Cases.

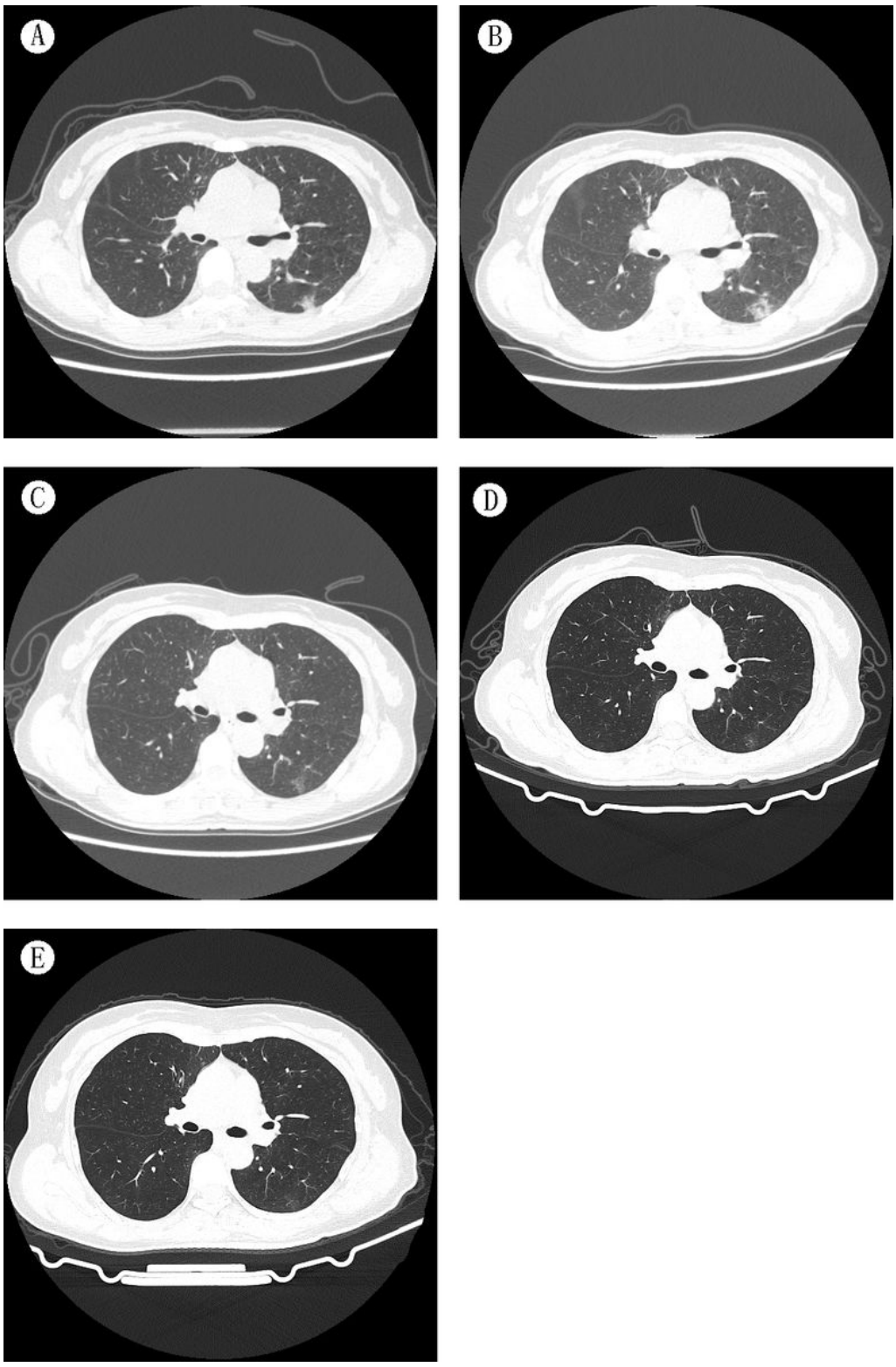

Figure 2

[No legend]

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