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30-Year-Old Woman With Cough, Dyspnea, and Anosmia



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A 30-year-old woman presented for the evaluation of acute cough in March 2020. Over the previous 4 days, she had experienced cough, dyspnea, and post-tussive emesis. Within the previous 3 days, she had developed diffuse myalgia and anosmia. She requested a telehealth visit with her primary physician due to progression of her symptoms.

Her medical history was notable for class III obesity with a body mass index of 47 kg/m². She had immigrated to the United States from East Africa 18 years prior. She took no regular prescription medications and used occasional over-the-counter ibuprofen for aches and pains. She reported living with multiple other family members — including her parents, sister, and three brothers — who had been ill with similar symptoms. A physical examination was not possible during the telephone encounter; however, the patient was able to speak in full sentences without difficulty. Review of systems was remarkable for clear sputum production, sore throat, chest tightness, and anorexia.

The patient was referred to the emergency department (ED) where she was afebrile with temperature of 37°C, heart rate between 95 and 102 beats/min, saturating 94% on room air, blood pressure of 123/77 mm Hg, and respiratory rate of 16 breaths/min. The patient was alert, oriented, and in no acute distress. Her mucous membranes were moist. Cardiovascular exam was notable for mild tachycardia without murmurs or rubs. Pulmonary examination showed normal air entry without wheezes or crackles, despite frequent, dry coughing. She used no accessory muscles of respiration. Her physical examination was otherwise unremarkable. Evaluation in the ED included a chest x-ray that was read as normal.

1. What is the most likely etiology of this patient's illness?

- Bacterial pneumonia with bloodstream infection
- Pulmonary autoimmune vasculitis
- Viral respiratory tract infection
- Pulmonary embolism
- Exacerbation of chronic obstructive pulmonary disease

Distinguishing bacterial versus viral pulmonary infection can be difficult, as they sometimes coexist. In this case, bacterial infection would be less likely given the recent sick contact and lack of consolidation on initial chest x-ray. Bacterial pneumonia is sometimes a complication of previous viral upper respiratory tract infections.¹ However, bacterial pneumonia is not usually accompanied by bloodstream infection and, when it is, patients may be more ill-appearing with systemic signs of inflammation including hypotension, tachypnea, tachycardia, fever, and elevated white blood cell count. Pulmonary manifestations of autoimmune vasculitis (eg, Churg-Strauss syndrome, granulomatosis polyangiitis, and microscopic polyangiitis) may look similar to infectious respiratory illnesses, yet autoimmune vasculitis usually presents with a more prolonged clinical course, frequently has other systemic manifestations such as renal involvement, and is often considered after infectious etiologies have been excluded. This patient is likely suffering from a viral illness, with high suspicion of coronavirus disease 2019 (COVID-19) given the rapid onset of symptoms and the increasing prevalence of COVID-19 in the community at the time of presentation. Pulmonary embolism may also involve fever and cough, but the history of sick contact and alternative diagnosis of

See end of article for correct answers to questions.

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viral respiratory tract infection makes this condition less probable. Chronic obstructive pulmonary disease exacerbation can cause cough and dyspnea, but it is less likely to include systemic symptoms as seen in this case. Nonetheless, patients with underlying lung disease are at increased risk of respiratory infectious pathogens, which may then trigger a chronic obstructive pulmonary disease exacerbation.

This patient's initial laboratory testing (normal range) demonstrated: hemoglobin 12.2 g/dL (12.0 to 15.5 g/dL), leukocytes $4.9 \times 10^9/L$ (3.92 to $5.13 \times 10^{12}/L$), lymphocytes $2.53 \times 10^9/L$ (0.95 to $3.07 \times 10^9/L$), potassium 4.2 mmol/L (3.6 to 5.2 mmol/L), sodium 136 mmol/L (135 to 145 mmol/L), creatinine 0.67 mg/dL (0.84 to 1.21 mg/dL), erythrocyte sedimentation rate 35 mm/h (0 to 29 mm/h), C-reactive protein 35.5 mg/L (≤ 10 mg/L), ferritin 75 $\mu\text{g}/L$ (24 to 307 $\mu\text{g}/L$), prothrombin time 13.6 s (10 to 14 s), international normalized ratio 1.2 (≤ 1.1), fibrinogen 375 mg/dL (200 to 393 mg/dL), D-dimer 395 ng/mL (≤ 500 ng/mL), lactate 1.0 mmol/L (0.5 to 1 mmol/L), alanine aminotransferase 26 U/L (7 to 55 U/L), aspartate aminotransferase 28 (8 to 48 U/L), lactate dehydrogenase 225 U/L (122 to 222 U/L), procalcitonin <0.06 ng/mL (≤ 0.15 ng/mL), interleukin-6 10.2 pg/mL (≤ 1.8 pg/mL), troponin T (fifth generation) <6 ng/L (≤ 10 ng/L), N terminal pro-brain natriuretic peptide 36 pg/mL (10 to 140 pg/mL), human chorionic gonadotropin 0.5 IU/L (<5 IU/L). As mentioned above, an initial radiograph of the chest did not reveal pulmonary opacities. Electrocardiogram showed sinus rhythm at 95 beats/min.

2. What is the next best test to order for this patient?

- Multiplex nucleic acid testing for respiratory pathogens
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real-time reverse-transcriptase polymerase chain reaction (RT-PCR)
- Nasopharyngeal influenza swab
- Sputum culture
- Computed tomography (CT) of the chest

While this patient does have a clinical presentation consistent with a viral upper respiratory tract infection, a respiratory pathogen panel would not be helpful given a high suspicion for COVID-19. At the time the patient presented, widely available respiratory pathogen panels (eg, FilmArray Respiratory Panel, BioFire Diagnostics, Salt Lake City, UT) did not detect COVID-19.² Currently, RT-PCR is the recommended testing for suspected COVID-19 cases in the United States.³ Patients with hallmarks of fever, cough, dyspnea, and close contact with a confirmed or suspected COVID-19 patient should receive testing.² At the time the patient presented, influenza was widespread and positive influenza testing would not exclude co-infection with COVID-19; this case describes a patient with a history that merits COVID-19 testing before influenza swab. Although bacterial pneumonia may be a complication of COVID-19, sputum culture would be of lesser benefit in this setting where suspicion for bacterial pneumonia is not as high. A recent study revealed that chest CT may be beneficial in diagnosis of COVID-19 when initial RT-PCR is negative yet clinical suspicion remains high.⁴ However, chest CT would not be the most practical first-line test, particularly for stable patients who have not yet had specific testing for COVID-19.

While in the ED, in addition to initial laboratory and imaging previously described, the patient also underwent infectious evaluation including blood cultures, urine antigens, and influenza swab.

3. What is the best recommended test for assessing this patient for COVID-19?

- Nasopharyngeal swab for viral culture
- Nasopharyngeal swab for RT-PCR
- Serologic antibody assay
- Sputum culture for RT-PCR
- CT scan of the chest

Because of safety concerns in handling COVID-19, viral culture is not recommended. RT-PCR is currently the best widely available standard test for individuals with symptoms and high clinical suspicion for

the virus as previously discussed. Nasopharyngeal or oropharyngeal sample collections are not considered aerosol-generating procedures for which airborne precautions such as an N95 mask would be necessary. At the time the patient presented, serologic antibody assays were under production and available through the Mayo Clinic Health System; however, they were not widely available. Recent analyses describing the clinical utility of serologic assays have also shown the poor diagnostic sensitivity of these assays during the first 14 days post-symptom onset (sensitivity range, 0% to 56.6%; Abbott SARS-CoV-2 immunoglobulin G assay and EUROIMMUN EI SARS-CoV-2 immunoglobulin G assay).⁵ Sputum culture would not be recommended due to absence of cough and because viral culture in the setting of COVID-19 may put microbiology workers at risk; therefore, a sputum culture was not collected during the patient's hospitalization. Chest CT scan may be useful in the setting of high clinical suspicion and negative initial SARS-CoV-2 RT-PCR testing (sensitivity of 97% with specificity of 25%), particularly in areas where the disease is widely spread.⁶ However, this would not have been the most cost-effective or beneficial method for large-scale testing and was not pursued in this case.

Following evaluation in the ED including a positive COVID-19 RT-PCR result, the patient was admitted to the hospital floor for continued observation and management of her respiratory illness which had worsened since her initial testing.

4. Which one of the following treatments would be the recommended for this patient?

- a. Chloroquine
- b. Remdesivir
- c. Azithromycin
- d. Corticosteroids
- e. Supportive care

Many agents are being studied for potential efficacy in treating COVID-19. These agents include chloroquine and remdesivir, which were shown to be active against SARS-COV-2

in vitro. Remdesivir showed reduction in time to clinical improvement in a multicenter, placebo-controlled trial, yet the finding was not statistically significant.⁷ Likewise, azithromycin and hydroxychloroquine showed a viral load decline in a nonrandomized clinical trial, with the caveats of QT prolongation and risk of cardiac arrest.⁸⁻¹⁰ Presently, there is insufficient evidence to support the treatment of COVID-19 with corticosteroids, and both the Centers for Disease Control and Prevention (CDC) and World Health Organization recommend against corticosteroids solely to treat COVID-19. Ultimately, existing drugs are still investigational and approved only for compassionate use or experimental trials. The current recommendation is supportive care for patients with COVID-19, with potential use of investigational agents only for patients who are enrolled in clinical trials, or those who are particularly sick and unstable.

Although supportive care is the mainstay of treatment for confirmed mild-to-moderate COVID-19 cases, this patient was enrolled in a clinical trial and received hydroxychloroquine 400 mg twice daily for 1 day followed by 200 mg twice daily for 4 days.

5. How should this patient be counseled about prognosis and next steps?

- a. She will likely experience mild symptoms; no further steps are needed
- b. She will likely experience severe symptoms; she should be admitted to the intensive care unit (ICU) and then quarantined
- c. This will likely be fatal; she should be admitted to the ICU and then quarantined
- d. She will likely experience mild symptoms; she should be quarantined at home until resolution of respiratory symptoms, fever without antipyretic medications, and two negative RT-PCR tests
- e. She will likely experience severe symptoms; she should be admitted and quarantined for 4 weeks

The vast majority of patients (>80%) will experience no or mild symptoms, with the most common symptom being fever, followed by fatigue.¹¹ This patient's body mass index of 47 kg/m² places her at elevated risk

for severe disease. However, given her younger age, benign medical history, initial presentation with mild-to-moderate respiratory symptoms, and reassuring laboratory testing, she would probably not experience severe symptoms, ICU care, or death. It is important for her to remain closely monitored by her outpatient providers and practice social distancing by home quarantine as well as supportive care until resolution of symptoms. Patients experiencing mild disease should not leave home until resolution of respiratory symptoms and fever without antipyretics because viral shedding may continue occur with minimal symptomology. For this patient who underwent COVID-19 testing, the CDC recommends that, before discontinuing precautions, she should have improvement of respiratory symptoms, resolution of fever without use of antipyretics, and two negative COVID-19 tests collected by nasopharyngeal swab (collected at least 24 hours apart), which makes this the correct answer.¹² If this patient follows the above CDC recommendations with a test-based approach or test-sparing with resolution of symptoms, then it is unnecessary for her to undergo quarantine for an extended period such as 4 weeks, even in severe cases.

Following a brief hospital stay with supportive care and enrollment in a hydroxychloroquine medication trial, the patient had improved symptomatically and was discharged to home with self-care and social distancing. She was afebrile and hemodynamically stable with a down-trending C-reactive protein before dismissal. Follow-up was scheduled via telephone visit to occur two days following discharge.

DISCUSSION

The COVID-19 pandemic has burdened health care systems in the United States and worldwide. It spread dramatically, impacting more people than the previous SARS-CoV-2 and Middle East Respiratory Syndrome (MERS)—CoV crises combined.² Recently, the CDC has documented a cumulative hospitalization rate of 20.0 per 100,000 cases with the highest rate in the >65-year-old

population (63.8 per 100,000 cases).¹³ At the time of writing, the CDC estimated the COVID-19 case-fatality ratio to be approximately 5%; however, this estimate might be inflated by testing limitations such as missing large numbers of people who are asymptomatic or minimally symptomatic.¹³

Best practices in diagnosing and treating the infection are uncertain, particularly as data emerges and evidence evolves daily. It is remarkable that the great majority of cases will not require hospitalization or ICU-level care. Currently, there is no randomized controlled trial evidence that specific treatments significantly improve outcomes in suspected or confirmed COVID-19 patients.¹⁴ Many potential therapeutics are currently investigational with a wide range of early results. As of April 2, 2020, there were at least 109 ongoing clinical trials of pharmacologic interventions for COVID-19.¹⁴ In particular, there were early reports from China in a series of more than 100 patients that those treated with chloroquine phosphate had shortened disease courses, improvement of lung imaging findings, and increased negative conversion rates.¹⁵ These results have not been replicated in the United States, and medications including chloroquine, hydroxychloroquine, and azithromycin all must be investigated with caution given the risks of QT prolongation and drug-induced sudden cardiac death.¹⁰ At the time of writing, remdesivir had recently gained approval for use by the US Food and Drug Administration in the United States for COVID-19; however, as mentioned previously, current clinical trials have only showed modest improvement of clinical course.⁷

Most patients present with mild-to-moderate symptoms to primary care providers who must determine the need for testing on a case-by-case basis.² Typically, COVID-19 involves viral respiratory tract-type symptoms such as fever, cough, fatigue, or dyspnea. Other symptoms include anosmia and gastrointestinal symptoms such as nausea or abdominal pain.^{2,16,17} Unfortunately, COVID-19 in the United States has disproportionately affected people of color.¹⁸ Potential risk factors for

more severe illness include obesity, hypertension, or underlying structural lung diseases as experienced by many patients living in the United States. Current therapy for COVID-19 is supportive; therefore, early identification, contact tracing, social distancing, and appropriate supportive care for patients with COVID-19 are essential for slowing the spread and burden of disease.

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CORRECT ANSWERS: 1. c. 2. b. 3. b. 4. e. 5. d