Severe bronchospasm following itolizumab infusion in a COVID-19 patient

Itolizumab is an anti-CD6 humanized IgG1 mAb that binds to domain 1 of CD6, a receptor present on T -effector cells, is responsible for priming, activation, and differentiation of T-cells.[1] There are several reported adverse reactions for chimeric, humanized, and fully human monoclonal therapeutics.

We are reporting severe infusion-related hypersensitivity reactions following itolizumab infusion in a 66-year-old male who was tested positive for COVID-19. He was admitted with features of severe COVID-19 acute respiratory distress syndrome. On the 6th day of his admission, his oxygen requirement increased to 15 L/min using a nonrebreathing facemask, and inflammatory markers such as serum ferritin 1100 mg/mL, lactate dehydrogenase (LDH): 648 U/L, C-reactive protein (CRP): 77.34 mg/mL, and IL-6 215.7 pg/mL were raised. So, infusion of the first dose of IV itolizumab (1.6 mg/kg) 100 mg [Alzumab™ Biocon Ltd., Bangalore, India] was started. The patient was afebrile and his baseline parameters were heart rate (HR) 90 bpm, blood pressure (BP) 130/70 mm Hg, oxygen saturation (SpO_2) 91, and respiratory rate (RR) 34 rpm. Itolizumab 100 mg was diluted in 250 mL of 0.9% normal saline and infused at 25 mL/h for the first hour. After 10 min of the start of

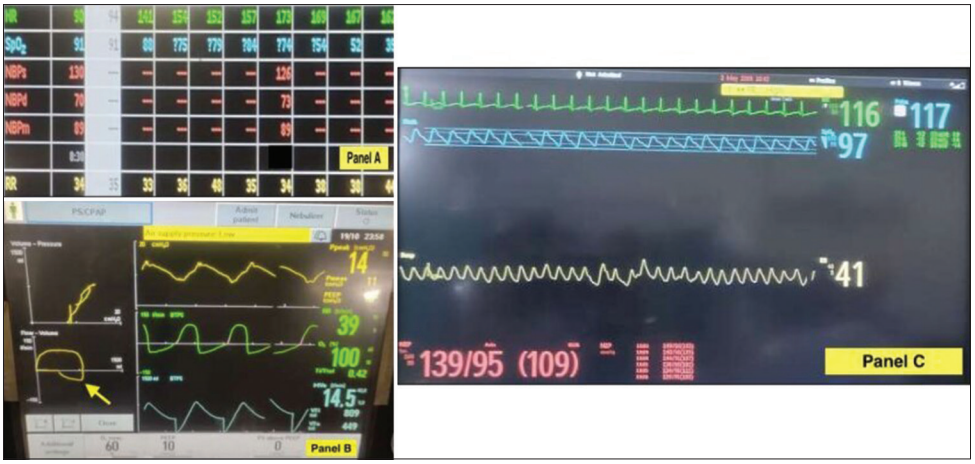

Figure 1: Panel A: Showing baseline vitals parameters and after 2 h of drug infusion (SpO_2 dropped from 91% to 35%). Panel B: Showing vitals parameters at 15 min interval after stoppage drug infusion (SpO_2 improved from 35% to 88%). Panel C: Arrow showing flow-volume loop with scooping of expiratory phase on ventilator display

the infusion, we noticed mild shivering, and it was managed by applying warming blankets. After 2 hours of the start of the infusion, around 50 mL of the drug was given. The patient complained of a moderate grade of shivering with an increase in heart rate of 162 bpm, BP 145/95 mm Hg, and RR 44 rpm with rapid fall in oxygen saturation to 35% Figure 1 [Panel A]. We immediately stopped the infusion and put this patient on continuous positive airway pressure (CPAP) mode with a fraction of inspired oxygen (FiO_2): 100 and positive end-expiratory pressure (PEEP): 12 cm H_2O. The flow-volume loop on ventilator graphics was suggestive of severe expiratory flow limitation Figure 1 [Panel B], so we made a probable diagnosis of severe bronchospasm due to severe serious infusion-related hypersensitivity reaction following itolizumab infusion. However, the entire event lasted for more than 190 min, and then SpO_2 reached 97%, HR came to 116 bpm and BP 139/95 mm Hg, and RR was 41 rpm. Figure 1 [Panel C] In clinical practice, mAbs infusion reactions have been observed to range from 12% to 15%.[2] These reactions are most likely to occur during the first dosing cycle and tend to decrease in severity and frequency upon subsequent infusions. This case is believed to be the first life-threatening case of itolizumab-induced bronchospasm. There are various methods to decrease itolizumab infusion–related reactions. They are (1) infusion should be given slowly in 5 to 6 h, (2) use premedication of hydrocortisone 100 mg i.v. and pheniramine 30 mg before the start of the infusion, (3) infusion set with an in-line filter with a pore size of 1.2 μm or less should be used, (4) drug desensitization to improve tolerance, and (5) switching to the subcutaneous (SC) route should be reconsidered. A written informed consent from the patient's relative was taken, and an adverse event reporting form was submitted.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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