Co-infection of COVID-19 and Influenza A in A Hemodialysis Patient: A Case Report

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2, a novel coronavirus that was first discovered in Wuhan, China in December 2019. With the growing numbers of community spread cases worldwide, the World Health Organization (WHO) declared the COVID-19 outbreak as a pandemic on March 11. Like influenza viruses, SARS-CoV-2 is thought to be transmitted by contact, droplets, and fomites, and COVID-19 has a similar disease presentation to influenza. Here we present a case of influenza A and COVID-19 co-infection in a 60-year-old man with end-stage renal disease (ESRD) on hemodialysis.

Case presentation: A 60-year-old man with ESRD on hemodialysis (HD) presented for worsening cough, shortness of breath, and diarrhea. The patient first developed a mild fever (100 °F) during hemodialysis three days prior to presentation and has been experiencing worsening flu-like symptoms, including fever of up to 101.6 °F, non-productive cough, generalized abdominal pain, nausea, vomiting, and liquid green diarrhea. He lives alone at home with no known sick contacts and denies any recent travel or visits to healthcare facilities other than the local dialysis center. Rapid flu test was positive for influenza A. Procalcitonin was elevated at 5.21 ng/mL with a normal white blood cell (WBC) count. Computed tomography (CT) chest demonstrated multifocal areas of consolidation and extensive mediastinal and hilar adenopathy concerning for pneumonia. He was admitted to the biocontainment unit of Nebraska Medicine for concerns of possible COVID-19 and was started on oseltamivir for influenza and vancomycin/cefepime for the probable bacterial cause of his pneumonia and diarrhea. GI pathogen panel and C. diff toxin assay were negative. On the second day of admission, initial nasopharyngeal swab came back positive for SARS-CoV-2 by RT-PCR. The patient received supportive care and resumed bedside hemodialysis in strict isolation, and eventually fully recovered from COVID-19.

Conclusions: Our case demonstrated that co-infection of influenza and SARS-CoV-2 can occur in patients with no known direct exposure to COVID-19. The possibility of SARS-CoV-2 co-infection should not be overlooked even when other viruses including influenza can explain the clinical symptoms.

Background

Coronavirus disease 2019 (COVID-19), a novel coronavirus disease that was first reported in Wuhan, China, is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. With the growing numbers of community spread cases worldwide, the World Health Organization (WHO) declared the COVID-19 outbreak as a pandemic on March 11, 2020[2]. As of April 23, 2020, a total of 2,630,778 cases have been reported in 185 countries, with 183,559 deaths[3]. The first COVID-19 case in the United States (U.S.) was confirmed on January 20, 2020[4], and in a mere three months, the number of confirmed cases in the U.S. roared to 842,264, with 46,785 deaths nationwide as of April 23, 2020[3]. In the majority of the cases in the U.S., public health officials cannot identify how or where they became infected, indicating widespread national community transmission[5]. Like influenza viruses, SARS-CoV-2 is thought to be mainly transmitted via respiratory droplets or direct contact[6], and COVID-19 has a similar disease

presentation to influenza, causing respiratory diseases that present as a broad-spectrum of illnesses from asymptomatic or mild to severe illness and, in some cases, death[7]. Here we present a case of COVID-19 and Influenza A co-infection in a patient who has no travel history or known exposure to suspected or confirmed COVID-19 cases in the United States.

Case Report

A 60-year-old man with end-stage renal disease (ESRD) on hemodialysis presented to the emergency department (ED) from home on March 18, 2020, with a chief complaint of fever, cough, shortness of breath, and diarrhea. He has a history of IgA nephropathy and a failed kidney transplant due to rejection in 2013. He lives alone at home in western Iowa and had no recent travel history or visits to any healthcare facilities except for a local dialysis center for routine dialysis.

The patient receives hemodialysis three times a week (Monday, Wednesday, and Friday) in a local dialysis center. The symptoms started on Monday, March 16, 2020, while he was at his routine dialysis when he began to feel feverish and experienced chills. His temperature taken at the dialysis center was 37·8°C. After dialysis, he developed a headache, non-productive cough, sore throat, runny nose, poor appetite with nausea, vomiting, and abdominal pain, which progressively worsened over the next two days. On March 17, he started to have generalized myalgias, mild shortness of breath, and diarrhea with liquid green stool without visible blood. He missed his hemodialysis on March 18 and presented to the ED.

On arrival at the ED, the patient was provided a mask and placed in a private room in accordance with the ED screening protocol. He was ill-appearing with a fever of 38·6°C. His respiratory rate was 23 per minute, and other vital signs were unremarkable. Physical examination was significant for diffuse rhonchi and bibasilar rales on auscultation. Chest X-ray (Figure 1) showed right midlung consolidation, and patchy left lower lung opacities, concerning for multifocal pneumonia. Rapid flu antigen test was positive for influenza A. A nasopharyngeal swab specimen was sent for real-time reverse-transcriptase polymerase chain reaction (RT-PCR) test to rule out COVID-19 infection. He was placed on contact and airborne isolation precautions with eye protection for concerns of probable COVID-19 as per the Center for Disease Control and Prevention (CDC) recommendations[4].

Lab workup was significant for elevated procalcitonin and lymphopenia (Table). The electrocardiogram showed normal sinus rhythm. Computed tomography (CT) chest (Figure 2) demonstrated multifocal areas of consolidation and tree-in-bud opacities within multiple lobes of the lungs compatible with multifocal pneumonia, as well as small bilateral pleural effusions and extensive mediastinal ad bilateral hilar adenopathy. CT abdomen and pelvis showed mildly dilated gas and fluid-filled loops of small bowel and bowel wall enhancement, reflecting possible partial distal obstruction/ileus and enteritis. Blood cultures were taken, and the patient was started on oseltamivir for influenza. He is anuric; therefore, we did not test urine streptococcal and legionella antigen. The patient was then admitted to a negative pressure room on an isolation ward while awaiting COVID-19 results.

On hospital day 2, his RT-PCR test was positive for SARS-CoV-2, confirming the diagnosis of COVID-19. The local health department was notified to investigate the source of infection. The patient was afebrile, reported feeling extremely fatigued, but his cough and shortness of breath improved. His primary complaint was severe liquid green diarrhea, although the GI pathogen panel and C. diff toxin assay were negative. The repeated procalcitonin level (Table) was elevated on day 2, suggestive of fivefold increased risk of severe SARS-CoV-2 infections[8]. The patient was continued on vancomycin and cefepime for the suspected superimposed bacterial pneumonia. Notably, he had multiple episodes of hypotension with systolic pressure in the high 80s (mmHg) to 90s with mean arterial pressure (MAP) in the low 60s. We administered 500 ml of lactated Ringer's solution for volume resuscitation. However, aggressive fluid resuscitation was avoided to prevent volume overload. Oral fluids were encouraged to maintain normal volume status. For his COVID-19, as there are no proven therapeutic options, the treatment is mainly supportive[4]. He was deemed not a candidate for the clinical trial with remdesivir due to his ESRD. Corticosteroids were not given as they may delay viral clearance and prolong the disease course[9].

Hemodialysis resumed at the bedside as per the CDC guidelines[10] on hospital day 3. He remained afebrile, and his blood pressure improved with midodrine and albumin after the dialysis.

Since hospital day 4, the patient started to feel better with increased appetite and improvement of diarrhea, cough, and shortness of breath. Blood cultures demonstrated no bacterial growth for 5 days. With a multidisciplinary approach and optimal medical management, he continues to show clinical improvement despite his comorbidities.

To optimize the use of personal protective equipment (PPE), the patient's dialysis schedule was changed to Tuesday, Thursday, and Saturday to decrease the dialysis days during his hospitalization. His volume status was closely monitored, as inadequate oral fluid intake and diarrhea could lead to hypovolemia and delay dialysis.

The patient was discharged home on hospital day 9 based on a test-based strategy as per CDC guidelines because of his history of solid organ transplant[11]. No outpatient dialysis precautions were recommended to the patient as he had two negative COVID-19 tests (≥24 hours apart)[11].

Discussion And Conclusion

Our case demonstrated that co-infection of influenza and SARS-CoV-2 could occur in patients with no known direct exposure to COVID-19. The patient presented with non-specific symptoms that were clinically indistinguishable from illnesses caused by other respiratory pathogens, and the rapid antigen tests in the ED confirmed influenza A infection. He lives alone and independently at home in western Iowa, has no recent travel history or visits to any healthcare facilities other than a local dialysis center three times a week for routine dialysis. At the time of his presentation, there was only one confirmed, travel-related case in the county where the patient lives, and the patient denied any direct contact with the first infected person. Although there was no community spread case in the county where the patient lives,

community transmitted cases were reported both in western Iowa and Omaha, Nebraska, at the time of this patient's presentation. Given the increase in the rapid community transmission of the COVID-19 pandemic, infectious disease team recommended that concomitant infection of COVID-19 needed to be ruled out in this high-risk patient with multiple comorbidities even when there was a lack of clear history of exposure and his symptoms could be easily explained by his positive rapid influenza antigen test. The local health department was notified of the positive COVID-19 results for the investigation of the source of infection. On March 21, 2020, this case was declared as the second confirmed case and the first confirmed community transmitted case in the area[12].

The severity of clinical presentations of COVID-19 ranges widely from asymptomatic, mild to severe illnesses requiring hospitalization and intensive care. As many infected persons remain asymptomatic or only develop mild symptoms, many cases go unidentified and unreported. In a study that analyzed the COVID-19 outbreak on the Diamond Princess cruise ship, 634 out of 3,063 tested people were found to be positive for SARS-CoV-2, and an estimated 17·9% of the infected remained asymptomatic throughout[13]. Another study on 565 Japanese nationals evacuated from Wuhan, China, found that people remained asymptomatic in 30·8% of the confirmed COVID-19 cases, an even higher percentage[14].

Around 14% of all infected cases worldwide progress to severe illness[7], and as of April 23, 2020, in 183,559 of 2,630,778 confirmed cases (6·97%) worldwide, patients eventually died[3]. Older adults (age >65 years) and patients with underlying medical conditions such as heart disease, lung disease, diabetes, and renal disease are at higher risk from severe COVID-19 illness[15]. In the United States, the preliminary description of outcomes among patients with COVID-19 indicates that fatality was highest in persons aged ≥85, ranging from 10% to 27%, followed by 3% to 11% among persons aged 65–84 years, 1% to 3% among persons aged 55-64 years, <1% among persons aged 20–54 years, and no fatalities among persons aged ≤19 years[16].

The most common symptoms of COVID-19 patients are fever (91·7%), cough (75%) fatigue (75%), and gastrointestinal symptoms (GI) (39·6%)[17,18]. Our patient initially developed mild fever, cough, and shortness of breath, but on admission (illness day 3) and during hospitalization, his main complaints were fatigue and diarrhea. The patient is unfortunately not eligible for the clinical trial of remdesivir at the University of Nebraska Medical Center due to his ESRD but has been improving clinically with dialysis and supportive care. By illness day 4 (hospital day 2), his shortness of breath, dry cough, and abdominal pain have improved. Since illness day 5 (hospital day 3), his severe diarrhea also improved with oral loperamide after Clostridium.difficile infection was ruled out.

A study done on 8274 close contacts in the Wuhan region where the virus was first discovered showed that 5·8% of COVID-19 patients had other respiratory pathogen co-infections[19]. In another study by Xia and colleges on 20 confirmed pediatric COVID-19 cases in Shanghai, China, 6 out of 20 children were coinfected with another respiratory pathogen[20]. In a recent research letter published on April 15, the rate of co-infections of COVID-19 with other respiratory pathogens was reported to be as high as 21% [21].

Given the increase in the rapid community transmission of the pandemic, the threshold for suspicion and testing for SARS-CoV-2 infection should be low in patients with fever, respiratory symptoms, or other symptoms that are fitting for COVID-19, even when there is evidence of infections by other respiratory pathogens[22-24]. Any missed COVID-19 cases can lead to significant adverse public health consequences. This case highlights the fact that co-infection of SARS-CoV-2 and other respiratory pathogens can occur in patients with no known direct COVID-19 exposure, and that it is important to test for COVID-19 in high-risk patients even when other etiologies could explain the symptoms.

Lessons learned from this case

1) There should be a high index of suspicion for SARS-CoV-2 infection in patients with fever and respiratory symptoms even when the patient is tested positive for other respiratory pathogens. Any missed COVID-19 cases will put the patient, other patients, health care providers, and the whole community at risk. A high index of suspicion, early testing, and a multidisciplinary approach to patient care are crucial for the treatment of COVID-19 pneumonia, especially in patients with multiple comorbidities.

2) With adequate testing and appropriate triaging of patients with suspected COVID-19, health care providers can be better-prepared in various health care settings, including imaging centers, dialysis facilities, and long-term care institutions.

3) With the widespread community transmission of COVID-19 in the U.S., patients presenting with other less typical symptoms including GI symptoms such as nausea, vomiting, and abdominal pain should also raise the clinicians' suspicion for possible COVID-19 infection.

Abbreviations

ESRD: End-stage renal disease

COVID-19: Coronavirus Disease 2019

WHO: World Health Organization

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

U.S.: The United States

WBC: White Blood Cell

CT: Computed Tomography

ED: Emergency Department

RT-PCR: Real-Time Reverse-Transcriptase Polymerase Chain Reaction

CDC: Center for Disease Control and Prevention

MAP: Mean Arterial Pressure

PPE: Personal Protective Equipment

Declarations

The data on the patient has not been reported in any other submission by the authors of this manuscript or by anyone else.

Ethics approval and consent to participate: Not applicable.

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Availability of data and materials: Not applicable.

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RJ drafted the manuscript, designed the table, and contributed to literature search. RV and AV worked on the manuscript, contributed to literature search, and made suggestions to improve the content. ER, CV, and DG worked on the manuscript and made suggestions to improve the content. SV supervised the work, designed the figures, contributed to literature search, and worked on the manuscript. All authors have read and approved the final manuscript.

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Table

Table. Laboratory results.

Laboratory Measures	Reference Range	Hospital Day 1 (Illness Day 3)	Hospital Day 2 (Illness Day 4)	Hospital Day 3 (Illness Day 5)	Hospital Day 4 (Illness Day 6)	Hospital Day 5 (Illness Day 7)	Hospital Day 6 (Illness Day 8)
White Cell Count (per µl)	4000 –11,000	8,700	–	15,300 (H)	7,400	6,100	6,800
Red Cell Count (per µl)	4,300,000 – 5,900,000	3,660,000(L)	–	3,190,000 (L)	3,400,000 (L)	3,270,000 (L)	3,400,000 (L)
Hemoglobin (g/dL)	13.3 - 17.3	11.3 (L)	–	9.9 (L)	10.4 (L)	10.2 (L)	10.4 (L)
Hematocrit (%)	39.0 - 52.0	33.5 (L)	–	30.1 (L)	31.8 (L)	31.0 (L)	32.1 (L)
Platelet Count (per µl)	150,000 – 400,000	226,000	–	157,000	179,000	189,000	199,000
Absolute Neutrophil Count (per µl)	1300 - 7500	7200	–	13,300 (H)	5500	3800	4700
Absolute Lymphocytes Count (per µl)	700 - 3900	800	–	1200	1200	1500	1300
Prothrombin Time (sec)	10.1 - 14.2	13.3	14.5 (H)	14.2	–	–	–
International Normalized Ratio	0.9 - 1.1	1.1	1.2 (H)	1.2 (H)	–	–	–
Sodium (mmol/L)	136 - 145	130 (L)	130 (L)	128 (L)	131 (L)	–	–
Potassium (mmol/L)	3.5 - 5.1	5.4 (H)	5.1	5.1	3.7	–	–
Chloride (mmol/L)	98 - 107	91 (L)	96 (L)	96 (L)	96 (L)	–	–

Anion Gap (mmol/L)	4 - 15	18 (H)	14	16 (H)	11	–	–
CO2 (mmol/L)	22 - 32	21 (L)	20 (L)	16 (L)	24	–	–
Blood Urea Nitrogen (mg/dL)	6 - 20	57 (H)	58 (H)	64 (H)	26 (H)	–	–
Creatinine (mg/dL)	0.64 - 1.27	8.42 (H)	9.63 (H)	10.90 (H)	6.68 (H)	–	–
Glucose (mg/dL)	70 - 139	53 (L)	245 (H)	97	69 (L)	–	–
Magnesium (mg/dL)	1.8 - 2.5	–	2.0	2.2	1.9	–	–
Calcium (mg/dL)	8.6 - 10.4	9.1	7.9 (L)	8.6	8.5 (L)	–	–
Total Protein (g/dL)	5.8 - 8.2	6.4	–	5.0 (L)	5.5 (L)	5.6 (L)	–
Albumin (g/dL)	3.5 - 5.1	3.0 (L)	–	2.3 (L)	2.6 (L)	2.5 (L)	–
Aspartate Aminotransferase (U/L)	15 - 41	95 (H)	–	66 (H)	68 (H)	60 (H)	–
Alanine Aminotransferase (U/L)	7 - 52	55 (H)	–	40	36	36	–
Alkaline Phosphatase (U/L)	32 - 91	104 (H)	–	111 (H)	92 (H)	91	–
Conjugated Bilirubin (mg/dL)	0.1 - 0.5	–	–	0.1	0.1	0.2	–
Total Bilirubin (mg/dL)	0.3 - 1.0	0.7	–	0.5	0.5	0.5	–
Lactic Acid (mmol/L)	0.5 - 2.0	1.3	–	0.8	–	–	–
Procalcitonin (ng/mL)	<0.10	5.21 (H)	–	17.30 (H)	15.30 (H)	–	10.00 (H)

(L) The value in the patient was below normal.
(H) The value in the patient was above normal.

Figures

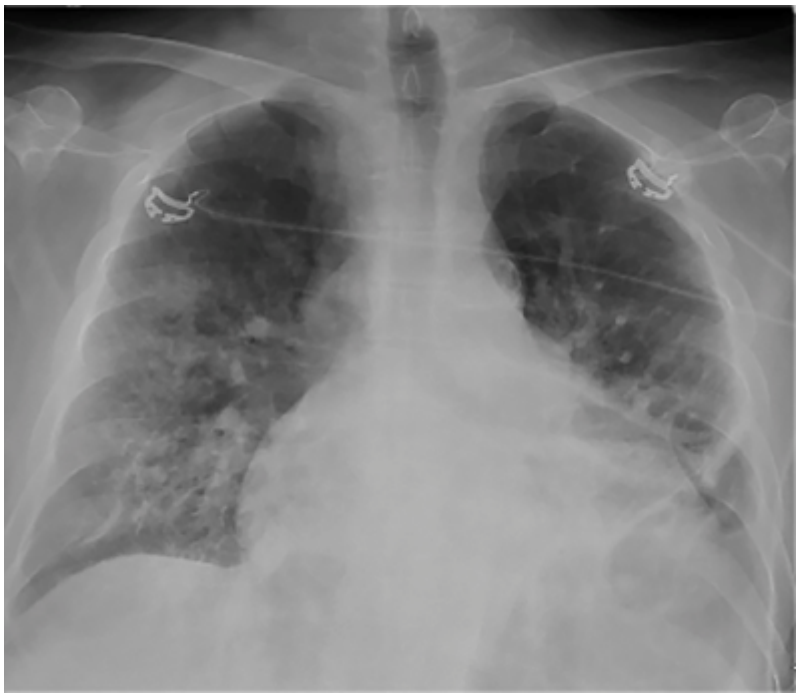

Figure 1

Anteroposterior chest X-ray showing new right midlung consolidation and left lower lung opacities.

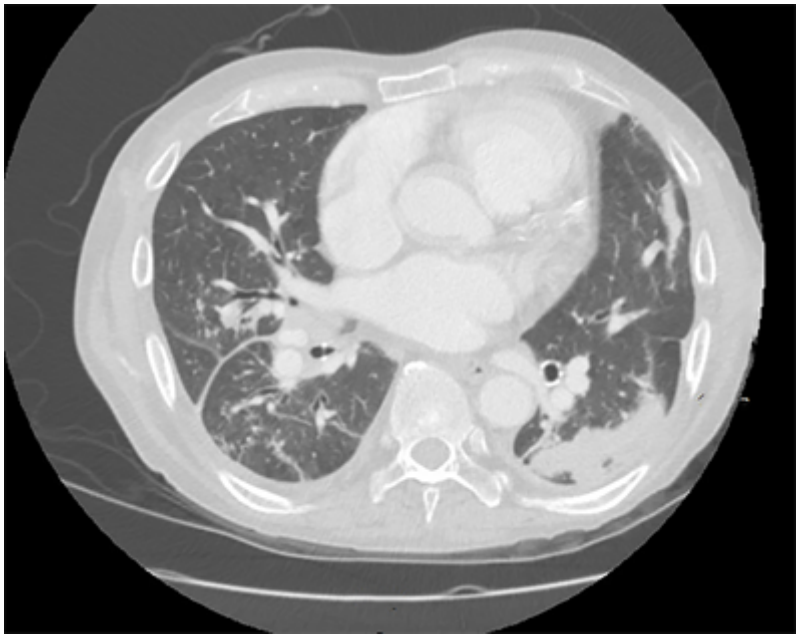

Figure 2

CT chest with no contrast showing multifocal pneumonia.