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CO-INFECTION WITH SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) AND HUMAN CORONAVIRUS HKU1 (HCOV-HKU1)

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ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and human coronavirus HKU1 (HCoV-HKU1) are two forms of human coronaviruses known to cause respiratory tract symptoms. A co-infection with both viruses is rare, particularly in the United States.

Case description: An 85-year-old male presented to the Emergency Department with recurrent falls, diarrhoea and cough, and whose viral panel was positive for both SARS-COV-2 and HCoV-HKU1. The patient developed bacterial pneumonia and was treated with antibacterial agents and glucocorticoids. His past medical history of atrial fibrillation required careful monitoring and subsequent discontinuation of remdesivir, a medication known to cause adverse cardiovascular effects in COVID-19 patients. The length of stay was also prolonged due to delirium and deconditioning. Ultimately, the patient required an urgent ablation followed by the placement of a permanent pacemaker, and anticoagulation therapy was initiated before discharge. The patient had a favourable outcome given the rarity of this case.

Discussion: COVID-19 patients co-infected with other human coronaviruses should be monitored for disease progression and superimposed bacterial infections. Providers should be cautious with the use of remdesivir in cases of co-infection and in severely ill COVID-19 patients who have a history of atrial fibrillation.

KEYWORDS

SARS-COV-2, co-infection, HCoV-HKU1, COVID-19

LEARNING POINTS

- This is a rare clinical case of a patient co-infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and human coronavirus HKU1 (HCoV-HKU1), two forms of coronaviruses; the report presents an epidemiological anomaly and a treatment framework.
- The importance of close monitoring of bacterial infections in coronavirus co-infections is reinforced.
- The cautious use of remdesivir in patients with a history of atrial fibrillation in severe or unique COVID-19 disease is recommended.

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an upper respiratory virus responsible for causing COVID-19, was first detected in Wuhan, China in 2019[1]. Symptoms commonly include fever, cough, dyspnoea, malaise, fatigue and sputum secretion, while common long-term symptoms include fatigue and shortness of breath[2,3]. For hospitalised patients with COVID-19 without the need for oxygen, current treatment protocols recommend treatment with remdesivir[4]. Human coronavirus HKU1 (HCoV-HKU1) is another human coronavirus, first identified in Hong Kong in 2005 and is known to cause upper respiratory tract infections[5]. Little is known about co-infection with these two variants of coronaviruses. We present a rare case of a patient infected with SARS-COV-2 and HCoV-HKU1 in the United States. We have treated approximately 5,000 COVID-19 patients at our mid-sized community hospital, including many with the developing and evolving sub-variants.

CASE DESCRIPTION

An 85-year-old Caucasian male presented to the Emergency Department due to recurrent falls, diarrhoea and cough. He reported shortness of breath and weakness and denied any fevers or chills. His past medical history was significant for type 2 diabetes mellitus, hyperlipidaemia, benign prostatic hyperplasia and atrial fibrillation (AF). He was a former smoker but reported no alcohol or recreational drug use. He had two COVID-19 vaccines in 2020, and none thereafter. The patient was admitted to the hospital for 18 days.

His initial physical examination showed a temperature of 37°C, blood pressure of 112/60 mmHg, heart rate of 75 bpm, respiratory rate of 28 and a body mass index of 20.8. Viral panel was positive for SARS-COV-2 and coronavirus type HKU1. Blood analysis revealed a white blood count of 2.4 $\times 10^9$/l, haemoglobin 13.4 g/dl, and haematocrit 39.8 *(Table 1)*. He was started on supplemental oxygen as O_2 saturation measured 89 to 92%. However, saturation improved, and supplementation was weaned off during the remainder of the hospitalisation and discontinued at discharge.

There was viral pneumonia with concomitant bacterial infection pneumonia due to a co-infection with two coronaviruses. Bacterial pneumonia was treated with ceftriaxone and a 5-day course of doxycycline; a 5-day course of 6 mg dexamethasone was administered. Remdesivir was started but was stopped prematurely after 48 hours due to poorly controlled atrial fibrillation/flutter with rapid ventricular rate, followed by bradycardia and sinus node dysfunction. This required an urgent atrial flutter ablation followed by the placement of a dual-lead pacemaker implant. Apixaban was initiated for stroke prophylaxis with a continuation of metoprolol succinate 25 mg bid for heart rate stabilisation. The patient experienced dysphagia and delirium with an extended length of stay in the hospital, and improved slowly with rehabilitation.

DISCUSSION

A co-infection with coronavirus HCoV-HKU1 and SARS-COV-2 has been previously reported but is rare. This case demonstrates a complicated course of an elderly male suffering a co-infection of two strains of coronavirus simultaneously that was managed with remdesivir and

Blood test	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Procalcitonin (ng/ml)	29.7	36.43	25.53	-	-	-	-	-
Alanine transaminase (U/l)	25	23	30	39	-	-	-	-
Aspartate aminotransferase (U/l)	50	-	-	53	-	-	-	-
Alkaline phosphatase (U/l)	47	-	-	-	-	-	-	-
Bilirubin (mg/dl)	2.1	-	-	-	-	-	-	-
C-reactive protein (mg/l)	-	-	-	246.7	-	-	-	-
Ferritin (ng/ml)	-	-	-	314.6	-	-	-	-
White blood count ($\times 10^9$/l)	2.4	2.2	-	7.9	7.3	-	12.3	10.6
Red blood count ($\times 10^{12}$/l)	4.44	3.78	-	3.95	3.70	-	4.11	4.16
Haemoglobin (g/dl)	13.4	11.5	-	12.1	11.0	-	12.3	12.4
Haematocrit (%)	39.8	34.4	-	35.4	33.4	-	36.4	37.0
Platelet count ($\times 10^9$/l)	149	105	-	152	156	-	202	259
HbA1C (%)	-	-	-	8.2	-	-	-	-

Table 1. Patient laboratory findings.

antibiotics. Underlying comorbidities and remdesivir were possible causative factors for difficult-to-control AF and bradycardia. The hospital course was also complicated by delirium and deconditioning requiring prolonged rehabilitation.

A similar co-infection of HCoV-HKU1 and SARS-COV-2 was reported in 2020 by Chuang et al. in a 34-year-old man[6]. They describe recovery as uneventful, and improvements were seen in chest radiography. In contrast, our patient presented with more atypical symptoms of a viral syndrome in the form of recurrent falls and had a complicated course with difficult-to-control AF. Although singular HCoV-HKU1 infections are not rare globally, co-infection with SARS-CoV-2 in symptomatic patients, especially those with atypical presentations, has been less commonly reported. Kanwar et al. highlighted that HCoV-HKU1 accounts for 1.6% of adult respiratory infections in the United States[7]. Adults with HCoV-HKU1 commonly report constitutional symptoms and upper respiratory tract symptoms. Singular HKU1 infections and HCoV co-infections often mirror single infections, but are associated with more adverse outcomes[8,9]. Additionally, Gaunt et al. highlighted the association between HCoV-HKU1 infections and febrile convulsions[10]. Considering co-infections is crucial, as they can lead to a broader range of symptoms and more severe outcomes, as demonstrated by our patient whose recurrent falls, diarrhoea and lack of rhinorrhoea and sore throat complicated the typical clinical presentation. This underscores the clinical value of thorough diagnostic evaluations in identifying such cases and tailoring treatment.

Co-infections with SARS-COV-2 are common in hospitalised patients, a majority of which are bacterial with the most common causative agents being hospital-acquired species, *Pseudomonas aeruginosa* and *Escherichia coli*[11,12]. A rare case of COVID-19 co-infection with Legionella was documented and the authors also emphasise the importance of monitoring for bacterial infections in hospitalised COVID-19 patients through early diagnosis and prevention[13]. Viral co-infection accounts are less common, accounting for 10–15% of co-infections, with influenza A or respiratory syncytial virus being the most common causative agents. These viral co-infections are significant as they account for longer hospital stays and longer ventilation durations[8,9]. Thus, identifying HCoV-HKU1 co-infections can inform infection control practices in hospital settings, helping to prevent the spread of multiple pathogens, particularly among immunosuppressed individuals. Given that multiplex polymerase chain reaction assays can detect multiple human coronaviruses simultaneously, the costs of detecting other coronaviruses may be offset[14]. Furthermore, anticoagulation therapy is required in COVID-19 infection in patients with AF[15]. A history of AF also complicated treatment with remdesivir as atrial flutter followed by bradycardia and sinus node dysfunction was observed. Remdesivir is known to have adverse effects on the cardiovascular system with QT prolongation, torsades de pointes, and bradycardia being documented[15,16]. Given bradycardia as a complication, there is no clear guidance on its discontinuation or management, and patients with past AF should be closely monitored alongside the progression of COVID-19 disease.

Given the rarity of coronavirus co-infections in the United States and the patient's complicated past medical history, this case highlights the possibility of simultaneous infection with two different strains of coronaviruses: the novel coronavirus 2019 and a pre-pandemic strain. It underscores patient-specific medical management as seen with the close monitoring of remdesivir in COVID-19 patients with a history of AF. The importance of a thorough viral panel is emphasised as physicians should not overlook the possibility of viral co-infections.

CONCLUSION

This case of an 85-year-old male with HCoV-HKU1 and SARS-COV-2 co-infection alongside superimposed bacterial pneumonia is a rare clinical presentation in the United States. Bacterial infections should be closely monitored in coronavirus co-infections. Cautious use of remdesivir is recommended in patients with a history of AF in severe or unique COVID-19 disease.

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