May 2020 Imaging Case of the Month: Still Another Emerging Cause for Infiltrative Lung Abnormalities

Prasad M. Panse MD
Clinton E. Jokerst MD
Michael B. Gotway MD

Department of Radiology
Mayo Clinic, Arizona
Scottsdale, Arizona 85054

Clinical History: A 46-year-old man with a history of well-controlled asthma presented to the Emergency Room with complaints of worsening non-productive cough for 4-5 days followed by fever to 104°F over the previous 3 days. The patient also complained of some chills and loose stools. The patient denied rhinorrhea, sore throat, congestion, and nausea or vomiting. The patient also denied illicit drug use, and drinks alcohol only occasionally and denied smoking.

The patient's physical examination showed a pulse rate of 79 / minute and a respiratory rate of 18 / minute, although his blood pressure was mildly elevated at 149/84 mmHg; he was afebrile with a temperature of 97.7 °F (36.5 °C). The patient's room air oxygen saturation was 98%. The physical examination showed some mild expiratory wheezes bilaterally, but was otherwise entirely within normal limits.

Which of the following represents the ***most appropriate*** step for the patient's management?

1. Obtain a complete blood count
2. Obtain a travel history
3. Obtain serum chemistries
4. Perform chest radiography
5. All of the above

Correct!
5. All of the above

All of the above steps are appropriate measures for this patient. It is conceivable that chest radiography could be deferred, given the normal oxygen saturation on room air, but obtaining a chest radiograph is certainly not inappropriate.

The patient was discharged home from the Emergency Room in stable condition with a prescription for a board-spectrum antibiotic. The patient returned to a different Emergency Room the following day with similar complaints, primarily complaining of the cough.

Which of the following represents the ***most appropriate*** step for the patient's management?

1. Obtain a complete blood count
2. Obtain a travel history
3. Perform chest radiography
4. Perform influenza testing
5. All of the above

Correct!
5. All of the above

Again, all of the above steps are appropriate measures for this patient. It is again conceivable that chest radiography could be deferred, given that normal oxygen saturation on room air, but obtaining a chest radiograph is certainly not inappropriate. In fact, given that the patient's cough has subjectively worsened, a chest radiograph is a reasonable test to perform.

Basic laboratory data showed a normal white blood cell count = 5.3 x 10^9 / L (normal, 3.4 – 9.6 x 10^9 / L) with a mildly reduced platelet count of 116 x 10^9 / L (135- 317 x 10^9 / L), no evidence of anemia, normal serum chemistries and normal renal function parameters. The patient's neutrophil count was normal, although the peripheral blood lymphocyte count was mildly reduced at 0.94 x 10^9 / L (normal, 0.95 – 3.07 x 10^9 / L). The patient's ferritin was also increased at 578 mcg/L (normal, 24 – 337 mcg/L) and the procalcitonin-S level was mildly elevated at 0.09 ng/dL (normal, ≤0.08 ng/dL). The patient was referred for chest radiography (Figure 1).

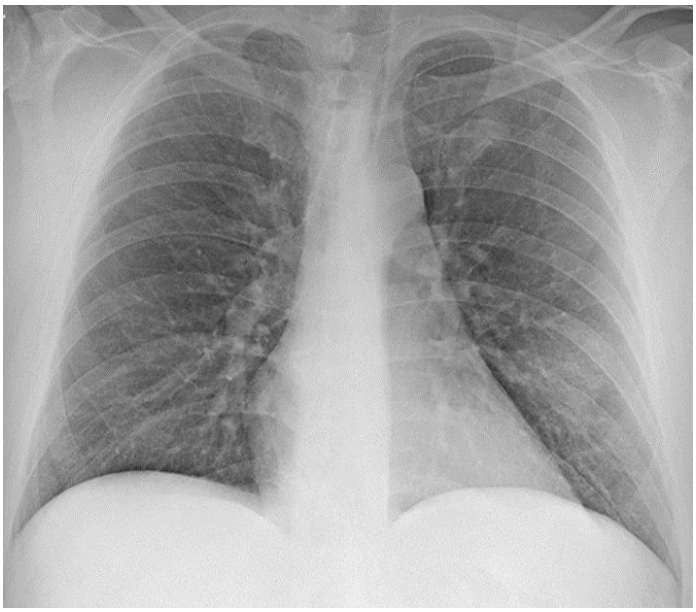

Figure 1. Frontal chest radiography.

Which of the following statements regarding the chest radiograph is ***most accurate***?

1. The chest radiograph shows focal rounded opacity at the left base
2. The chest radiograph shows mediastinal and peribronchial lymph node enlargement
3. The chest radiograph shows multifocal bilateral areas of consolidation
4. The chest radiograph shows normal findings
5. The chest radiograph shows numerous small nodules

Correct!

1. The chest radiograph shows focal rounded opacity at the left base

The heart size is normal and the mediastinal and hilar contours are within normal limits; no evidence of intrathoracic lymph node enlargement is seen. No pleural abnormality is present. Focal somewhat rounded increased opacity at the left base is present, but this abnormality is isolated; no right lung abnormalities are seen. There is no evidence of small nodules.

The patient was questioned regarding recent travel, and he indicated that he has been in New York City in early March 2020, riding the subways, attending various shows, until the shows and other public gatherings were canceled due to the COVID-19 pandemic. He noted his respiratory symptoms began just after he returned from his vacation.

Which of the following courses of action is the ***most appropriate next step*** for the management of this patient?

1. Contact local infection control
2. Isolation of the patient
3. Real time reverse-transcription–polymerase chain- reaction (RT-PCR) testing for SARS-CoV-2 (COVID-19)
4. Supportive care
5. All of the above

Correct!
5. All of the above

All of the steps listed are appropriate for this patient. The patient has developed symptoms consistent with COVID-19 infection following exposure to a region with a high prevalence of this infectious agent, and therefore he should be regarded as a "suspected case" of COVID-19 infection. As this infection is highly contagious, without an available vaccine or a currently proven effective therapy, infection control and supportive care measures remain the cornerstone of therapy.

Influenza testing and testing for streptococcal infection were both negative. COVID-19 RT-PCR nasal swab testing was also negative.

Which of the following statements regarding the management of this patient is ***most accurate***?

1. Bronchoscopy should be performed to more confidently exclude COVID-19 and other infections
2. Chest CT should be performed
3. Chest radiography should be immediately repeated
4. COVID-19 infection has been effectively excluded
5. The patient should remain isolated

Correct!
5. The patient should remain isolated

The sensitivity for the RT-PCR nasal swab for COVID-19 infection varies according to the source cited, but recent data suggest the test may be at least 90% sensitive, perhaps greater, for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens. This test is not infallible, however, with false negative results reported. This observation has led a number of investigators to suggest that CT scanning may prove useful for detecting lung abnormalities indicative of COVID-19 infection. Nevertheless, the CT findings of COVID-19 infection, while often suggestive in the proper context [one of high pre-testing probability due to a combination of typical symptoms, recent exposure to an infected individual, and/or a relatively high prevalence of COVID-19 infection in the community are non-specific and can be seen with other infectious and non-infectious disorders. Furthermore, negative CT results have been encountered in the presence of proven infection. Finally, CT scanning for COVID-19 infected patients exposes transport personnel and CT technologists- these exposures could lead to additional infections- and at least one hour is required for decontamination of the CT suite following scanning of an infected individual, which curtails CT availability for other patients who need this resource. Bronchoscopy is not required either- this procedure will needlessly expose staff when the proper course of management still remains supportive care and isolation. Repeat chest radiography would be indicated for a change in respiratory status, but is not necessarily required at this point.

The patient was still stable and was sent home to self-quarantine. He returned to the Emergency Room 2 days later with complaints of worsening shortness of breath and continued fever. Chest radiography (Figure 2) was repeated.

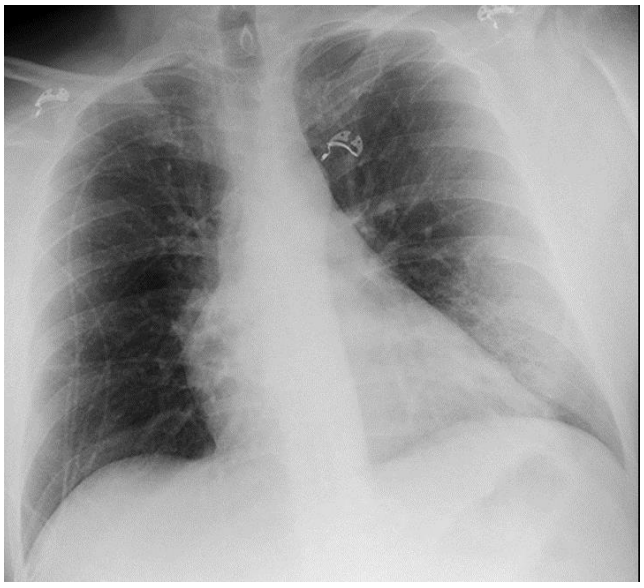

Figure 2. Frontal chest radiography performed several days following presentation chest radiography (Figure 1).

Which of the following statements regarding the chest radiograph is ***most accurate***?

1. The chest radiograph has now normalized
2. The chest radiograph shows new interlobular septal thickening
3. The chest radiograph shows progressive, multifocal, bilateral consolidation
4. The chest radiograph shows the previously noted somewhat rounded opacity at the left base on the presentation chest radiograph (Figure 1) has slightly worsened
5. The chest radiograph shows the previously noted somewhat rounded opacity at the left base has cavitated

Correct!

4. The chest radiograph shows the previously noted somewhat rounded opacity at the left base on the presentation chest radiograph (Figure 1) has slightly worsened

The chest radiograph appears fairly similar to the presentation chest radiograph (Figure 1), perhaps with slight worsening of the somewhat rounded opacity at the left base, but there is no evidence of cavitation. The mediastinum appears normal and no pleural abnormalities or interlobular septal thickening is present. The right lung remains clear.

In the Emergency Room, the patient was oxygenating well, with room air oxygenation saturation of 97%. Unlike his presentation, however, he was now complaining of substernal chest pain, and his white blood cell count was now 11.4 x 10^9 / L (normal, 3.4 – 9.6 x 10^9 / L). His D-dimer was mildly elevated at 707 ng/mL (normal, ≤500 ng/mL) and his C-reactive protein level was also elevated at 25 mg/L (normal, ≤8 mg/L). Repeat RT-PCR nasal swab testing for COVID-19 infection was performed and found to be positive, and the patient was admitted. Given his COVID-19 infection, hydroxychloroquine / chloroquine therapy was anticipated.

Which of the following courses of action is the ***most appropriate next step*** for the management of this patient?

1. Perform bronchoscopy
2. Perform CT pulmonary angiography
3. Perform ECG
4. Perform unenhanced chest CT
5. Routine admission to the hospital

Correct!
3. Perform ECG

The patient has no defined risk factors for venous thromboembolism and testing along these lines is probably not required, particularly given that he has a focal abnormality on his chest radiograph which can be explained on the basis of infection, as can his symptoms; the focal appearance of chest radiographic abnormality would be very atypical for thromboembolic disease. The elevation of his D-dimer is potentially attributable to his COVID-19 infection. As noted above, chest CT is not routinely indicated for COVID-19 infected patients, particularly when chest radiographic abnormalities have already been noted. Given that the patient is being admitted and has known COVID-19 infection, the admission should not be "routine;" rather protective measures, such as a respirator for the patient to wear, or admission to a room capable of providing negative air pressure, is required. Furthermore, hospital staff caring for the patient should also be appropriately protected through the use of a combination of airborne precautions. Given that hydroxychloroquine and chloroquine has been approved to treat COVID-19 infected patients by the Food and Drug administration under an emergency use authorization, and that these medications can be associated with dysrhythmia owing to prolongation of the Q-T interval, obtaining an ECG prior to the initiation of hydroxychloroquine and chloroquine is appropriate.

The patient was admitted to an intermediate care unit for monitoring and, given his wheezing, albuterol therapy was initiated. The patient was empirically started on azithromycin and ceftriaxone therapy, and an ECG was performed, after which hydroxychloroquine treatment was begun, following consultation with infectious disease. Testing for various respiratory pathogens was initiated as was testing for tuberculosis. Unenhanced chest CT was also recommended by infectious disease (Figure 3).

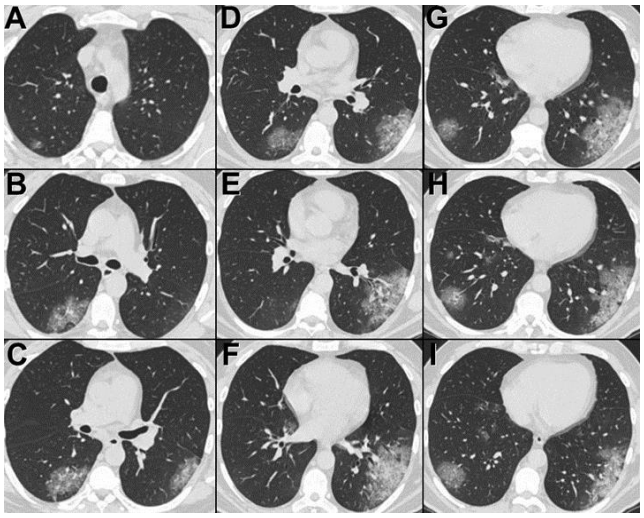

Figure 3. Representative images from the axial unenhanced chest CT displayed in lung windows.

Which of the following statements regarding the chest CT is ***most accurate***?

1. The chest CT shows bronchiectasis
2. The chest CT shows features most consistent with a bacterial pneumonia
3. The chest CT shows features suggesting fibrotic lung disease
4. The chest CT shows findings suggesting unsuspected metastatic pulmonary malignancy
5. The chest CT shows findings typical for those reported in patients with COVID-19

Correct!

5. The chest CT shows findings typical for those reported in patients with COVID-19

The unenhanced chest CT shows patchy, multifocal, somewhat rounded or oblong areas of ground-glass opacity preferentially distributed in the subpleural lower lungs bilaterally. The areas of ground-glass opacity show internal mild interlobular septal thickening and intralobular interstitial thickening. This imaging features, while ultimately rather non-specific, are those commonly reported in patients with COVID-19 pulmonary infection. Areas of consolidation may also occur, and both the “crazy paving” and the “reverse (ground-glass opacity) halo” signs have been reported at chest CT as well. While bacterial pneumonias may take multiple forms and is difficult to entirely exclude bacterial infection in this circumstance, the presence of ground-glass opacity alone would be unusual for a bacterial pulmonary infection. Rather, bacterial infections commonly present as areas of consolidation with air bronchogram formation, centrilobular nodules (often with branching configurations) and airway thickening. No bronchiectasis is present, and the morphology of the lung parenchymal opacities is not suggestive of metastatic malignancy; the latter typically appears as multiple nodules or masses, with or without cavitation.

The patient continued to spike fevers to approximately 102 °F, although his dyspnea and cough had improved mildly. The patient had become frustrated with his care and felt he could take care of himself at home, and left the hospital against medical advice.

He was subsequently readmitted to another hospital due to worsening shortness of breath with minimal activity accompanied by chest heaviness, now 12 days after his initial diagnosis. He felt he had been improving somewhat after he initially left the hospital, but now his symptoms were worsening. His oxygen saturation was now 94% on 3L oxygen, decreasing to 90% with walking. In the Emergency Room, laboratory data showed a mildly elevated white blood cell count of 9.9 x 10^9 / L (normal, 3.4 – 9.6 x 10^9 / L), but without fever. His heart and respiratory rates were 86 / minute and 18 / minute, respectively. Frontal chest radiography (Figure 4) was performed.

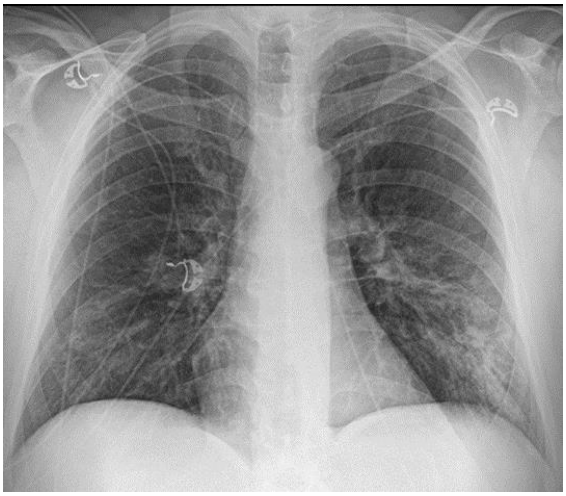

Figure 4. Frontal chest radiograph at second Emergency Room presentation (now 12 days after his initial diagnosis).

Which of the following statements regarding the chest radiograph is ***most accurate***?

1. The chest radiograph shows identical findings to the presentation chest radiograph (Figure 1)
2. The chest radiograph shows new pleural effusions
3. The chest radiograph shows overall improvement
4. The chest radiograph shows overall interval worsening
5. The chest radiograph shows resolution of previously noted lung opacity with new lung opacities in previously uninvolved areas

Correct!
4. The chest radiograph shows overall interval worsening

The frontal chest radiograph shows patchy peribronchovascular thickening in the left lower lobe at the site of the previously noted somewhat rounded opacity at presentation chest radiography (Figure 1). Very faint abnormalities are now visible in the right lower lobe. Overall, the chest radiographic appearance has worsened compared to presentation, with new areas of involvement now visible (right lower lobe) and worsening of pre-existing abnormalities. No pleural effusion or lymphadenopathy is present.

The patient's C-reactive protein level was trending downward compared with his initial hospitalization, as was his D-dimer level, the latter now 612 ng/mL (normal, ≤500 ng/mL). Repeat COVID-19 testing was positive. His ECG was normal and unchanged and initial troponin measurement was within the normal range.

Which of the following courses of action is the ***most appropriate next step*** for the management of this patient?

1. Cardiac MRI
2. Continue supportive care
3. Perform bronchoscopy
4. Perform CT pulmonary angiography
5. Perform repeat unenhanced chest CT

Correct!
2. Continue supportive care

The patient's symptoms are completely consistent with COVID-19 infection. Apparent clinical worsening with progression of radiographic abnormalities during the second week of COVID infection has been noted, with patients who improve subsequently showing such improvement 3-4 weeks following the diagnosis of COVID-19 infection; this patient is exactly within the time window when clinical and radiographic worsening may be seen. He again has no risk factors for pulmonary embolism, and his D-dimer level is actually lower than presentation, and therefore investigation for suspected acute pulmonary embolism is probably unnecessary. While the patient's substernal chest pain should raise the possibility of cardiac disease, including ischemic heart disease and myocarditis, the patient's ECG is normal and unchanged, and his troponin levels are within the normal range, making these diagnoses unlikely. The patient's substernal chest pain is a common phenomenon in the setting of repeated coughing and may be explainable on that basis. Finally, cardiac MRI would potentially expose transportation staff and technologists to COVID-19 infection, and should be undertaken only if absolutely necessary. Bronchoscopy is not indicated as the patient has an established infection that explains his complaints and imaging findings, and performing bronchoscopy is unlikely to provide management-altering information despite needlessly exposing staff to COVID-19 infection.

The patient underwent CT pulmonary angiography (Figure 5).

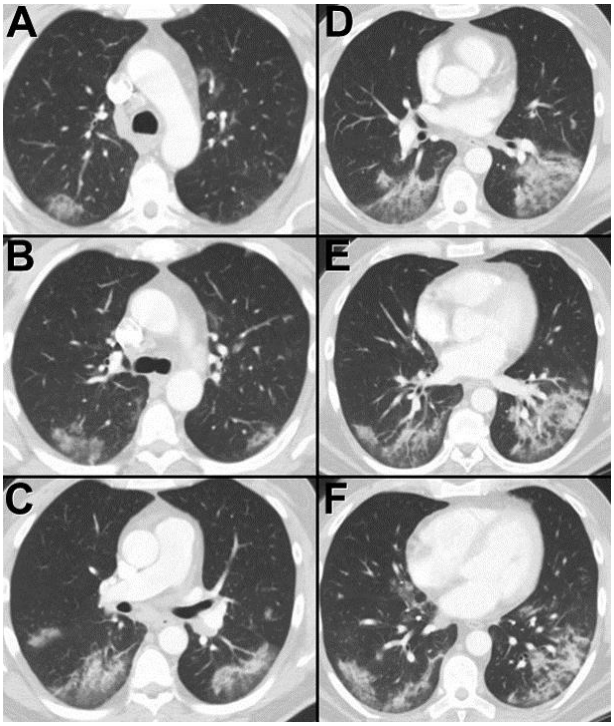

Figure 5. Representative images in lung windows from the CT pulmonary angiography.

Regarding the CT pulmonary angiogram (Figure 5), which of the following statements is ***most accurate***?

1. CT pulmonary angiography shows acute pulmonary embolism
2. CT pulmonary angiography shows myocarditis
3. CT pulmonary angiography shows new pleural effusions
4. CT pulmonary angiography shows pericarditis
5. CT pulmonary angiography shows progression of the pulmonary abnormalities seen previously (Figure 3)

Correct!

5. CT pulmonary angiography shows progression of the pulmonary abnormalities seen previously (Figure 3)

The CT pulmonary angiogram shows no evidence of acute or chronic thromboembolic disease and no pleural abnormalities are present. While CT pulmonary angiography cannot exclude myocarditis or ischemic heart disease, there is no visible coronary calcium, no pericardial effusion is present, and the myocardium appears to enhance normally. The pulmonary opacities seen at the initial unenhanced chest CT (Figure 3) have worsened, showing an overall greater extent and transitioning from a more “pure” ground-glass opacity appearance to a more consolidative appearance.

The patient was readmitted and isolated. Over the next two days, his remained afebrile and his shortness of breath and chest pain improved. His oxygenation improved to 98% on room air. The patient was discharged home with instructions to continue quarantining for 14 days, given his persistent positive COVID-19 testing.

Diagnosis: COVID-19 (Coronavirus Disease 2019 / SARS-CoV-2) pneumonia

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