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A case of 2019 novel coronavirus infected pneumonia with twice negative 2019-nCoV nucleic acid testing within 8 days

Zhongrui Ruan[1], Peng Gong [2], Wei Han[1], Minqiang Huang, [1] Ming Han [1]

[1]Department of Emergency, The Shenzhen University General Hospital, Shenzhen University, Shenzhen, Guangdong 518000, China

[2]Department of General surgery, The Shenzhen University General Hospital, Shenzhen University, Shenzhen, Guangdong 518000, China

Zhongrui Ruan and Peng Gong contributed equally to this work.

Correspondence to: Ming Han, Department of Emergency, The Shenzhen University General Hospital, Xueyuan avenue no.1098, Shenzhen, Guangdong 518000, China. E-mail: mhan@stu.edu.cn

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To the Editor: Since December 2019, unexplained pneumonia cases have been reported in hospitals in Wuhan, Hubei province. Then, it has been confirmed that the pneumonia cases were infected by a novel coronavirus called 2019 Novel Coronavirus (2019-nCoV). As the exact sources of the virus, the time of virus shedding after infection and viral propagation are still undefined, there are still great challenges in controlling the virus spreading and the treatment of infection. Up to now (Feb 04,2020), there have been 19,731 confirmed cases in China, among which 725 cases in Guangdong province. Shenzhen, as one of the cities with the largest floating population in Guangdong Province, has the highest number of confirmed cases of infection (245 cases). Therefore, rapid diagnosis of infection cases and early isolation are extremely important for the overall prevention and control work [1].

In recent days, network media reported that there existed confirmed 2019-nCoV infected pneumonia cases who got negative nucleic acid testing more than two times at early stage. But the detailed reports are still absent. Therefore, we reported here the history and clinical data of a confirmed case with negative 2019-nCOV nucleic acid testing within 8 days, and final positive test confirmed on the 11th days of onset in Shenzhen University General Hospital.

A 47-year-old woman, who traveled to Wuhan on Jan 13, 2020 with her mother (who was later confirmed to be infected by 2019-nCoV.) got an intermittent fever (highest temperature: 37.9℃) on Jan 20, 2020, accompanied by coughing. Two days later, she was admitted to the Third People's Hospital of Shenzhen. Initially, her blood test showed normal white blood cell count (4.94×10^9/L) and decreased lymphocyte count (1.06×10^9/L), the oxygen saturation was 99%. After admission, the patient received atomized inhalation of interferon twice daily. However, 2019-nCoV nucleic acid testing by sampling from throat swab on Jan 22 and Jan 28 failed to show positive results.

On Jun 29, 2020, the patient was transferred to Shenzhen University General Hospital for further isolation and clinical observation. At admission (day 9 of onset), the patient had worsened headache and cough, but her body temperature (36-37.2℃) and oxygen saturation (99%) remained relatively normal. Her blood test showed normal white blood cell count (5.81×10^9/L) and decreased lymphocyte count (0.91×10^9/L). Chest CT scan showed bilateral ground-glass opacity [Figure 1]. Besides atomized inhalation of interferon, oseltamivir (75mg) was orally administered twice daily.

On Jan 31 (day 11 of onset), blood gas analysis of this patient showed dramatic deterioration (PO_2 65.5 mmHg, PCO_2 39.2 mmHg, SO_2 93.6%). 2019-nCOV nucleic acid testing was performed again by sampling from nasal swabs. The result showed positively 2019-nCoV infected, which was verified by CDC at the same time.

According to the New Coronavirus Infection Pneumonia Protocol (version 6) published by China Health Committee, two consecutive negative respiratory 2019-nCoV nucleic acid testing (at least one day apart) are required for exclusion of 2019-nCoV infected pneumonia [2]. However, there are still cases who cannot be excluded due to their highly suspected epidemiological history, typical clinical, laboratory, and radiological characteristics. According to this case, the patient had an exact epidemiological history, pulmonary imaging changes, and typical clinical symptoms. However, virus nucleic acid sequence has not been detected for 8 days after onset, until the 11st days after onset, indicating the presence of non-parallel relationship between 2019-nCoV nucleic acid testing and clinical symptoms.

At present, nasal and throat swabs are often used for 2019-nCoV nucleic acid testing sampling. There were studies on influenza virus test showing that influenza viruses of different sub-types

had respective affinity for settled sites, resulting in different positive detection rate from different sampling sites [3]. To date, the exact biological characteristics of 2019-nCoV are still undefined, including variant sub-types or settled sites [4]. Therefore, for this case, we suspected that changes of sampling site from throat to nasal might contribute to positive detection. As of press time, we had four patients with negative throat swabs who later tested positive for nasal swab. Recent reports demonstrate that the digestive system is another rout of 2019-nCoV infection [5], also suggesting that the settled sites of 2019-nCoV maybe individual differences.

Accordingly, for the highly suspected population, multiple sampling from multi-sites would be beneficial for 2019-nCoV detection at much earlier stage. Additionally, the status of the patients shortly before sampling should also be taken into consideration, since antiviral nebulization treatment might influence the positive detection rate. Efforts should be done to improve the efficiency of virus detection at early stage for the better prevention and control spread of 2019-nCoV.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflict of Interest

None

Reference

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Figure legends:

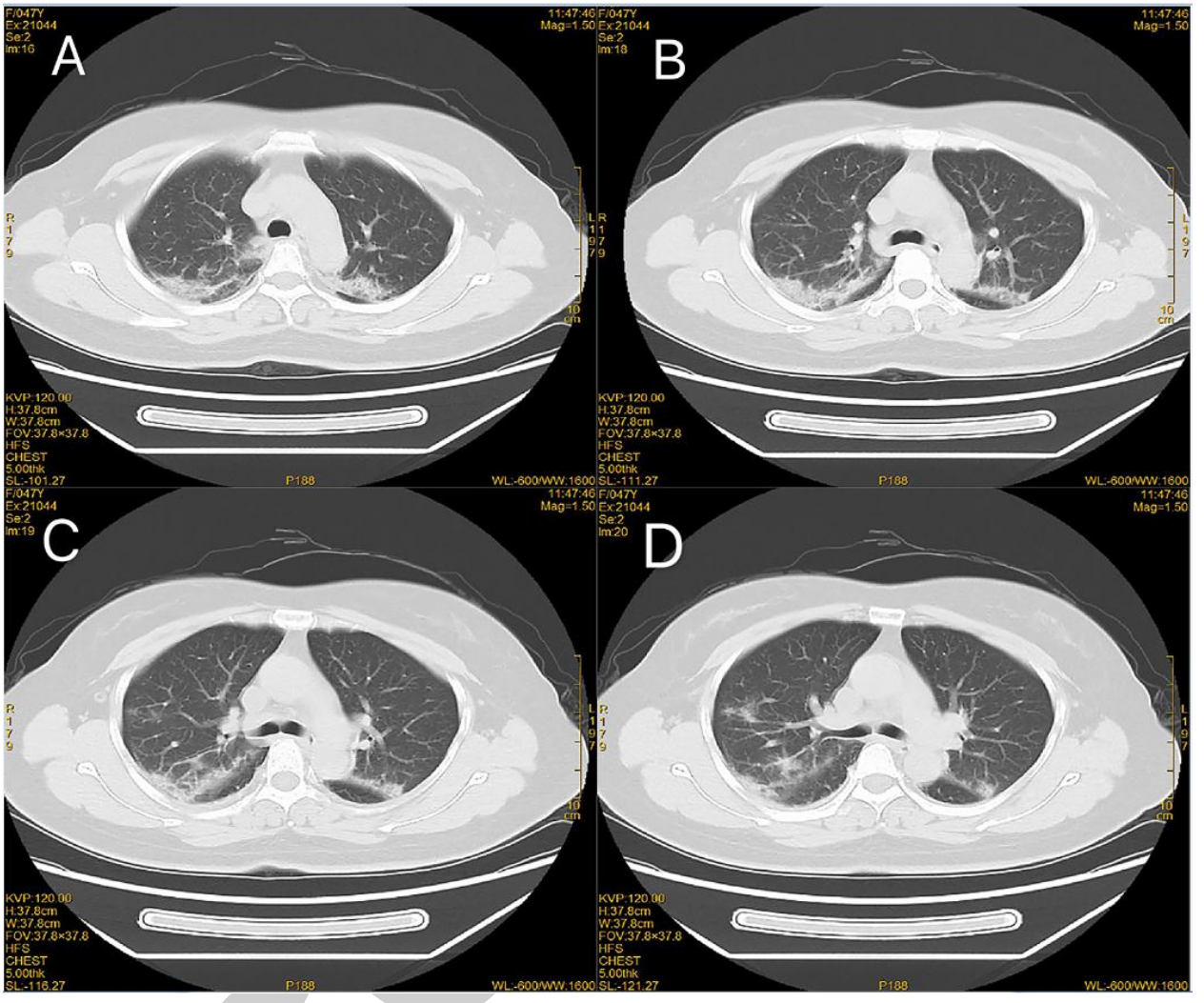

Figure 1. The continuous chest CT scans of the patient. A, multiple ground-glass density shadows in the lower lobe of both lungs at the level of the aortic arch showing; B-D, continuous faults extending downward.