ELSEVIER

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

A 78-Year-Old Woman With Diarrhea and Respiratory Failure

Check for updates

Rafael Mahieu, MD; Maxime Léger, MD; Marie Dubillot, MD; and Julien Demiselle, MD

CASE PRESENTATION: A 78-year-old woman was admitted to the ED with a 10-day history of diarrhea and recent onset of dry cough, fever, and asthenia. She had a medical history of obesity (BMI 32) and arterial hypertension treated with irbesartan. In the context of a large-scale lockdown in France during the COVID-19 pandemic, she only had physical contact with her husband, who did not report any symptoms. She required mechanical ventilation because of severe hypoxemia within 1 hour after admission to the ED.

CHEST 2021; 159(3):e159-e162

Physical Examination Findings

At admission, the patient's temperature was 36°C, her BP was 132/75 mm Hg, respiratory rate was 22 breaths/min, and pulse oximetry was 84% on room air. Skin mottling was observed. Lung auscultation revealed diffuse crackles. Abdominal examination was normal.

Diagnostic Studies

Arterial blood gases on oxygen therapy at 12 L/min with a non-rebreather mask showed Pa_{O_2}, 70 mm Hg; Pa_{CO_2}, 35 mm Hg; and lactate, 1.1 mmol/L (normal value, <2 mmol/L). The WBC count was normal (9,830/mm^3) with a slight increase in absolute neutrophil count (7,840/mm^3) and a normal lymphocyte count. Procalcitonin was slightly increased at 0.45 ng/mL. Results of hepatic tests were normal.

Chest radiograph performed while the patient was receiving mechanical ventilation showed bilateral interstitial infiltrates (Fig 1).

On the day of admission, a nasopharyngeal swab was performed for influenza A and B, respiratory syncytial viruses, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). An endotracheal aspirate for bacterial cultures was also performed. Bacterial cultures and real-time nucleic acid amplification tests for viruses were negative.

The CT scan performed on day 4 revealed bilateral ground-glass opacities and a segmental pulmonary embolism (PE) (Fig 2). A second sample from tracheal swab was negative for SARS-CoV-2.

AFFILIATIONS: From the Centre Hospitalier Universitaire d'Angers, Service de maladies infectieuses et tropicales (R. Mahieu), Angers, France; the Département Anesthésie-Réanimation (M. Léger and M. Dubillot), UBL Université d'Angers, Angers, France; and the Centre Hospitalier Universitaire d'Angers, Médecine Intensive Réanimation (J. Demiselle), Angers, France.

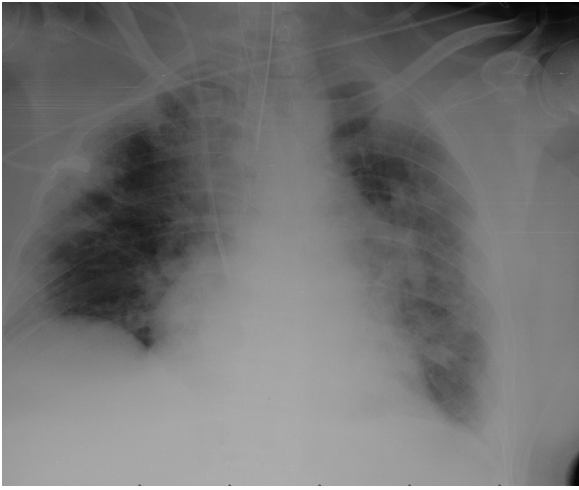**CORRESPONDENCE TO:** Rafael Mahieu, MD; e-mail: rafael.mahieu@chu-angers.fr

Figure 1 – *Chest radiograph showing bilateral infiltrates.*
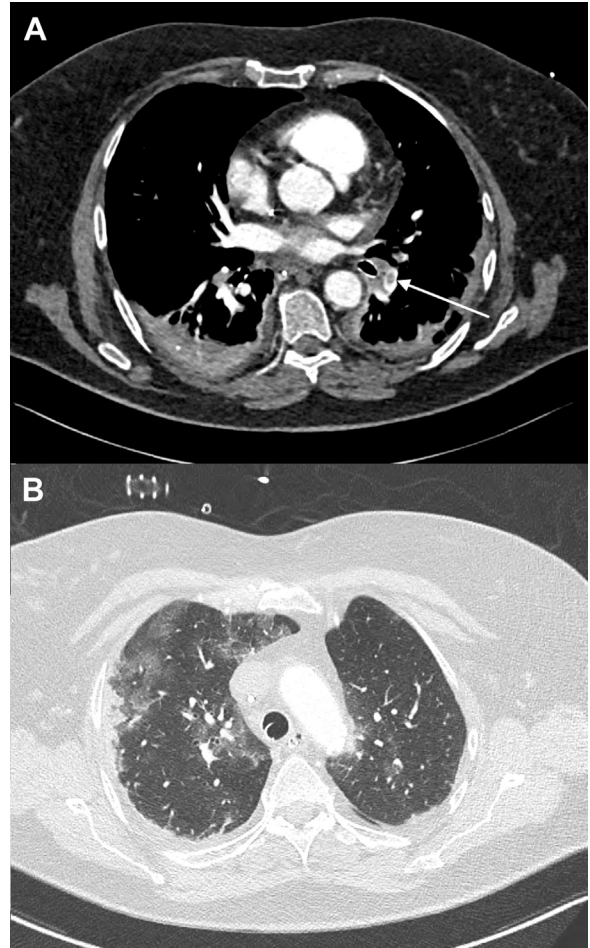
A

B

Figure 2 – *CT scan showing segmental pulmonary embolism (2A) and peripheral ground-glass opacities (2B). White arrow indicates a segmental pulmonary embolism.*

What is the diagnosis?

Diagnosis: Severe coronavirus disease 2019 pneumonia

Discussion

Definitive coronavirus disease 2019 (COVID-19) diagnosis relies on a positive sample for the SARS-CoV-2 virus. Real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) of a respiratory sample is used to confirm the clinical diagnosis. When performed on upper respiratory specimens, the sensitivity of this technique is low, ranging from 32% to 72%. Sensitivity of rRT-PCR is higher when performed on nasopharyngeal swabs compared with oropharyngeal swabs, and sputum samples are more sensitive than pharyngeal samples. Only 20% of patients with COVID-19 pneumonia, however, have a productive cough. Contrary to SARS-CoV infections, in which RNA peaks at 7 to 10 days after symptom onset, SARS-CoV-2 viral loads in throat swab and sputum samples peak soon after symptom onset, and sampling can be performed as soon as symptoms occur. A first negative test should be interpreted with caution, in particular when clinical suspicion is high (for example, in a high-prevalence region). The negative likelihood ratio for nasopharyngeal swab during COVID-19 has been estimated at 0.3, and it does not formally rule out COVID-19. Performing at least a second test is highly recommended to rule out COVID-19 when there is no alternative diagnosis. A second or third test has been associated with increased yields of 25% and 10%, respectively. In a very-low-prevalence area or when clinical suspicion is low, COVID-19 pneumonia may then be ruled out. In contrast, additional testing may be considered in high prevalence areas. Lower respiratory tract samples such as BAL fluid specimens have the potential to confirm or exclude the diagnosis with the highest positive rates (sensitivity of 93%). BAL is, however, an invasive, time-consuming, technically complex, and aerosol-generating procedure (with possible viral exposure for medical staff). When the diagnosis remains unclear, BAL may be performed only in highly selected patients, if the results will change clinical management. Similar results have been found for other respiratory viruses, in particular in immunocompromised hosts, with a 40% increase in the yield of samples when BAL is performed. The very high specificity of rRT-PCR (above 95%) enables the confirmation of COVID-19 pneumonia for all sample sites, and a positive result should be considered definitive, without need for further testing.

CT scanning has been proposed as a means of providing early diagnosis in patients suspected to have COVID-19. The typical pattern is described as peripheral ground-glass opacities (GGO) associated with multilobar involvement and bilateral distribution. The high prevalence of pulmonary consolidation (31%-72%) during COVID-19 pneumonia makes the differentiation of bacterial, SARS-CoV-2, and other viral pneumonia challenging, whereas pleural effusion is particularly rare. Chest radiographs (CXR) at presentation is useful in searching for an alternative diagnosis and may identify lung consolidation. However, CXR may lack sensitivity for detecting GGO, and a chest CT scan should be performed when CXR is normal, in particular for rRT-PCR negative patients. In patients with positive rRT-PCR, CT scan sensitivity ranges from 77% to 97% and specificity is 56%. The frequency of CT findings seems to be related to infection time course, because 56% of patients with COVID-19 may have a normal CT scan between day 0 and day 2 after symptom onset, decreasing to 9% between day 3 and day 5 and 4% after day 6. Therefore, a normal CT scan performed 5 days after the onset of symptoms and a negative rRT-PCR should allow the clinician to safely rule out COVID-19 pneumonia, in particular when the prevalence of the disease is low. The low specificity of the CT scan (between 50% and 60%) is associated with a high risk of false positives, and clinicians must remain vigilant and consider alternative diagnoses for patients with suspected COVID-19 pneumonia.

Because of the high incidence of PE during COVID-19 (up to 25%), performing a CT pulmonary angiography is mandatory in the case of sudden clinical worsening in a patient with a suspected or confirmed case of COVID-19. Performing a CT pulmonary angiography instead of standard noncontrast chest CT in all patients with suspected COVID-19 is not recommended. No D-dimer threshold is validated to rule out or detect PE during COVID-19.

Because no gold standard for COVID-19 pneumonia diagnosis is yet available, a case-by-case approach has been proposed, and further studies including serological testing will probably specify more precisely the diagnostic accuracy of each test.

Serological testing for IgM and IgG antibodies against SARS-CoV-2 in serum is a promising approach with good sensitivity (77.3% and 83.3% for IgM and IgG, respectively) and negative predictive value (80% and 83.8% for IgM and IgG, respectively). The median

seroconversion time for IgM and IgG is 10 and 15 days, respectively, and titers vary with disease severity (the more severe the disease, the higher the antibody level). In a patient with a CT scan suggesting COVID-19 with repeated negative rRT-PCR tests, serology may help confirm diagnosis.

Overall, the diagnostic approach to a patient with suspected COVID-19 is based on the time from the onset of symptoms, the type of specimens used for rRT-PCR and the result of the CT scan. For patients in the early stages (in the first 5 days) with a normal CT scan and a negative rRT-PCR in an upper respiratory sample, a second CT scan can be obtained after day 5, and the diagnosis of COVID-19 should be considered when typical GGO is observed. When repeated rRT-PCR tests are negative with typical findings on a CT scan, additional testing (lower respiratory tract sample or serological assay if available) should be performed. Ruling out the diagnosis of COVID-19 in the context of a pandemic is based on the specific pretest probability of COVID-19 in each region of the world. In most situations, a combined approach including CT scan and repeated rRT-PCR if negative is mandatory to rule out the diagnosis. In complex situations, serology could help to confirm or rule out the diagnosis, but the diagnostic accuracy is limited in the early phase of the disease.

Clinical Course

Because the clinical presumption for COVID-19 was high with typical findings on the CT scan, a third sample was obtained on a second tracheal aspirate and confirmed COVID-19 diagnosis on an RT-PCR assay targeting the RNA-dependent RNA polymerase (RdRp) gene of SARS-CoV-2. This test was performed 4 days after the admission, 12 days after the onset of symptoms. The patient was extubated after 7 days of mechanical ventilation. Subsequent chest radiograph showed significant decrease in the pulmonary infiltrate.

Clinical Pearls

1. COVID-19 diagnosis can be confirmed by SARS-CoV-2 rRT-PCR on respiratory samples.

2. Repeating rRT-PCR after a first negative test can significantly improve the diagnostic yield.

3. The sensitivity of rRT-PCR varies between the different types of clinical samples, with the highest sensitivity for lower respiratory samples.

4. CT scan has a sensitivity greater than 90%, with a maximum performance after day 5 from the onset of symptoms, but a specificity of approximately 50%.

5. Bilateral ground-glass opacities are the typical pattern on chest CT scans in patients with COVID-19.

Acknowledgments

Suggested Readings

Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology*. 2020:200463.

Boonyaratanakornkit J, Vivek M, Xie H, et al. Predictive value of respiratory viral detection in the upper respiratory tract for infection of the lower respiratory tract with hematopoietic stem cell transplantation. *J Infect Dis*. 2020;221(3):379-388.

Caruso D, Zerunian M, Polici M, et al. Chest CT features of COVID-19 in Rome, Italy. *Radiology*. 2020201237.

Loeffelholz MJ, Tang Y-W. Laboratory diagnosis of emerging human coronavirus infections: the state of the art. *Emerg Microbes Infect*. 2020;9(1):747-756.

Pan Y, Zhang D, Yang P, Poon LLM, Wang Q. Viral load of SARS-CoV-2 in clinical samples. *Lancet Infect Dis*. 2020;20(4):411-412.

Rubin GD, Ryerson CJ, Haramati LB, et al. The role of chest imaging in patient management during the COVID-19 pandemic. *Chest*. 2020;158(1):106-116.

Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069.

Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA*. 2020;323(18):1843-1844.

Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. https://www-bmj-com.proxy.insermbiblio.inist.fr/content/369/bmj.m1808; 2020. Accessed August 24, 2020.

Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med*. 2020;382(12):1177-1179.