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ANAPHYLAXIS FOLLOWING THE INTRAVENOUS ADMINISTRATION OF CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR IN A HAEMODIALYSIS PATIENT

Dong-Jin Oh, Department of Internal Medicine, Myongji Hospital, Goyang, Korea

Anaphylactic shock developed immediately after the first administration of 100 µg intravenous (IV) bolus injection of continuous erythropoietin receptor activator (CERA, pegylated epoetin-β) in a 49-year-old man undergoing haemodialysis. He had previously received multiple doses of 4000 units of epoetin-α IV injection without complication. He exhibited typical anaphylactic symptoms of dyspnea, chest tightness, vomiting, cyanosis, low systolic blood pressure (60 mmHg), and bradyarrhythmia. Administration of antihistamine, epinephrine, and short-acting corticosteroid, and cardiopulmonary resuscitation was performed and the patient fully recovered.

There had been no prior history of chronic allergic diseases such as allergic rhinitis, urticaria, angioedema, or bronchial asthma. There were no additional IV medications including IV iron when pegylated epoetin-β was administered. He was haemodialysed with biocompatible Fx60 (Fresenius Medical Care, Homburg, Germany) high-flux dialyzer. His chronic medications were oral iron, calcium carbonate, amlodipine, oral vitamin-D agent. He did not receive ACE inhibitors or other drugs with a risk of anaphylaxis at the time. After the event, skin tests with erythropoietin (EPO)-α, EPO-β, darbepoetin-α were performed. Surprisingly, a strong positive skin test was observed for darbepoetin-α. Subsequent to this, we titrated (EPO)-α from low to usual dosage (1000 → 2000 → 4000 → 6000 units/injection) without significant side-effects and achieving a stable haemoglobin level of 11.6 gm/dL with (EPO)-α.

Darbepoetin-α is a second-generation erythrocyte-stimulating agent that is a super-sialylated analogue of EPO having three times longer of half-life than that of EPO-α.¹ Alternative bioengineering techniques to prolong the half-life of EPO further resulted in the development of CERA (methoxypolyethyleneglycol-epoetin-β), which is a pegylated derivative of EPO-β with an elimination half-life of around 130 hours when administered either intravenously or subcutaneously.¹

One case report of a delayed type hypersensitivity reaction with pruritus, macropapular lesion after administration of epoetin-β and darbepoetin-α.² They suggested that pegylated epoetin-β may be a good alternative for treating chronic anaemia in patients with CKD and intolerance to epoetin-β and darbepoetin-α.² In the present case, the development of

anaphylactic reaction to pegylated epoetin-β was unexpected because he was previously treated safely with IV epoetin-α administration. Additional analysis of the administered dose or related product doses to exclude contamination or batch failure was not undertaken and re-challenge was declined by the patient. However, no other patient receiving treatment in our institution had any adverse response to CERA. In addition, there was no positive skin reaction with either epoetin-α or epoetin-β in this patient and there was no alternative agent implicated at the time of anaphylaxis.

To my knowledge, this case represents the first case of anaphylaxis following the intravenous administration of CERA in a haemodialysis patient. Clinicians should be aware of the potential for anaphylaxis with any administered product including epoetins.

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PROBABLE BULLOUS PEMPHIGOID RELATED TO ARTERIOVENOUS SHUNT INFECTION

Chia-Ter Chao^{1,2} and Chun-Fu Lai^{1,2}, ¹Nephrology Division, Department of Internal Medicine, National Taiwan University Hospital Jin-Shan Branch, and ²Nephrology Division, Department of Internal Medicine, National Taiwan University Hospital, Taiwan

An 86-year-old male with diabetes mellitus related end-stage renal disease, started maintenance hemodialysis 1.5 years ago, with left forearm arteriovenous graft (AVG). He reported puncture site swelling and fever for one week. Physical examinations revealed one erythematous bulging lesion near AVG anastomotic area, with bloody/purulent discharge. Blood and pus culture yielded methicillin-susceptible *Staphylococcus aureus* (MSSA) consecutively, and vascular duplex showed peri-graft hematoma with infective component. AVG infection was confirmed, and dialysis access was replaced with one tunnelled dialysis catheter. However,