CASE REPORT

OPEN

Bebtelovimab-Induced Bradycardia Leading to Cardiac Arrest

Christina Gearges, MD, MBA[1]
Hibah Haider, MD[1]
Vishal Rana, MD[1]
Zahra Asghar, MD[1]
Anjali Kewalramani, MD[1]
Zachary Kuschner, MD[1,2]

BACKGROUND: Bebtelovimab is a monoclonal antibody used to prevent progression of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Complications of SARS-CoV-2 infection can include cardiac effects including sinus bradycardia.

CASE SUMMARY: We describe the case of an 86-year-old male infected with SARS-CoV-2 who experienced bradycardia with cardiac arrest immediately following infusion of Bebtelovimab with return of spontaneous circulation obtained following 1 minute of chest compressions and administration of atropine. His bradycardia resolved, and he was extubated on hospital day 1, found to be neurologically intact, and discharged on hospital day 9.

CONCLUSIONS: Due to the time course of the patient's symptomatology, we attribute the bradycardic arrest to the Bebtelovimab infusion. This case illustrates the need for further research into the etiology of bradycardia due to SARS-CoV-2 infection and to examine potential links to monoclonal antibody infusion. It also serves as important caution to maintain close cardiac monitoring while administering monoclonal antibodies for SARS-CoV-2.

Monoclonal antibodies (MABs) have been used to prevent worsening of symptoms and severe illness of COVID-19 syndrome, a severe complication of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Bebtelovimab is a new MAB that has been approved for emergency use and used specifically for Omicron variants of SARS-CoV-2 (1). The mechanism of action of bebtelovimab on the Omicron variant is that it neutralizes the SARS-CoV-2, B.1.1.7, B.1.351, and B.1.617.2 variants (2). Bebtelovimab acts on the LY-CoV1404 epitope: a highly potent SARS-CoV-2 spike glycoprotein receptor-binding domain (2). MABs have been effective at reducing hospitalizations and halting progression of symptoms in SARS-CoV-2-infected patients. This case reports an unusual case of sinus bradycardia with cardiac arrest due to infusion of bebtelovimab.

CASE SUMMARY

An 86-year-old male with a past medical history of chronic lymphocytic leukemia in remission since 2015, hypertension, atrial fibrillation, diabetes mellitus type 2, and hyperlipidemia presented to the emergency department with progressive shortness of breath and cough for one month. Thirty days prior to admission, an outpatient x-ray of the chest showed a right lower lobe opacification consistent with pleural effusion for which the patient was treated with augmentin and underwent diuresis. CT of the chest in the emergency department showed persistence of the opacification despite treatment. At the time of presentation he endorsed shortness of breath without any associated symptoms and denied complaints of fever, chills, or chest pain, and or sick contacts, and recent travel. Vitals were within normal limits: temperature of 98.6°F, heart rate of 74 beats/min, respiratory rate

DOI: 10.1097/CCE.0000000000000747

of 18 breaths/min, blood pressure of 110/59 millimeters mercury (mm Hg) and oxygen sat of 91% on room air. On physical examination, the patient was in no acute distress, and examination was notable only for diminished breath sounds and rales of the right lower lobe, normal heart tones without murmurs, bilateral lower extremity edema without erythema, or tenderness. The remainder of his examination was otherwise unremarkable.

Routine screening for procedural clearance with SARS-CoV-2 polymerase chain reaction returned positive for SARS-CoV-2. Patient had a high-sensitivity troponin of 79 initially and down trended to 72, pro-brain natriuretic peptide (pro-BNP) of 5,476, white blood cell (WBC) 11.27, and blood urea nitrogen/creatinine (BUN/Cr) of 27/1.58. The remainder laboratory investigations were all within normal limits; including lactate, complete blood count (CBC), comprehensive metabolic panel (CMP), tryptase, and Procalcitonin level. Plain radiographs of the chest revealed a right-sided small–to-moderate pleural effusion and Interventional Radiology performed thoracentesis yielding 1,100 cc of clear yellow fluid of which tests returned consistent with a transudative effusion with negative cultures. There were no immediate complications from the procedure, which was well tolerated. One hour after thoracentesis, the patient was administered bebtelovimab for his current SARS-CoV-2 infection, which was administered over 30 seconds as per standard protocol. Approximately 1 minute after completing the infusion, the patient became unresponsive with agonal respirations and was found to be bradycardic to 38 beats/min on telemetry without a palpable pulse. Chest compressions were initiated, and he was ventilated with bag valve mask. His heart rate remained between 37 and 39 beats/min, and 1 mg of atropine was administered with improvement in heart rate to 110 beats/min and recover of a pulse. The patient remained obtunded and was intubated and admitted to the ICU. No rash, skin changes, or bronchorrhea were noted by the resuscitation team in the emergency department.

In the ICU, the patient rapidly recovered his mental status, followed commands, and was extubated on postarrest day 1 and found to be neurologically intact. He developed intermittent bradycardia with heart rate ranging from 40 to 50 beats/min and hypotension with systolic blood pressure (SBP) in the 80 mm Hg and mean arterial pressure (MAP) in the 50 mm Hg. Blood pressure improved to SBP 110 and MAP 70 mm Hg with low-dose norepinephrine infusion, which he required for 2 days after which his vasopressor requirement resolved. He was able to recall the events leading up to his cardiac arrest and denied pruritus, rash, worsening shortness of breath, chest pain, palpitations, or vision changes, and stated that he felt well until he awoke intubated. An electrocardiogram following the arrest demonstrated sinus bradycardia with normal intervals and without ST elevations or depressions, and troponins following the arrest were 70 and 62. The patient was initially given 1 dose of empiric dexamethasone; however, given he had no hypoxemia, he was determined to not meet criteria for steroid therapy in COVID-19, and further doses were held. Transthoracic echocardiography was performed and demonstrated LVEF of 60–65%, right ventricular systolic pressure greater than 60 mm Hg (suggesting pulmonary HTN), and IVC dilatation. He was transferred out from the ICU on hospital day 6 and discharged from the floor to continue outpatient workup on day 9. Informed consent was obtained by the patient for publication.

DISCUSSION

SARS-CoV-2 infection has effects on multiple organ systems, which include cardiac effects such as arrhythmias, cardiomyopathies, myocarditis, and acute coronary syndromes (3). It has been reported that 7.2–33% of patients with COVID-19 syndrome experienced sinus bradycardia, which resolved with treatment of the infection (4, 5). The mechanism of action of SARS-CoV-2 on the cardiac system is potentially multifactorial and typically dependent on disease severity (3). It has been proposed that the angiotensin-converting enzyme 2 receptors permit infection of the myocardium leading to bradycardia (6). It is unlikely that the bradycardia with cardiac arrest in our case was due to SARS-CoV-2 infection given his normocardic heart rate and lack of severe symptoms prior to receiving MAB infusion. Due to the time course of onset of bradycardia, we attribute this to bebtelovimab infusion. Bebtelovimab has a half-life of 11.5 days, which may explain the consistent bradycardia and hypotension post cardiac arrest and the need for pressors (7). Bebtelovimab has been associated with anaphylactic reactions; however, this is unlikely in our patient given the lack of anaphylactoid symptoms and improvement without administration of epinephrine, which—for unclear reasons—was not administered during the arrest. Bebtelovimab has been associated with vasovagal syncope (8). However, the patient denied prior vasovagal events, and although bradycardia

due to a cardioinhibitory response is one explanation for his cardiac arrest, the lack of preceding prodromal symptoms such as lightheadedness, nausea, diaphoresis, or shortness of breath would be unusual. An alternative suggestion is that our case may be due to a primary effect of bebtelovimab on either cardiac tissue—inducing primary bradycardia or on venous capacitance—inducing hypotension with secondary bradycardia—though these possibilities require more research before such a relationship can be presumed to exist.

CONCLUSIONS

To the author's knowledge, this is the first case of bradycardia and the first case of bradycardia-mediated cardiac arrest due to bebtelovimab infusion. The mechanism is, at this time, unclear and may be due to a vasovagal event or an as-yet unelucidated cardiovascular mechanism. Future research is warranted to better understand both the etiology of SARS-CoV-2-induced bradycardia and to investigate cardiac effects of bebtelovimab. This case serves as an important caution for providers administering bebtelovimab and a reminder to maintain close observation with cardiac monitoring during infusion.

The patient gave informed consent in writing to the publication of this article, and the signed consent form is maintained on file by the corresponding author.

1 *Internal Medicine, Mather Hospital, Northwell Health, Zucker School of Medicine at Hofstra University, Port Jefferson, NY.*

2 *Critical Care, Long Island Jewish Medical Center, Northwell Health, Zucker School of Medicine at Hofstra University, Queens, NY.*

Drs. Gearges, Haider, Rana, Asghar, Kewalramani, and Kuschner provided care to the patient. Drs. Gearges and Kuschner drafted the article, and all authors contributed substantially to its revision.

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: cgearges@northwell.edu

REFERENCES

1. Iketani S, Liu L, Guo Y, et al: Antibody evasion properties of SARS-CoV-2 Omicron sublineages. *Nature* 2022; 604:553–556
2. Westendorf K, Žentelis S, Wang L, et al: LY-CoV1404 (bebtelovimab) potently neutralizes SARS-CoV-2 variants. *Cell Rep* 2022; 39:110812
3. Douedi S, Mararenko A, Alshami A, et al: COVID-19 induced bradyarrhythmia and relative bradycardia: An overview. *J Arrhythm* 2021; 37:888–892
4. Hu L, Gong L, Jiang Z, et al: Clinical analysis of sinus bradycardia in patients with severe COVID-19 pneumonia. *Crit Care* 2020; 24:257
5. Zhou M, Wong CK, Un KC, et al: Cardiovascular sequalae in uncomplicated COVID-19 survivors. *PLoS One* 2021; 16:e0246732
6. Xu X, Chen P, Wang J, et al: Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Sci China Life Sci* 2020; 63:457–460
7. Black D: Bebtelovimab. Sanford Guide Web Edition. Available at: https://webedition.sanfordguide.com/en/druginformation/antiviral-gents/coronavirus/bebtelovimab. Accessed February 14, 2022
8. ClinicalTrials.gov: A Study of Immune System Proteins in Participants With Mild to Moderate COVID-19 Illness – Full Text View. Available at: https://clinicaltrials.gov/ct2/show/NCT04634409. Accessed July 1, 2022