Late Hypersensitivity Reaction to COVID-19 Antibody Infusion: A Case Report

Abstract: Antibody therapy has shown to be effective in preventing hospitalization among patients infected with SARS-CoV-2. Rare hypersensitivity reactions have been reported to occur within one hour of infusion onset which prompted regulators to require a minimum of one hour of observation. We report a case of a hypersensitivity reaction that occurred after this time frame.

Keywords: sars-cov-2, drug hypersensitivity, antibodies, monoclonal.

INTRODUCTION

Monoclonal antibody therapy is a mainstay of treatment for a multitude of pathologies including cancer, multiple sclerosis, asthma and rheumatoid arthritis (Ecker, D. M. et al., 2015, January). On November 20, 2020 the Federal Drug Administration (FDA) granted emergency use authorization to casirivimab and imdevimab (REGN-COV2), an antibody treatment regimen for patients infected with SARS-CoV-2. Casirivimab and imdevimab are monoclonal antibodies that are directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells. They have been shown to reduce the rate of hospitalization by two thirds (from 9% to 3%) in patients at high risk of disease progression (S. Food and Drug Administration. 2021). Although typically uneventful, rare adverse events have occurred. As a consequence, guidelines recommend monitoring patients for complications for an hour post infusion (Regeneron Pharmaceuticals Inc. 2021). We report a case of a hypersensitivity reaction to REGN-COV2 that occurred sixty-two minutes after the one-hour observation period. Proper recognition that hypersensitivity reaction may occur beyond one-hour post infusion is essential, as intervention is crucial.

CASE REPORT

In December 2020, a 53-year-old male with multiple myeloma was referred to the emergency room for monoclonal antibody therapy after testing positive for SARS-CoV-2. The patient presented with four days of body aches, a low-grade fever, sore throat, and a cough.

At the emergency department, the patient was afebrile, in no acute distress, with an oxygen saturation of 94% on room air. Current medication included oral chemotherapy agents daratumumab and pomalidomide for multiple myeloma. The patient had no known allergies.

The patient met the high-risk criteria for which emergency usage of monoclonal antibody was warranted. After appropriate consultation regarding the risks and benefits of treatment, 1200 mg of casirivimab and 1200 mg of imdevimab were administered.
During the infusion the patient was observed and noted to be resting comfortably with stable vitals and no adverse reactions. After the one-hour observation period, the observation-discharge-examination revealed that the patient appeared safe and appropriate for discharge. The patient was provided with a pulse oximeter and counseled on appropriate use; he was instructed to return to the emergency department should his oxygen saturation level fall below 90%. After being discharged, and sixty-two minutes post observation while waiting for his ride home, he developed rigors and became transiently tachycardic (160 beats per minute), tachypneic (35 breaths per minute), hypotensive (77/50 mmHg), febrile (38 Celsius) and hypoxic (88 percent oxygen saturation on room air). He was quickly given IV normal saline, acetaminophen, steroids and oxygen. His repeat vital signs revealed sinus tachycardia at 126 beats per minute, BP 104/67 and pulse ox 92%. The patient was admitted and labs were drawn. Abnormal labs included a glucose of 158, bicarb of 17 mmol/L, LDH of 335 Units/L, fibrinogen >700mg/dl and lactic acid of 4.8mmol/L. A chest x-ray was performed and demonstrated bilateral multifocal infiltrates.

**DISCUSSION**

Monoclonal antibodies are used in a myriad of pathologies and hypersensitivity is a common potential adverse effect in almost all such therapies. Known side effects of REGN-COV2 include fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia, chest pain or discomfort, weakness, altered mental status, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, fatigue, and diaphoresis (Regeneron Pharmaceuticals Incorporation. 2019). A clinical trial was conducted in which 518 participants received various doses of REGN-COV2. The trial determined that adverse events were rare, occurring in only 1-2% of participants (Regeneron Pharmaceuticals Incorporation. 2021). Only one case of anaphylaxis occurred and it was within one hour of infusion. Four cases of infusion related reactions were reported, which included pruritus, pyrexia, chills, urticaria, abdominal pain and flushing. Due to the relative rarity of severe hypersensitivity reactions and their proximity to infusion time, guidelines from the FDA provided that patients should be observed for one hour after the infusion is complete.

The exact mechanisms by which hypersensitivity reactions occur during and post monoclonal antibody therapy administration remains an active area of active research. Regardless of the mechanism, hypersensitivity related reactions require immediate identification and appropriate management and treatment. Determination of the severity of the reaction during or post the infusion period will dictate the treatments administered. Urgent intervention is indicated for life threatening reactions and can decrease mortality.

Although the sudden deterioration of our patient is consistent with a hypersensitivity reaction we cannot definitively exclude other pathologies. Massive replication of SARS-CoV-2 and a resulting cytokine storm could be a possible etiology of this patient’s condition (Tan, C. et al., 2021). This cytokine storm typically presents with acute respiratory distress syndrome, multi-organ failure and coagulation abnormalities (Hojyo, S. et al., 2020). Another possible cause of the patient’s symptoms was a pulmonary embolism but the patient had a non-significant D-dimer level of 198ng/ml. In addition, his speedy recovery post administration of steroids, IV fluids and oxygen make both a cytokine storm and pulmonary embolism less likely. Severe hypersensitivity reaction remains the most likely diagnosis.

**CONCLUSION**

Our patient case is of significance because, to our best knowledge, it is the first report of a hypersensitivity reaction following the one-hour period requiring immediate treatment with a fluid bolus, acetaminophen, steroids, and supplemental oxygen. Epinephrine was not initiated due to no airway constriction, difficulty speaking or swelling. It was available at the bedside, but the patient’s blood pressure normalized after fluid administration.

Recognition that hypersensitivity reactions may occur post the one hour waiting period is essential. We were fortunate the patient remained in the hospital when this adverse reaction occurred and appropriate care was timely rendered. The patient had a good outcome.

**REFERENCES**


