Dear Editor,

Rabbit anti-thymocyte globulin (rATG) is a T-cell-depleting immunosuppressive agent that is widely used in both living and cadaveric renal transplantation. Its dosage and usage vary among different transplant centers. rATG may be associated with a number of adverse effects such as increased posttransplant infections and possibly malignancy. Various immunological reactions have been reported in the literature with rATG use such as serum sickness syndrome, non-cardiogenic pulmonary edema, refractory hypotension, and fatal anaphylaxis. We report here a case of acute lung injury (ALI) with cytokine syndrome due to rATG with heightened immune reaction with each subsequent dose.

A 46-year-old woman was admitted electively for living unrelated kidney transplantation with basic disease being diabetic nephropathy. She was planned for a living unrelated renal transplant with donor being her brother-in-law. The donor and recipient were 0/1/2 A/B/DR HLA matched. CDC and flow crossmatch were negative including SARS COVID 19 RT PCR. She was asymptomatic on the day of transplant. Induction Immunosuppression was planned with intravenous corticosteroids and rATG, to be given at a dose of 3.5 mg/kg in three divided doses.

On the morning of surgery before being shifted to the operation theatre, she received rATG 50 mg in 250 mL 0.9% normal saline with premedication of pheniramine and acetaminophen. Thirty minutes after the infusion, she developed sudden shortness of breath. Physical examination revealed bilateral chest crepitations mainly in the basal region. Lab investigations were sent and revealed serum procalcitonin was 0.3 ng/ml (normal value <0.15 ng/mL), hemoglobin was 10.1 gm/dL, total leucocyte count of 9800 cells/mm$^3$ and platelet counts of 1,91,000/mm$^3$. A high-resolution CT (HRCT) scan of the chest was suggestive of bilateral lung infiltrates (right more than left). Blood cultures revealed no growth. It was decided to postpone the surgery. She was started on empiric antibiotics for a presumed diagnosis of pneumonia and sent home. Serial chest X-rays showed persistent right lower lobe infiltrates though with decreasing intensity.

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After 24 days of the initial event, she was admitted again for renal transplant surgery. Repeat HRCT scan of the chest showed resolution of previous lung infiltrates. Blood cultures revealed no growth. It was decided to postpone the surgery. She was started on empiric antibiotics for a presumed diagnosis of pneumonia and sent home. Serial chest X-rays showed persistent right lower lobe infiltrates though with decreasing intensity.

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Postoperative days 1 and 2 remain uneventful with no history of fever, cough, or any breathlessness. There was good urine output with improving serum creatinine levels. Her vitals remain stable and oxygen saturation was 99% on room air. On postoperative day 3, she again received 50 mg of IV ATG over 3 h with pre-medications. Five hours post-infusion, she had a sudden cardiac arrest and brief CPR 2 mins was done. Injection epinephrine (1:10000) i.v. was given and the return of spontaneous circulation achieved quickly in less than 2 min. The patient was subsequently intubated and put on ventilatory support. Chest X-ray was done and showed bilateral lower zone infiltrates. The patient was put on inotropic support and dose was titrated as per blood pressure. For suspected acute coronary
event, a coronary angiography was done which revealed normal coronary arteries. IL-6 levels were sent to corroborate with possibility of cytokine release syndrome and they were high: 15.26 pg/mL (normal range <7.00 pg/mL). Holter monitoring revealed normal sinus rhythm.

On postoperative day 5, she was extubated with no inotropic requirement. All these previous episodes of pulmonary edema, hypotension with escalating severity were likely due to rATG hypersensitivity. No further infusion of rATG was given. Pulmonary edema was managed with injection torsemide on titrated doses. She was discharged after 6 days with a nadir serum creatinine of 0.8 mg/dL. During subsequent follow-up, her allograft remained stable. Her serum creatinine continues to be 0.9 mg/dL at 3 months post-transplantation.

**Discussion**

rATG is made by immunizing rabbits who are devoid of any pathogens with a cell suspension of human thymocytes.\(^4\) rATG is widely used as an induction agent in renal transplantation especially in high-risk cases.\(^3\) In the present case, there was heightened severity of symptoms with each subsequent dose of rATG. Also, each time there was recovery by conservative measures only which further strengthen the association of sudden onset pulmonary infiltrates with rATG. Isolated ALI due to rATG is sparsely reported in literature. There are few case reports of ALI with rATG in cases other than renal transplantation.\(^5\) rATG can increase pulmonary capillary endothelium permeability by increasing TNF-α and interleukin levels similar to sepsis.\(^5\) rATG induced acute lung injury without other signs of hypersensitivity is a rare finding. More studies are needed in future to elucidate the pathogenesis and thus to prevent such complications if possible.

**Declaration of patient consent**

Informed and written consent was obtained from all individual participants included in the study.
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Nil.

Conflicts of interest
There are no conflicts of interest.

Nimish Gupta, Sagar Gupta, Ritesh Mongha¹, Sanjay Aggarwal¹
Department of nephrology, Metro Heart Institute with Multispeciality, Sector 16a, Faridabad, Haryana, India | Department of Urology, Metro Heart institute with Multispeciality, Sector 16a, Faridabad, Haryana, India

Address for correspondence:
Dr. Nimish Gupta,
Consultant Nephrology, Metro Heart Institute with Multispeciality, Sector 16a, Faridabad, Haryana, India.
E-mail: nimish392005@gmail.com

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