Letters

Differential Diagnosis for Coronavirus Disease (COVID-19): Beyond Radiologic Features

We read the recent *AJR* article "Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management" with great interest [1]. The authors suggested that chest CT could be useful as a standard method for rapid diagnosis of COVID-19 with a low rate of missed diagnoses (3.9%, 2/51) [1]. Because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, spreads through human-to-human transmission, not all patients infected with SARS-CoV-2 will show positive results on a reverse transcription–polymerase chain reaction (RT-PCR) test before chest CT shows signs of COVID-19 [2]. Because early and accurate diagnosis of suspected COVID-19 is essential for isolation or treatment to be as effective as possible, we would like to share our thoughts concerning the diagnostic process that should be used for patients with suspected SARS-CoV-2 infection if initial RT-PCR test results are negative.

In our opinion, the factors relevant to a differential diagnosis are exposure history, RT-PCR test results, CT findings, laboratory test results, and clinical manifestations of SARS-CoV-2 infection. With information about each of these factors, suspected cases can be confidently placed into one of the following five categories: definitely COVID-19, very probably COVID-19, probably COVID-19, probably not COVID-19, and very probably not COVID-19.

With regard to the first category, RT-PCR is considered to be the reference standard for screening SARS-CoV-2 infection. If the initial RT-PCR test returns positive results for SARS-CoV-2, the patient should be considered to definitely have COVID-19, regardless of whether other factors are also present.

Patients with negative initial RT-PCR results but a combination of other relevant factors, such as a history of exposure to an infected person, presence of typical chest CT features, laboratory test results indicative of COVID-19, and clinical manifestations of cough and fever, should be considered to very probably have COVID-19. One recent study from an area with a high rate of infection suggested that chest CT had sensitivity of 98% for diagnosis of COVID-19 with RT-PCR testing as the reference standard [2]. In patients with COVID-19 in whom laboratory tests showed abnormal results of the kind typically associated with the disease, fever and cough were the most commonly seen clinical manifestations [3, 4].

One previous study reported that the mean interval ± SD between initially negative and subsequently positive RT-PCR results was 5.1 ± 1.5 days (range, 4–8 days); the mean interval between initially positive to subsequently negative RT-PCR results was 6.2 ± 2.3 days (range, 4–15 days) [2]. In light of the delay in RT-PCR detecting the virus, patients with a negative initial RT-PCR test result, a history of exposure to an infected person, and a progression of CT findings matching the characteristic time frame should be considered to probably have COVID-19. CT findings have been reported to vary at different stages of the disease [3, 5]. An appearance consisting primarily of ground-glass opacification (GGO) with comparatively less consolidation was reported to be the principal manifestation on CT images obtained before onset of symptoms and for up to 1 week after symptom onset. GGO decreased in the more advanced stages of COVID-19 pneumonia, but consolidation or mixed consolidation and GGO increased, and reticular patterns were seen in the later stages (more than 1 week after symptom onset) [3]. Because time interval and CT findings appear to be closely related, patients whose CT findings track this course should be classified as probably being infected with SARS-CoV-2.

Patients in the fourth category have a history of exposure to an infected person, but initial screening RT-PCR test results are negative, and CT findings do not show the typical progression for COVID-19 within the applicable time frames.

Patients with a history of exposure to an infected person but none of the other factors should be considered to very probably not be infected.

When faced with a possible case of COVID-19, radiologists should comprehensively analyze the exposure history, CT findings, laboratory test results, and clinical manifestations to properly categorize the situation if the initial RT-PCR test results are negative. Because initial RT-PCR results are not always positive in patients with SARS-CoV-2 infection, chest CT images could play an important role in detecting lesions in the pulmonary parenchyma [6, 7]. In other words, chest CT and RT-PCR results should both be considered verification methods for comprehensive diagnosis in patients with suspected COVID-19, in combination with exposure history, laboratory result, and clinical manifestations.

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References

1. Li Y, Xia L. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *AJR* 2020 Mar 4 [Epub ahead of print]
2. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology* 2020 Feb 26 [Epub ahead of print]
3. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020 Feb 24 [Epub ahead of print]
4. Guan WJ, Ni ZY, Hu Y, et al.; China Medical Treatment Expert Group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 Feb 28 [Epub ahead of print]
5. Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. *Radiology* 2020 Feb 13 [Epub ahead of print]
6. Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. *Radiology* 2020 Feb 19 [Epub ahead of print]
7. Hao W. Clinical features of atypical 2019 novel coronavirus pneumonia with an initially negative RT-PCR assay. *J Infect* 2020 Feb 21 [Epub ahead of print]