New-Onset Seizures After Bamlanivimab Infusion

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Abstract

Since the beginning of the COVID-19 pandemic, industry and healthcare providers have investigated methodologies to manage infection of SARS-CoV-2. One treatment breakthrough has been the introduction of monoclonal antibodies to prevent worsening SARS-CoV-2 infection in non-hospitalized patients diagnosed with COVID-19. These monoclonal antibodies, like bamlanivimab, bind to the SARS-CoV-2 spike protein and prevent its ability to binding to human ACE2 receptors. This is a case of a 91 year-old man with no prior seizure history who developed new-onset seizures after bamlanivimab infusion.

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Abstract

Since the beginning of the COVID-19 pandemic, industry and healthcare providers have investigated methodologies to manage infection of SARS-CoV-2. One treatment breakthrough has been the introduction of monoclonal antibodies to prevent worsening SARS-CoV-2 infection in non-hospitalized patients diagnosed with COVID-19. These monoclonal antibodies, like bamlanivimab, bind to the SARS-CoV-2 spike protein and prevent its ability to binding to human ACE2 receptors. This is a case of a 91 year-old man with no prior seizure history who developed new-onset seizures after bamlanivimab infusion.

Case

A 91 year-old-man with a past medical history of Hodgkins Lymphoma, iron deficiency anemia, and heart failure with preserved ejection fraction presented with a one-week history of generalized weakness and malaise.

He developed paresthesias in his hands on the morning of admission, which prompted his son to bring him to the emergency room. Upon arrival, the patient's vital signs were: blood pressure of 138/56 mmHg; pulse of 58 bpm, respiratory rate of 17 breaths/min, 100% SpO2 on no supplemental oxygen. Initial chest radiograph and EKG were unremarkable. The patient's respiratory pathogen panel by RNA PCR was positive for SARS-CoV-2; he was transferred to an observation unit for treatment with bamlanivimab.

He underwent the 30 minute infusion without complications. Due to his age and comorbidities, he was planned to be observed overnight prior to discharge the following morning. Seven hours after administration of bamlanivimab, the patient was reported to have an acute change in mental status and oxygen saturation declining to 80s, for which he was placed on 2L supplemental oxygen. Saturation subsequently increased to

97%. Twelve hours after bamlanivimab, the patient had a 10-second, witnessed seizure followed by a drop in oxygen saturation to 86%. The patient was placed on 6L supplemental oxygen and oxygen saturation increased to 98%. He was seen staring at the ceiling and no longer responding to verbal or light physical stimuli, appearing to be in a postictal state. He was withdrawing to pain without asymmetry on neurological exam. Three hours after the initial seizure, the patient had two additional seizures lasting approximately two minutes each which were treated with lorazepam. The patient was also placed on non rebreather mask after his oxygen saturations decreased to 80% during these two consecutive episodes. He was started on levetiracetam 500mg every 12 hours for seizure prophylaxis in addition to dexamethasone and remdesivir.

Electroencephalography monitoring performed over the following 72 hours demonstrated initial portion of diffuse attenuation followed by intermittent periods of 5-6Hz background without epileptiform activity. CT of the brain showed no acute intracranial hemorrhage or mass effect, moderate bilateral periventricular and subcortical foci of decreased attenuation, deemed likely related to chronic microvascular ischemic changes of the brain. MRI of the brain demonstrated age-appropriate involutional and microvascular angiopathic changes, without acute infarct or space-occupying lesions. The patient's mental status subsequently returned to his baseline prior to admission.

Discussion

Patients have presented with a wide ranging symptoms of COVID-19. Seizures have been a documented presentation of COVID-19 occurring at various stages of illness and even in individuals without underlying neurological illness.[1,2,3,4] Beta coronaviruses SARS-CoV and MERS-CoV have been associated with neurological symptoms are attributed to the upregulation of proinflammatory cytokines following initial viral pneumonia.[5]

Potential mechanisms that could contribute to seizures in COVID-19 include interaction with angiotensin-converting enzyme 2 (ACE2) in neuronal and glial cells, and cytokine storm effects, specifically mediated by IL-6.[6] Cytokine release syndrome (CRS) has also been documented after administration of well-known monoclonal antibody treatments[7].

The BLAZE-1 study, which led to the emergency use authorization of bamlanivimab, reported no cases of seizures or serious adverse effects– other than anaphylaxis– in the 101 patients that received bamlanivimab. However, only 3% of participants (9 patients) in BLAZE-1 who received bamlanivimab were 75 years of age or older and there was no reported correlation of adverse events to age groups, making adverse effects in older adults even less certain.[8] When applying the Adverse Drug Reaction Probability Scale, often known as the Naranjo Algorithm, to this case, the likeliness of bamlanivimab causing seizures in this case is "Possible" (score 3 of 13)[9], suggesting a temporal sequence of events related to bamlanivimab. This may also be explained by characteristics of the patient's diagnosis of COVID-19.

Conclusion

We describe a case of a patient receiving bamlanivimab infusion for COVID-19. Based on the uncertainty of causality in this case, it may be worthwhile to monitor older adults who receive bamlanivimab for longer than the recommended 60 minutes after administration. Further study of potential side effects of novel therapeutic agents against COVID-19, specifically pertaining to the geriatric population, is advised.

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