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Alert for non-respiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: A case report of familial cluster with three asymptomatic COVID-19 patients

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jmv.25776.

Abstract：

At present, Coronavirus Disease 2019 (COVID-19) is rampaging around the world. However, asymptomatic carriers intensified the difficulty of prevention and management. Here we reported the screening, clinical feathers, and treatment process of a family cluster involving three COVID-19 patients. The discovery of the first asymptomatic carrier in this family cluster depends on the repeated and comprehensive epidemiological investigation by disease control experts. In addition, the combination of multiple detection methods can help clinicians find asymptomatic carriers as early as possible. In conclusion, the prevention and control experience of this family cluster showed that comprehensive rigorous epidemiological investigation and combination of multiple detection methods were of great value for the detection of hidden asymptomatic carriers.

Key words: COVID-19; Family cluster; Incubation period

Coronavirus Disease 2019 (COVID-19) has become a serious threat to global public health, resulting in more than approximately 80,000 new cases and 3,000 deaths till February 29, 2020. Finding infectious patients and cutting off transmission routes were the important methods to the control of COVID-19. However, the emergence of asymptomatic carriers has brought great challenges to the control of COVID-19[1]. We reported the screening and treatment process of a family cluster involving three COVID-19 patients, starting with a urticaria patient in dermatology department. Through this case report, we would like to emphasize the importance of systematic epidemiological investigation and combined application of different detection methods for controlling COVID-19.

Patient A

Patient A was in good health and denied the history of "hypertension, diabetes, heart disease, hepatitis, and tuberculosis". Patient A has no history of food allergy, drug allergy, and chronic urticaria. Patient A has been living in the local area for nearly 3 months, has never been to Wuhan, and has no contact history with wild animals. Patient A developed generalized sporadic erythema on February 4, 2020, and had been treated in dermatology department of our hospital as a urticaria patient. After anti allergy treatment, the systemic sporadic erythema gradually subsided. On February 8, Patient A had a little skin rash on the limbs and came back to the dermatology department for further consultation. After repeated verification, the disease control experts of our hospital found that Patient A had contact with relatives from Xiangyang City, Hubei Province on January 21, 2020. Our disease control experts conducted a comprehensive epidemiological investigation and examination on the family members and close contacts of Patient A. During the course of the epidemiological investigation, patient A recalled that there seemed to be a slight dry cough in the past week. Finally, our disease control experts found three asymptomatic COVID-19 patients in the family members and close contacts of Patient A.

The patient was admitted to our hospital on February 8, 2020. The temperature of patient A was normal during hospitalization, and there was no obvious expectoration, chest pain and shortness of breath. The results of the examination on admission were as follows: C-reactive protein < 5.00 mg/L, leukocyte $6.71*10^9$/L, lymphocyte ratio 23.7%, lymphocyte count $1.59*10^9$/L, neutrophil $4.4*10^9$/L, neutrophil percentage 65.1%;

procalcitonin 0.08 ng/ml. CT examination February 8, 2020 showed that there were multiple patchy and ground glass shadows with uneven density and fuzzy edge in the outer zone of both lungs (Fig1.A). According to the imaging findings and close contact history with COVID-19 patients, patient A was clinically diagnosed as COVID-19 patient.

Patient A was given ribavirin antiviral, interferon atomization, anti allergy and symptomatic support after admission. Second CT examination on February 10, 2020: multiple ground glass shadows in both lungs, considering infectious lesions in both lungs (Fig1.B). Examination results on February 11, 2020 were as follows: C-reactive protein < 5.00 mg/L, leukocyte $5.03*10^9$/L, lymphocyte ratio 32.8%, lymphocyte count $1.65*10^9$/L, neutrophil $2.9*10^9$/L, neutrophil percentage 58.0%; procalcitonin < 0.01 ng/ml. Third CT examination on February 13, 2020: compared with CT on February 8, 2020, partial absorption of lesions in both lungs (Fig1.C). The results of nucleic acid detection of COVID-19 on February 8, 9 and 12 were all negative.

Patient B

Patient B (elder sister of patient A) was in good health and denied the history of "hypertension, diabetes, heart disease, hepatitis, and tuberculosis". Patient B has lived in Xiangyang City, Hubei Province for the last three months. Patient B has been to the local farmer's market, but has no direct contact with wild animals. On January 21, 2020, patient B came to the local area from Hubei Province to visit her younger sister (Patient A). On February 8, 2020, the patient B received the epidemiological investigation from the disease control experts of our hospital. CT examination on February 8, 2020 showed that there were multiple patchy

and ground glass shadows in both lungs (Fig2.A and Fig2.B). Therefore patient B was admitted to our hospital for further examination and treatment.

The patient B has no fever, cough, and expectoration during hospitalization. The results of the examination on admission were as follows: C-reactive protein < 5.00 mg/L, leukocyte $4.7*10^9$/L, lymphocyte ratio 30.0%, lymphocyte count $1.4*10^9$/L, neutrophil $2.8*10^9$/L, neutrophil percentage 60.1%; procalcitonin 0.08 ng/ml. The result of nucleic acid detection of COVID-19 on February 10 was positive. Patient B was given ribavirin plus interferon antiviral and symptomatic treatment after admission. CT examination on February 10, 2020 showed that there were multiple patchy and ground glass shadows in both lungs (Fig2.C and Fig2.D). Examination results on February 11, 2020 were as follows: C-reactive protein < 5.00 mg/L, leukocyte $4.85*10^9$/L, lymphocyte ratio 29.9%, lymphocyte count $1.45*10^9$/L, neutrophil $2.9*10^9$/L, neutrophil percentage 58.8%; procalcitonin < 0.01 ng/ml.

Patient C

Patient C (son of patient A) was in good health and denied the history of "hypertension, diabetes, heart disease, hepatitis, and tuberculosis". Patient C has been living in the local area for nearly 3 months, has never been to Wuhan, and has no contact history with wild animals. On February 8, 2020, patient C received the epidemiological investigation from the disease control experts of our hospital and was admitted to our hospital for further examination and treatment.

The patient C has no fever, cough, and expectoration during hospitalization. The results of the examination on admission were as follows: C-reactive protein < 5.00 mg/L, leukocyte $4.8*10^9$/L, lymphocyte ratio 46.0%, lymphocyte count $2.2*10^9$/L, neutrophil $2.0*10^9$/L, neutrophil percentage 41%. CT examination February 8, 2020 showed that no obvious lesions were found in both lungs (Fig3). The result of nucleic acid detection of COVID-19 on February 11 was positive. Patient C was given ribavirin plus interferon antiviral and symptomatic treatment after admission. Examination results on February 11, 2020 were as follows: C-reactive protein < 5.00 mg/L, leukocyte $5.97*10^9$/L, lymphocyte ratio 31.2%, lymphocyte count $1.86*10^9$/L, neutrophil $3.6*10^9$/L, neutrophil percentage 60.7%; procalcitonin < 0.01 ng/ml.

Discussion

This case report of familial cluster highlighted the importance of rigorous epidemiological investigation again. The first patient in this familial cluster developed urticaria but without respiratory symptoms and fever. The rash gradually subsided after treatment in our dermatology department. When this urticaria patient came to the hospital for further consultation, our disease control expert repeatedly verified the epidemiological investigation records, and finally found suspicious clues from the close contacts with this patient. This family cluster case brought us some useful hints: First of all, the design of epidemiological survey must be comprehensive and rigorous to avoid missing important clues. Secondly, it is necessary for disease control experts to repeatedly verify the epidemiological investigation data of patients in the high-risk period to prevent patients from omitting important epidemic information due to subjective and objective reasons.

The first patient in this case report had urticaria but no respiratory symptoms and fever. It was reported that there were 889 asymptomatic cases (1.2%) out of 72,314 COVID-19 patients[1]. Screening asymptomatic carriers played an important role in controlling epidemic situation. It was valuable to carry out nucleic acid detection of COVID-19 in outpatients had suspected contact history with COVID-19 patients to find the asymptomatic carriers.

In this case, the results of multiple viral nucleic acid tests of patient A were all negative, suggesting that we should be alert to the negative effects of false negative rate of nucleic acid detection on the prevention and control of COVID-19. It was reported that the sensitivity of RT-PCR method on throat swab samples ranged from 30% to 60% due to the limitations of sample collection and detection method[2]. Chest CT scan could provide important diagnostic information for the detection of viral nucleic acid[2]. Ground glass shadow was the most common CT manifestation (56.4%) in 1099 COVID-19 patients[3]. The sensitivity of Chest CT scan was 97.0% (580/601) in a diagnostic accuracy study based on 1014 COVID-19 patients[2]. A Rapid IgM-IgG Combined Antibody Test for COVID-19 has been developed for COVID-19 patients[4]. In 397 patients with COVID -19 confirmed by RT-PCR and 128 healthy controls, the sensitivity and specificity of this detection method were 88.7% and 90.6% respectively[4]. These previous studies demonstrated that chest CT and serum antibody detection method were helpful to screen asymptomatic COVID-19 patients.

In general, the current case suggests that comprehensive rigorous epidemic investigation and the combination of multiple detection methods could help to identify asymptomatic COVID-19 patients.

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Figure

Figure1. Chest CT examination of patient A on February 8, 2020 (A), February 8, 2020 (B), and February 8, 2020 (C)

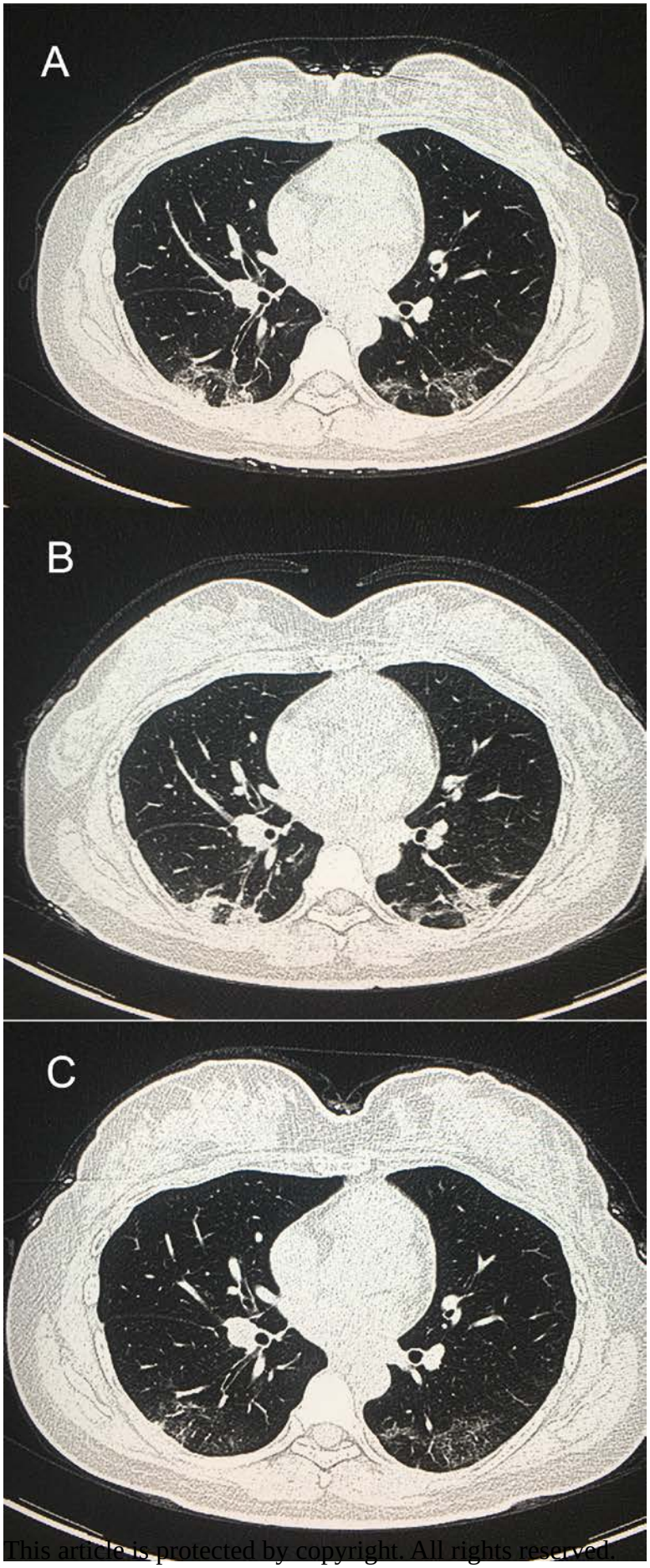

Figure2. Chest CT examination of patients B: (A) Right upper lung on February 8, 2020; (B) Lower lung on February 8, 2020; (C) Right upper lung on February 10, 2020; (D) Lower lung on February 10, 2020.

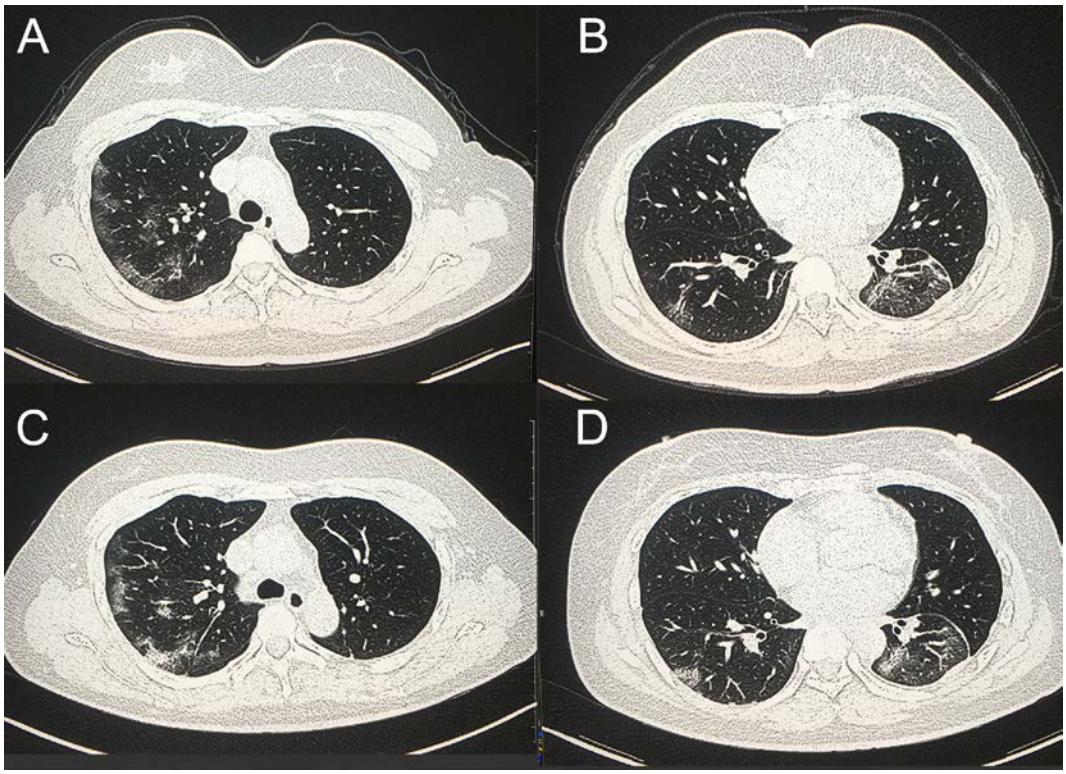

Figure3. Chest CT examination of patients C in different CT sections on February 8, 2020: (A) Double upper lobes; (B) Double upper lobes and dorsal segments of lower lobes; (C) Right middle lobe, left upper lingual lobe and double lower lobes; (D) Right middle lobe, left upper lingual lobe and double lower lobes.