Radiology

Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing

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Declaration of interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Summary statement

In patients at high risk for 2019-nCoV infection, chest CT evidence of viral pneumonia may precede positive negative RT-PCR test results.

Abstract

Some patients with positive chest CT findings may present with negative results of real time reverse-transcription–polymerase chain- reaction (RT-PCR) for 2019 novel coronavirus (2019-nCoV). In this report, we present chest CT findings from five patients with 2019-nCoV infection who had initial negative RT-PCR results. All five patients had typical imaging findings, including ground-glass opacity (GGO) (5 patients) and/or mixed GGO and mixed consolidation (2 patients). After isolation for presumed 2019-nCoV pneumonia, all patients were eventually confirmed with 2019-nCoV infection by repeated swab tests. A combination of repeated swab tests and CT scanning may be helpful when for individuals with high clinical suspicion of nCoV infection but negative RT-PCR screening

Abbreviations

PT-PCR=reverse-transcription–polymerase chain- reaction

GGO=ground glass opacity

Introduction

In December 2019, an outbreak of 2019-nCoV pneumonia began in Wuhan (Hubei, China) and spread rapidly [1]. Without a therapeutic vaccine or specific antiviral drugs, early detection and isolation becomes essential against novel coronavirus. The use of chest computed tomography (CT) as a screening tool for patients with suspected 2019-nCoV not well understood. In our experience, some patients with likely 2019-nCoV infection may have initial negative reverse transcriptase (RT) polymerase chain reaction (PCR) results. Reasons for false negative RT-PCR may include insufficient cellular material for detection and improper extraction of nucleic acid from clinical materials.

The purpose of the study was to describe CT imaging features of five patients with initial negative or weakly positive RT-PCR results but high suspicion of 2019-nCoV infection.

Materials and methods

This study was approved by Medical Ethical Committee (Approved Number.2020002), which waived the requirement for patients' informed consent referring to the CIOMS guideline.

Clinical evaluation

Laboratory-confirmed 2019-nCoV patients with initial negative RT-PCR results in the database of Radiology Quality Control Centre, Hunan province were collected. Diagnosis of 2019-nCoV was determined according to the following three methods: isolation of 2019-nCoV or at least two positive results by real-time RT-PCR assay for 2019-nCoV or a genetic sequence that matches 2019-nCoV. From 167 laboratory-confirmed cases, a total of five patients (1 woman, 4 men; age range, 25- 66 years) who underwent CT scanning from 3 cities in Hunan Province, China, were included in this study. Three patients were evaluated in Changsha, 1 in ChangDe, and 1 in XiangTan China.

Available clinical history, laboratory, and epidemic characteristics were collected. According to the guideline of 2019-nCoV (Trial Version 5) [2], the patients were typed into four group, mild, common, severe and fatal types. All patients underwent CT scanning on the same day when initial mouth swab test was performed.

Imaging Interpretation

Two thoracic radiologists (with 10 years of experience) blinded to the clinical data reviewed the CT images independently and resolved discrepancies by consensus. All images were viewed on both lung (width, 1500 HU; level, −700 HU) and mediastinal (width, 350 HU; level, 40 HU) settings. The presence or absence of nine image features was recorded: ground-glass opacities (GGO), consolidation, mixed GGO and consolidation, traction bronchiectasis, bronchial wall thickening, reticulation, subpleural bands, vascular enlargement and lesion distribution. The detailed definitions of the above features were as described in [3] . We divided each lung into three zones: upper (above the carina), middle (below the carina up to the inferior pulmonary vein), and lower (below the inferior pulmonary vein) zones [4]. A semi-quantitative score was assigned for each lung zone: score 0, 0% involvement; score 1, less than 25% involvement; score 2, 25% to less than 50% involvement; score 3, 50% to less than 75% involvement; and score 4, 75% or greater involvement. There were 6 lung zones per patient; the maximal score was 4 times 6 zones resulting in a score of 24.

Results

167 patients were evaluated; of these 5 (3%) patients initially had negative RT-PCR but positive chest CT with pattern consistent with viral pneumonia (figure 1). After positive CT findings, all patients were isolated for presumed 2019-nCoV pneumonia. Repeat swab testing and RT-PCR tests 2019-nCoV infection in all patients. In 7 patients (4%), CT was initially negative while RT-PCR was positive. In 155 patients (93%), both RT-PCR and CT were concordant for 2019-nCoV infection. Of the 5 patients with negative RT-PCR and positive CT at initial presentation, the median CT involvement score was 4. The highest CT involvement score was 14 while the minimum was 2.

The description of 5 patients with positive CT and negative RT-PCR results are presented below:

Patient 1: A 62-year-old male with recent travel history to Wuhan, China, the epicenter of the 2019-nCoV outbreak[5], was admitted to the hospital with fever and mild cough of 6 days duration. The chest CT showed multi-focal ground glass opacity (GGO) and parenchyma consolidation, predominantly involving subpleural regions of both lung (Figure 2). The CT involvement score was 14. During isolation for presumed 2019-nCoV pneumonia, the patient became dyspneic and developed type I respiratory failure five days after admission. The second swab test of 2019-nCoV was positive five days after CT scanning.

Patient 2 : A 60-year-old male with fever of 39°C was referred for hospital evaluation. His wife had been previously diagnosed with 2019-nCoV pneumonia. His CT images showed multi-focal GGO and mixed consolidation that most appeared at peripheral area of lung. (Figure 3). The CT involvement score was 11. The first swab test was negative and the male patient was quarantined at home. Over the next week, multiple swab tests returned negative results but his symptom remained. On day 8, the swab test was positive and the patient was hospitalized for further treatment.

Patient 3: A 25-year-old female appeared with cough, dizziness and debility but had no fever. Her RT-PCR results were weakly positive on the first swab test. Both her parents were diagnosed with 2019-nCoV pneumonia. She was quarantined at home. A second mouth swab test conducted the next day was negative, but a CT at that time that showed bilateral subpleural GGO indicating viral pneumonia (Figure 4). The CT involvement score was 4.Two days after CT examination, the third swab test result was positive for 2019-nCoV, confirming CT results.

Patient 4: A 66-year-old male with ongoing fever was admitted to hospital. His social history was positive for close contact with an individual having confirmed 2019-nCoV pneumonia. A swab test and RT-PCR for 2019-nCoV was negative. CT scanning was performed at the same time and showed patchy GGOs in the subpleural regions of both lungs suggesting viral pneumonia. The CT involvement score was 3. The patient was kept under observation and home isolation. During the period of isolation (2 days after chest CT scanning), the swab test turned positive, confirming prior CT results.

Patient 5: A 29-year-old male with onging fever was admitted to hospital. He had a travel history to Wuhan during the 2019-nCoV outbreak. A swab test and CT scanning were performed. The CT images showed multi-focal mixed GGO and parenchyma consolidation involving the subpleural regions of both lungs suspicious for viral pneumonia. The CT involvement score was 2. Two RT-PCT tests were both negativ and the patient was kept on home-isolation. A third swab test was positive 8 days after CT scanning. The patient was sent to hospital for isolated treatment.

Discussion

Based on clinical data obtained from the Radiology Quality Control Centre, Hunan province, we evaluated radiographic characteristics of 5 patients with confirmed 2019-nCoV infection and initial negative or weakly positive RT-PCR. All patients presented characteristic radiographic features of 2019-nCoV pneumonia from the first scan and then were confirmed by positive repeat swab test during the isolated observation or treatment. The review of these five cases suggested typical CT findings can help early screening suspected cases and may predict severe complications such as acute respiratory diseases.

According to current diagnostic criteria, laboratory examination such as swab test has become a standard and formative assessment for the diagnosis of 2019-nCoV infection [2]. However, the current laboratory test is time-consuming, and a shortage of supply test kits may not meet the needs of a growing infected population. RT-PCR testing for 2019-nCoV may be falsely negative due to laboratory error or insufficient viral material in the specimen.

Previous radiographic studies showed that the majority of cases had similar features on CT images, like GGO or mixed GGO and consolidation. 2019-nCoV pneumonia is likely to have a peripheral distribution with bilateral, multifocal lower lung involvement [6-8]. In the context of typical clinical presentation and exposure to other individuals with 2019-nCoV, CT features of viral pneumonia may be strongly suspicious for 2019-nCoV infection despite negative RT-PCR results. In these cases, repeat swab testing and patient isolation should be considered.

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References

[1] WHO. Novel coronavirus–China. Jan 12, 2020[EB/OL]. http://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/ (accessed Jan 19, 2020).
[2]China National Health Commission. Diagnosis and treatment of pneumonitis caused by new coronavirus (trial version 5). Beijing: China National Health Commission, 2020. http://www.nhc.gov.cn/yzygj/s7653p/202001/4294563ed35b43209b31739bd0785e67.shtml (accessed Feb 5, 2020).
[3] AJLAN A M, AHYAD R A, JAMJOOM L G, et al. Middle East respiratory syndrome coronavirus (MERS-CoV) infection: chest CT findings[J]. AJR Am J Roentgenol, 2014,203(4):782-787.
[4]OOI G C, KHONG P L, MULLER N L, et al. Severe acute respiratory syndrome: temporal lung
changes at thin-section CT in 30 patients[J]. Radiology, 2004,230(3):836-844.
[5]Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020 Jan 24. doi: 10.1056/NEJMoa2001017. [Epub ahead of print]
[6] Kanne, J. Chest CT Findings in 2019 Novel Coronavirus (2019-nCoV) Infections from Wuhan, China: Key Points for the Radiologist. Radiology 2020. https://pubs.rsna.org/doi/10.1148/radiol.2020200241. Published online February 4, 2020.
[7] Chung M et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology 2020. https://pubs.rsna.org/doi/10.1148/radiol.2020200230. Published online February 4, 2020.
[8] Song F et al. Emerging Coronavirus 2019-nCoV Pneumonia. Radiology 2020. https://pubs.rsna.org/doi/10.1148/radiol.2020200274. Published online February 6, 2020.

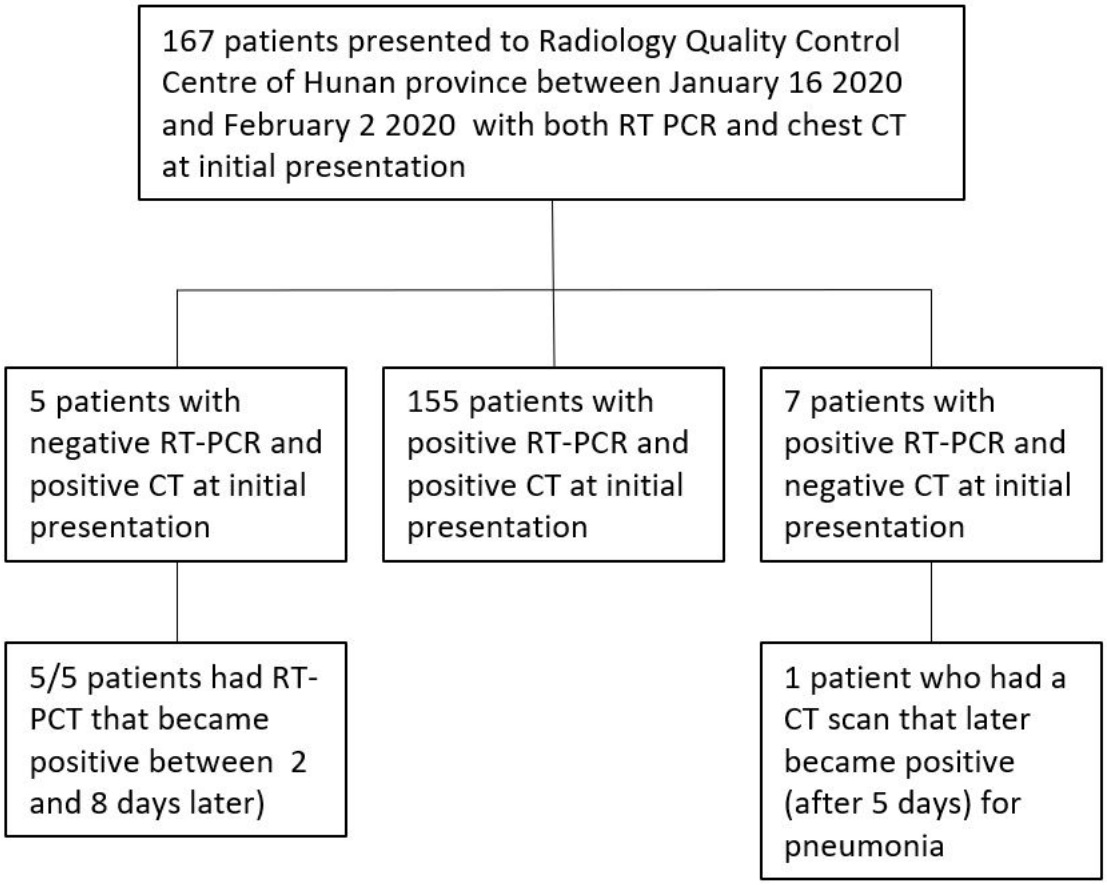

Figure 1: Patient flowchart. Of 167 patients screened, 5 (3%) had negative RT-PCR results and chest CT findings compatible with 2019-nCoV pneumonia.

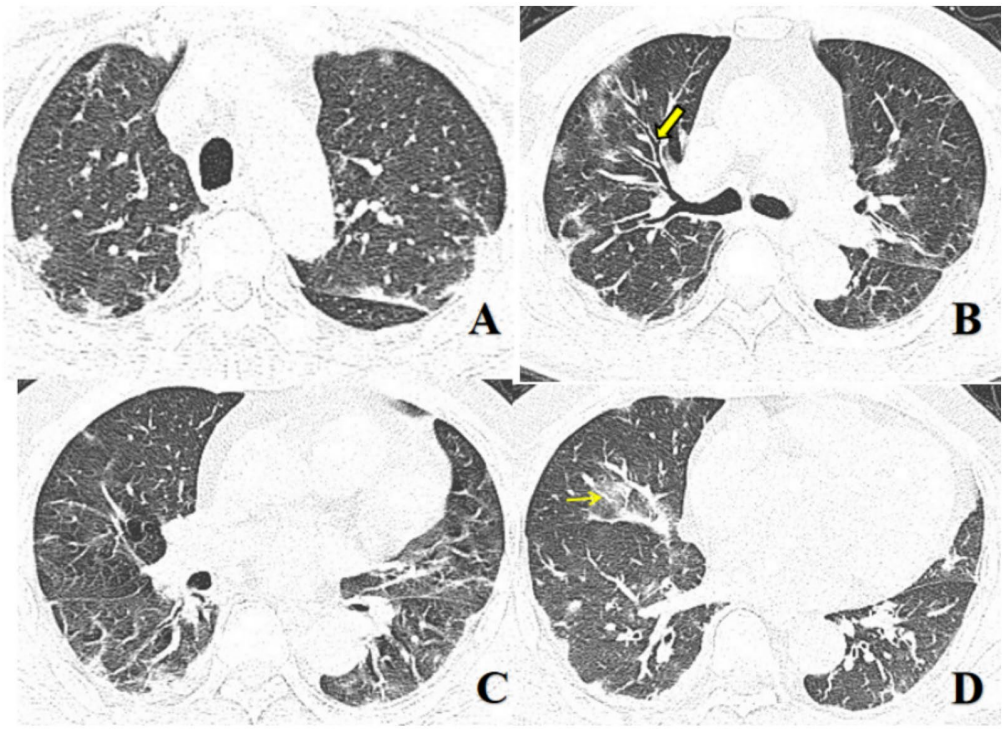

Figure 2: Chest CT imaging of patient1.A-D, CT images show bilateral multifocal GGOs and mixed GGO and consolidation lesions. Traction bronchiectasis(fat arrow) and vascular enlargement are also presented (thin arrow).

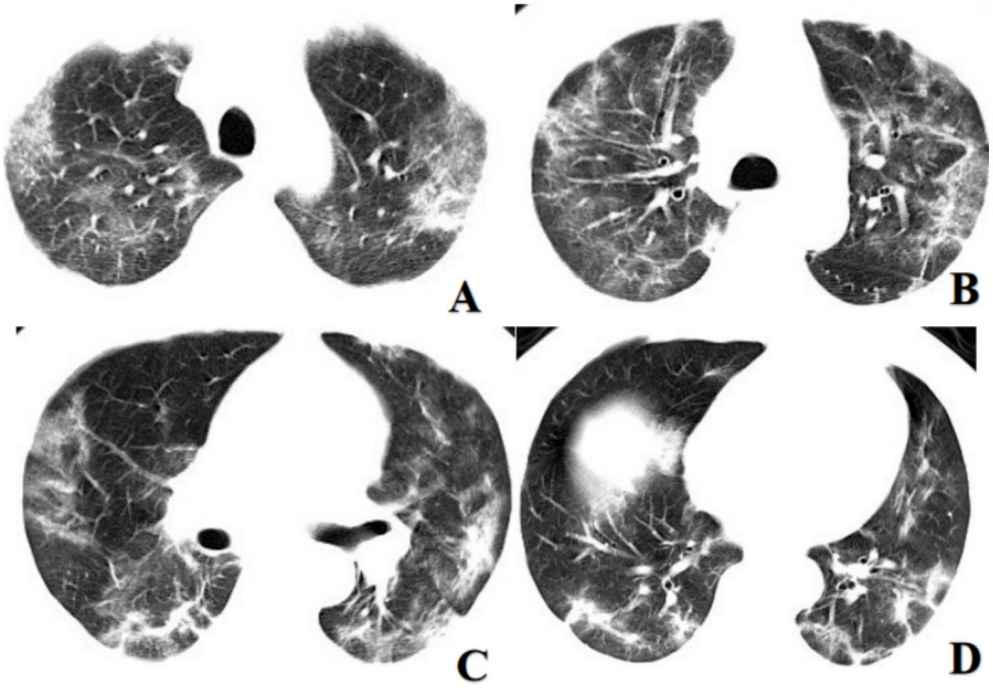

Figure 3: Chest CT imaging of patient 2. A-D, CT images showed multi-focal GGO and mixed consolidation that most appeared at peripheral area of both lungs. The CT involvement score was 11.

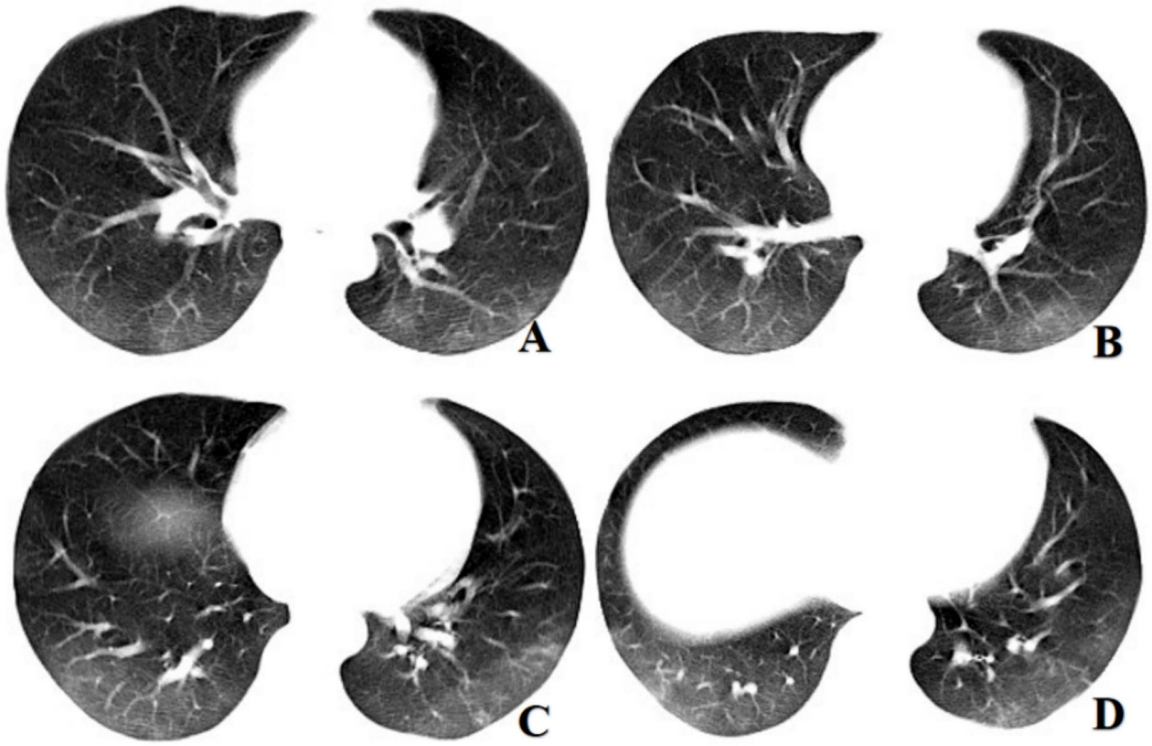

Figure 4: Chest CT imaging of patient 3. A-D, CT images showed bilateral subpleural bandlike areas of GGO compatible with viral pneumonia.