

Computed Tomographic Imaging of 3 Patients With Coronavirus Disease 2019 Pneumonia With Negative Virus Real-time Reverse-Transcription Polymerase Chain Reaction Test

Junqing Xu,¹ Ruodai Wu,¹ Hua Huang,¹ Weidong Zheng,² Xinling Ren,³ Nanshan Wu,¹ Bin Ji,¹ Yungang Lv,¹ Yumeng Liu,¹ and Rui Mi¹

¹Department of Radiology, Shenzhen University General Hospital, Shenzhen University Clinical Medical Academy, Shenzhen, China, ²Department of Clinical Laboratory, Shenzhen University General Hospital, Shenzhen University Clinical Medical Academy, Shenzhen, China, and ³Department of Respiratory Diseases, Shenzhen University General Hospital, Shenzhen University Clinical Medical Academy, Shenzhen, China

We reported computed tomographic (CT) imaging findings of 3 patients with coronavirus disease 2019 (COVID-19) pneumonia with initially negative results before CT examination and finally confirmed positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse-transcription polymerase chain reaction assay.

Keywords. chest CT; covid-19 pneumonia; rt-PCR.

The current outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously novel coronavirus 2019 [2019-nCoV]), which emerged in Wuhan, China, has spread rapidly and is now confirmed in multiple countries [1–3]. The World Health Organization has recently declared that COVID-19 a public health emergency of international concern [4]. The diagnosis of COVID-19 needs a fluorescent reverse-transcription polymerase chain reaction (RT-PCR) kit for nucleic acid detection [1–3]. Our finding emphasizes the disturbing possibility that swabs are not sensitive for COVID-19 at early stages of the clinical presentation.

MATERIALS AND METHODS

We recruited 3 patients from 29 January to 2 February 2020 in Shenzhen University General Hospital who showed negative results before computed tomographic (CT) examination

and were finally confirmed positive for SARS-CoV-2 by real-time RT-PCR (rRT-PCR) assay. All 3 patients had a definitive history of exposure to close contact with confirmed patients.

The specimens collected included nasopharyngeal swab and blood sample; samples were transported as routine. The nasopharyngeal swab was placed into a sterile sampling tube containing 1 mL of virus delivery medium, covered, and sealed. Serum samples were stored in disposable serum storage tubes. The detection of SARS-CoV-2 was performed with rRT-PCR kit (Daan, Guangzhou Daan Clinical Laboratory Center) in the laboratory department in our hospital and the local Center for Disease Control and Prevention. Validation was tested on positive and negative controls on each batch of tests.

Chest CT scans were performed on a Revolution 256 row CT scanner (General Electric Company) and imaged with 1.25-mm slice thickness CT. The CT images were read independently by 2 radiologists with > 10 years' experience on chest CT who were blinded to the clinical data.

EPIDEMIOLOGICAL, CLINICAL, AND IMAGING TIME COURSE

Figure 1 describes the timeline of the epidemiological exposure, clinical and laboratory examinations, and CT imaging during the course of illness. Here we define the last day of exposure as day 0. A 47-year-old woman (patient 1) became ill with fever of 37.9°C; her fever came down the following day and the patient started coughing occasionally, which developed into frequent dry cough with occasional phlegm. CT examination was carried out on the third day. Patient 2 (age 45 years, female) and patient 3 (age 65 years, female) both experienced an onset of fever and a sore throat and dry cough; their symptoms had not evidently changed up to the time of CT examination and the collection of the first positive nasopharyngeal swabs. CT examination was performed on the first and fourth day in patients 2 and 3, respectively. The time of PCR of SARS-CoV-2 testing is shown in Figure 1.

CT IMAGING FEATURES

All 3 patients had abnormal CT findings. CT imaging of patient 1 (Figure 2) showed that the disease was in the progressive stage. The bilateral, multifocal fusion structure of ground glass opacity (GGO) and multilobular infiltration were clearly documented, and an air space nodule could be seen in the left upper lobe lesion. Images of patients 2 and 3 (Figure 3) show peripheral multifocal GGOs, and interlobular septal thickening ("crazy-paving" pattern) could be seen in some regions.

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Correspondence: J. Xu, Shenzhen University Hospital, Shenzhen University Clinical Medical Academy, Shenzhen, China (junqingxu@126.com).

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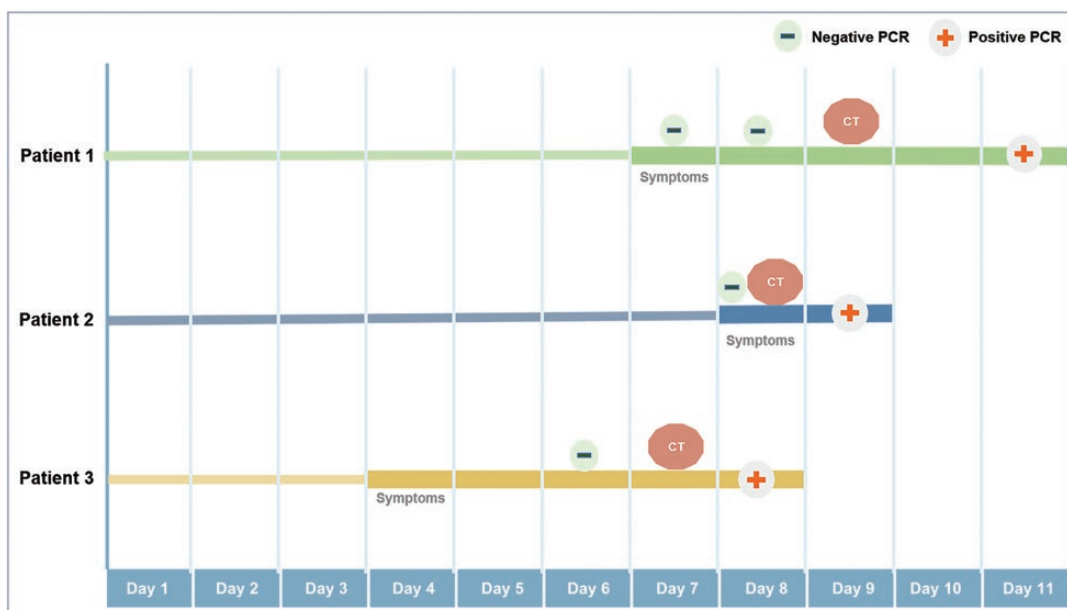


Figure 1. Epidemiological exposure, clinical, laboratory, and computed tomographic imaging timeline during the course of illness. Abbreviations: CT, computed tomography; PCR, polymerase chain reaction.

DISCUSSION

The CT imaging of patients 2 and 3 had similar features, with both showing mild pneumonia. CT features included peripheral

multifocal GGOs, which are common CT findings in patients with COVID-19 pneumonia [5–8]. In patient 1, the disease was in the progressive stage, with bilateral features, multifocal fusion structure of GGOs, and multilobular infiltration, whereas

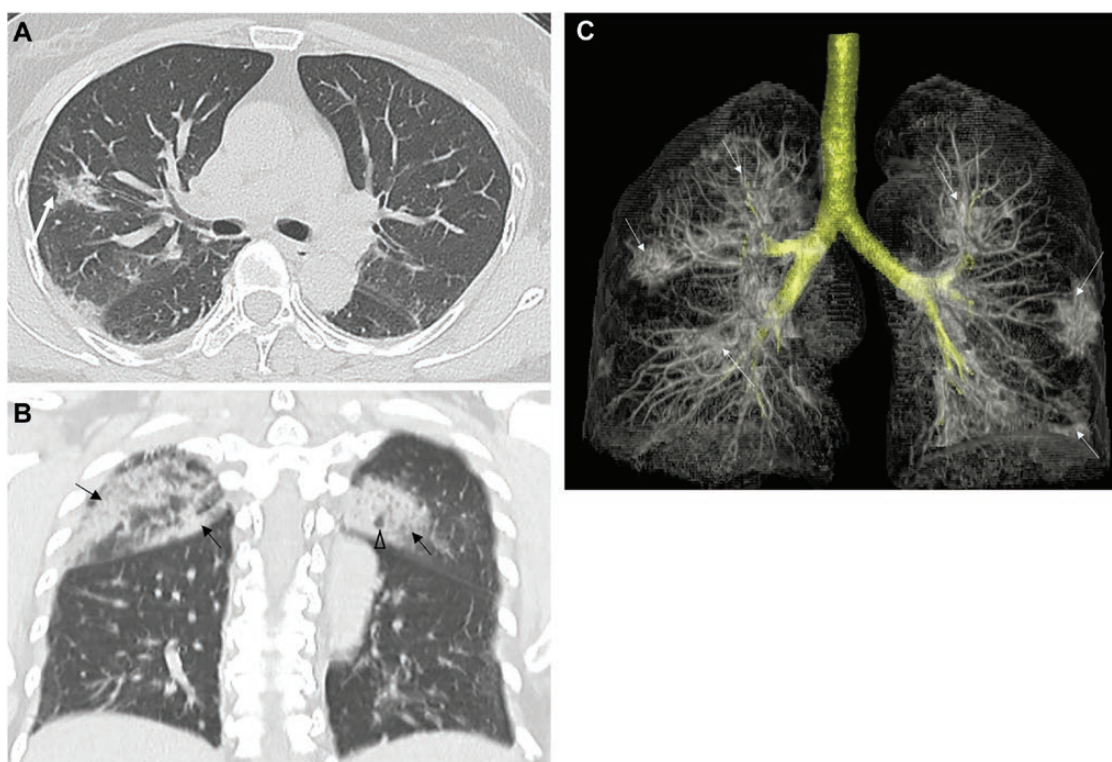


Figure 2. Patient 1 (47-year-old woman) presenting with fever and cough. *A*, Axial computed tomographic (CT) scan shows multifocal ground glass opacities; the white arrow shows an air bronchogram sign. *B*, Coronal reconstructed CT image (3-mm thickness) shows merged large pieces of ground glass opacities in both lungs (black arrows), and an air space nodule can be seen in the left upper lobe (triangle). *C*, Three-dimensional volume-rendered reconstruction shows diffuse bilateral confluent and patchy ground glass opacities (white arrows) and multilobular infiltration.

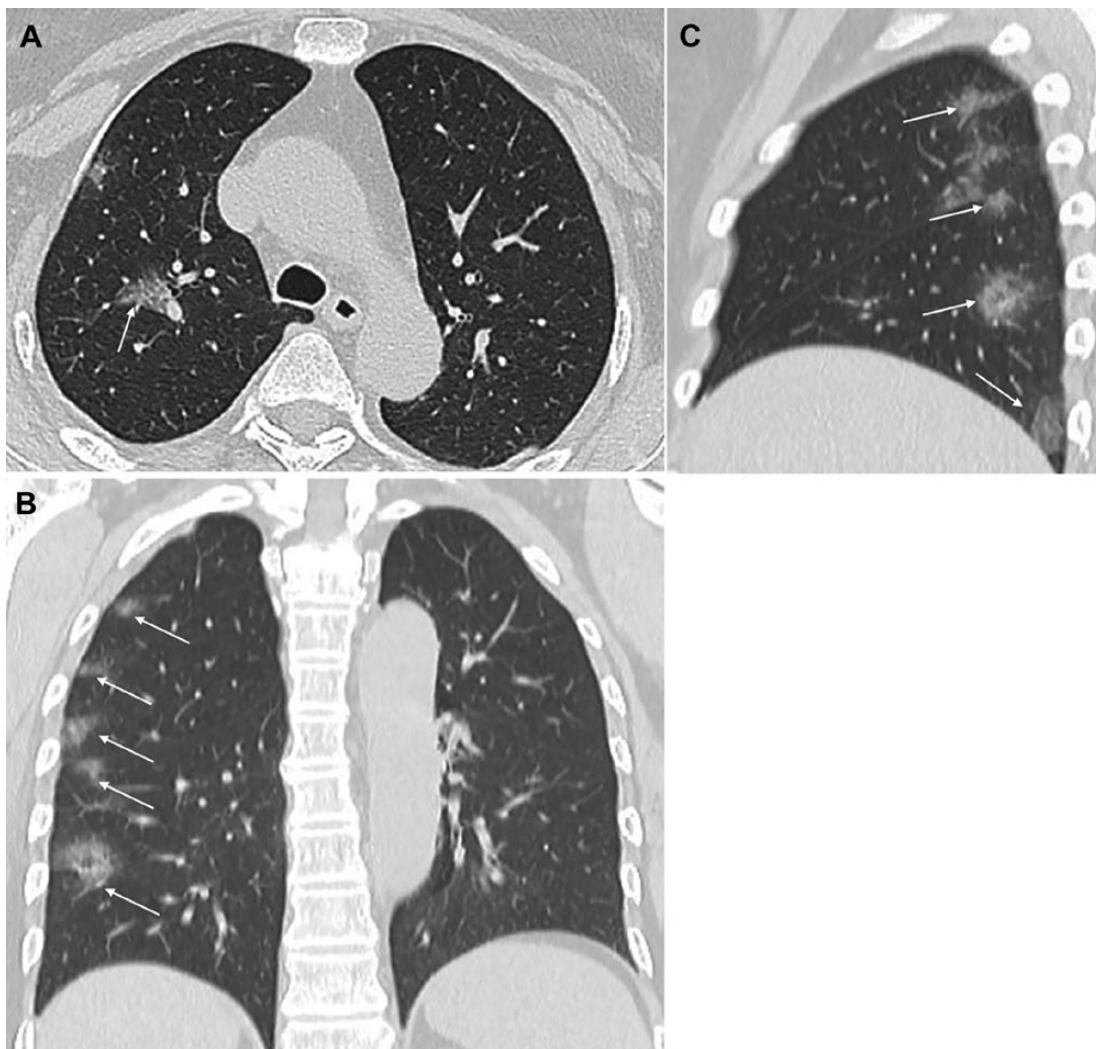


Figure 3. Patient 3 (65-year-old woman) presenting with fever and cough. A, Axial computed tomographic (CT) scan shows multifocal ground glass opacities; the white arrow shows interlobular septal thickening ("crazy-paving" pattern). Coronal (B) and sagittal (C) reconstructed CT images (3-mm thickness) show multiple peripheral ground glass opacities (white arrows).

the PCR was still negative. Chest CT may be helpful in some situations such as early detection of severe or critical cases.

Detection of the nucleic acid of virus was still negative in the 3 patients on the sixth to eighth day after onset of disease. Such patients may be missed if the surveillance case definition focuses heavily on early virus detection. These cases show the challenges in the management of COVID-19 pneumonia and suggest that PCR testing of nasopharyngeal swabs probably is not sensitive for COVID-19 at early stages of the clinical presentation. Ongoing efforts may be needed for epidemiologists to seek the use of nasopharyngeal swabs or other specimens, such as noninvasive saliva obtained at a single point in time, from complicated situations as a tool to rule in or rule out SARS-CoV-2 infection for clinical or epidemiologic purposes.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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