Cardiopulmonary Arrest After Severe Anaphylactic Reaction to Second Infusion of Infliximab in a Patient with Ankylosing Spondylitis

To the Editor:

Infliximab is an anti-tumor necrosis factor- α (TNF- α) chimeric monoclonal antibody widely used to treat chronic inflammatory diseases such as rheumatoid arthritis, Crohn's disease, ankylosing spondylitis (AS), and psoriasis. Infusion reaction to infliximab occurs in approximately 5% of patients¹. Although severe anaphylactic reactions including hypotension, arrhythmia, and bronchospasm have been reported, there is no report of cardiopulmonary arrest strongly connected with the infliximab infusion. We describe a patient with AS who developed cardiopulmonary arrest after an anaphylactic reaction to the second infliximab infusion.

A 37-year-old man with no history of allergy or coronary artery event received infliximab infusion for AS at our hospital. His symptoms were refractory to nonsteroidal antiinflammatory drugs, and he had been treated with salazosulfapyridine (1000 mg/day) alone for 2 years. One year before starting infliximab infusion, his electrocardiogram (ECG) showed no abnormality. In prescreening ultrasound cardiogram wall motion and aortic valve function were normal. The first infusion (5 mg/kg, total dose 275 mg) did not cause any adverse reactions. After canceling 2 appointments, he received the second infusion 12 weeks after the first treatment, without premedication. Three minutes after starting the infusion, he rapidly developed dyspnea and skin redness. Infusion was immediately stopped. He lost consciousness and developed cardiopulmonary arrest. The ECG monitor showed ventricular tachycardia (VT). Within 2 minutes, he recovered to sinus rhythm without use of a defibrillator. He was treated for anaphylaxis with epinephrine, methylprednisolone, chlorpheniramine maleate, and famotidine. In the emergency room, he was intubated and continuous vasopressor was administered.

Upper airway symptoms and skin redness improved daily. Seventy hours after the event, he developed VT that resolved spontaneously. ECG showed prolonged QT interval and ST-T depression in V1–6. There were no abnormalities in cardiac enzymes or coronary arteriographic or electrophysiological findings. Coronary artery spasm was suspected as the cause of VT, while prolonged QT may have been associated with H1/2 blocker administration. Anaphylaxis has been identified as a cause of coronary artery spasm^{2,3}. After treatment for ventilator-associated pneumonia, he was discharged on Day 17 without sequelae.

The recommended timing of infliximab infusion is 0, 2, and 6 weeks, followed by every 8 weeks. Although the risk of infusion reaction to infliximab increases when administered years after the previous infusions⁴, we doubt whether the 12-week interval between first and second infusions in our patient was associated with the severe anaphylactic reaction. This interval is not markedly different from the standard interval of 8 weeks, and usually a 12-week interval after fourth infusion results in no significant increase of infusion reaction. Therefore, this case indicates that life-threatening anaphylactic reactions to infliximab may not be predictable based on the laboratory examinations currently performed. The formation of human

anti-chimeric antibodies (HACA), particularly IgE isotype, has been shown to relate to hypersensitivity to infliximab infusion^{5,6}. However, examination of anti-infliximab IgG and IgE antibodies is not available for routine clinical practice. Although history of allergy sometimes gives clues to the allergic reaction, this case had no history of allergy, and serum IgE in this patient was only 11 IU/ml. Generalized premedication could be a strategy to reduce the risk of infusion reaction, but steroid-based premedication would not decrease the incidence or severity of infusion reaction to infliximab⁷.

Our report emphasizes the potential risk of unpredictable severe anaphylactic reaction to infliximab. A more sophisticated algorithm and examination may be required in order to predict infusion reaction to biologics.

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