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Suspected Anti-Thymocyte Globulin induced severe Intraoperative anaphylaxis in a Cadaveric Donor Renal Transplant recipient: A case report

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Abstract
Anti-thymocyte globulin related anaphylaxis is rare but life-threatening. Thymoglobulin is a purified, pasteurized, rabbit-derived T-cell depleting polyclonal gamma immunoglobulin, obtained by immunization of rabbits with human thymocytes, commonly used for treatment of acute rejection in renal transplantation and induction immunosuppression. We report a case of a cadaveric renal transplant recipient who developed intraoperative anaphylactic shock, likely triggered by thymoglobulin administration. This case report signifies the importance of prompt diagnosis and management of intraoperative anaphylaxis, as early intervention is crucial for achieving a successful outcome. Communication between the anaesthesia team, nephrologists and surgeons played a key role in taking the decision of continuing the transplant.

Keywords: Anaphylaxis, Anti-thymocyte globulin, Renal Transplant.

INTRODUCTION

Anti-thymocyte globulin (Thymoglobulin) is an IgG fraction purified polyclonal immunoglobulin from the rabbit serum, immunized against human T-lymphocytes. Thymoglobulin is frequently used in renal transplantation for both, treatment of acute rejection episodes and induction immunosuppression and also in bone marrow aplasia treatment. [1-5] It is now the basis of standard renal transplantation regime for immunosuppression induction intraoperatively. [6,7]. Rabbit-protein hypersensitivity is the main contraindication to thymoglobulin [8] Thymoglobulin related anaphylaxis is uncommon; however, it can occur in patients with rabbit antigen-associated previous exposure, triggering an exaggerated allergic reaction, potentially leading to anaphylaxis, as a result of an anamnestic immune response.[9]. We report a case of serious anaphylactic shock following anti-thymocyte globulin administration during a cadaveric-donor renal transplantation.

CASE REPORT

A 22-year-old male patient, American Society of Anaesthesiology (ASA) physical status III, known case of hypertension, on multiple antihypertensives, secondary to End Stage Renal Disease due to Autosomal Dominant polycystic kidney disease, undergoing Maintenance Hemodialysis through Left sided Radial Arteriovenous Fistula, thrice per week, since 5 years, presented for Cadaveric Donor Kidney Transplant. There was no known history of drug allergies. His pre-operative serum potassium was 5.2 mmol/L and serum creatinine was 7 mg/dL. Pre-operative vital signs were: temperature 98.2°F, blood pressure 152/90 mm Hg, heart rate 62 beats/minute, respiratory rate 18 breaths/minute and arterial blood oxygen saturation 99%.

The patient was undergoing renal transplantation for the first time. Surgery was performed in a latex-free operating room. General anaesthesia induction was smooth and uneventful, 8.5 mm, cuffed oral endotracheal tube was easily secured in the tracheal lumen. After intubation, the monitor showed, oxygen saturation 100%, heart rate 68 beats/minute, peak airway pressure 20 mm Hg, blood pressure 134/84 mm Hg, and end tidal CO_2 30 mm Hg. Later, lumbar epidural catheter was placed for intraoperative and postoperative analgesia, followed by the placement of ultrasound guided, single puncture right sided double lumen Internal Jugular Vein (IJV) catheter. After fifty minutes of induction, Anti-Thymocyte Globulin drip 75 mg, was started in 100 ml normal saline over four hours iv, via the smaller lumen port of the IJV catheter following the iv pre-medications, which included pheniramine maleate 22.75 mg, paracetamol 300 mg and methylprednisolone 500 mg. Within 2 minutes of starting ATG, there was a drop in oxygen saturation to 95%, and rise in the peak airway pressure to 30 mm Hg. We assured the pulse oximeter was in the right position and contact, also confirmed the patency of ongoing Cisatracurium infusion and the depth of anesthesia. We also turned off the nitrous oxide; following the above measures, oxygen saturation returned to 99%. After a couple of minutes, the peak airway pressure and end tidal CO_2 elevated, with oxygen saturation 92%. The Anti-Thymocyte globulin infusion was stopped (1.25 mg infused). We ruled out, if there was any kinking of endotracheal tube along its oral course or leak throughout the circuit upto the ventilator, sample line and sodalime concerns, if any and also ensured, if the endotracheal cuff was adequately inflated. Auscultation revealed bilateral wheezing. We made the required ventilatory changes, increasing the positive end expiratory pressure and minute ventilation, with 100% FiO_2 and shifting to pressure control mode, but all in vain. Endotracheal suctioning was done and the endotracheal tube was replaced with 8 mm cuffed tube, under vision with direct laryngoscopy, which did not yield any positive results as well. Meanwhile, we asked the surgeons to loosen up the Thompson's retractor at the chest site and stop the surgery, portable chest radiograph was ordered. The surgical step involved during the event, included the renal bed being ready and the graft was to be transplanted. The dose of muscle relaxant was repeated, iv doses of diphenhydramine 25 mg, dexamethasone 8 mg and hydrocortisone 200 mg were administered, along with the puffs of salbutamol and budesonide through endotracheal tube, following which, bradycardia (47/min) and a drop in blood pressure to 60/34 mm Hg, not responding to bolus crystalloid, with further fall in oxygen saturation to 77%, peak airway pressures alarming to 50 mm Hg and end tidal CO_2 70 mm Hg, with inspiratory tidal volume of 50 ml, were noted. Revised auscultation indicated silent chest. Anticipating an impending anaphylactic cardiovascular collapse, we gave a bolus dose of 0.1 mg (1 ml of 1:10,000) epinephrine iv; following the adrenaline administration, all the monitor and ventilator alarms got miraculously silenced within a couple of minutes, with gradual restoration of vitals to normal range and improved minute ventilation, on the subsequent readings and minimal wheezing with audible vesicular breath sounds, on auscultation. Patient was put in

Trendelenburg position. Arterial blood gas drawn at the time showed respiratory acidosis: (pH 7.1/pO_2 95/pCO_2 86/HCO_3 28/BE-5.2). An intraoperative trans-oesophageal echocardiogram was not suggestive of myocardial infarction or pulmonary embolism (no right ventricle dysfunction), and showed a hyperdynamic left ventricle. Ultrasound of the chest showed no evidence of pneumothorax or acute haemorrhage. Chest radiograph showed a normal cardiac shadow with IJV catheter insitu, and no evidence of haemothorax or pneumothorax. The patient had no documented latex or rabbit allergy. After detailed discussion of the intraoperative events and potential consequences with the patient's family, nephrologist, and the surgical team and after confirming that informed consent was obtained, the decision was made to proceed with the kidney transplant. Double diluted Anti-Thymocyte globulin intravenous infusion was started, at 75 mg in 250 ml normal saline over 8 hours, as per the nephrologist's advice after the assurance of complete stability of patient vitals and good ventilation. The renal transplant was successfully concluded and patient was extubated uneventfully. His intraoperative immunologic studies were significant for elevated tryptase 70 ng/ml (<15 ng/ml) and histamine 98 ng/ml (<65 ng/ml).

DISCUSSION

Anaphylaxis under general anaesthesia presents as an enormous challenge to the anaesthesiologist, requiring quick application of the THINK FAST, ACT FAST approach, in terms of limited interval to rule out the differential diagnoses, the involvement of multiple intravenous drugs, the patient being covered in drapes, and implementation of immediate intervention. Anaphylaxis is essentially, a clinical diagnosis, hence early diagnosis and prompt intervention are critical to enhancing the chances of patient survival. Cases of Thymoglobulin-induced anaphylaxis are sporadic, with only a limited number reported in the medical literature. [6, 9-12] Of those, one patient experienced severe thymoglobulin-related IgE reaction, but tryptase and skin tests were not done in one of the two renal transplant recipients [11] while, in the other case, like our case, skin test was not done to confirm thymoglobulin anaphylaxis but tryptase level was notably increased.[12]. In this case, the induction and maintenance of anaesthesia were uncomplicated, but shock developed within minutes of initiating the thymoglobulin infusion. There was no history of rabbit exposure or allergy in our case. While Anti-Rabbit IgE testing was not available in our hospital setting, elevated tryptase and histamine levels, along with the rapid development and intensity of the shock, strongly supported an IgE mediated anaphylactic origin, pointing its association with thymoglobulin, based on the sequence of events.

Anaphylaxis under general anaesthesia may present as severe bronchospasm with difficult ventilation, as the first indication, like in our case, and at times be the only sign of anaphylaxis in these patients.[13] We quickly ruled out common causes of bronchospasm first and discontinued the Anti-Thymocyte globulin infusion, whilst anticipating anaphylaxis-induced bronchospasm as a diagnosis of exclusion. Thymoglobulin infusion is generally well tolerated without major complications when patients receive appropriate pre-medications, and the infusion is administered slowly under close medical supervision to minimize the risk of cytokine release syndrome, ensuring patient safety.

Adrenaline and fluid therapy form the mainstay of treatment. Had adrenaline not been administered promptly in our case, it would have quickly escalated to the need for cardiopulmonary resuscitation. Earliest possible administration of intravenous adrenaline controls the catastrophe by reversing the vasodilation and inflammatory marker release, sufficiently with smaller and fewer doses, saving further need of vasopressor infusions that could be required with delayed administration, effectively illustrating

the adage 'a stitch in time saves nine. Antihistamines and corticosteroids form the second line of treatment to prevent further relapse.[14]

CONCLUSION

Timely diagnosis and management of intraoperative anaphylactic reactions, poses a potential challenge to the anaesthesiologist, as they can prove fatal, if not promptly intervened. Prompt identification and timely management of intraoperative anaphylaxis can be life-saving. Effective communication is the key between medical providers, as this coordinated and synergistic approach not only enables medical professionals to respond effectively, adapt to unanticipated challenges, but also improves overall patient outcomes through timely and efficient management during critical emergencies.

DECLARATION OF PATIENT CONSENT

Patient has given his consent for his clinical information to be reported in the journal.

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Nil

CONFLICTS OF INTEREST

There are no conflicts of interests

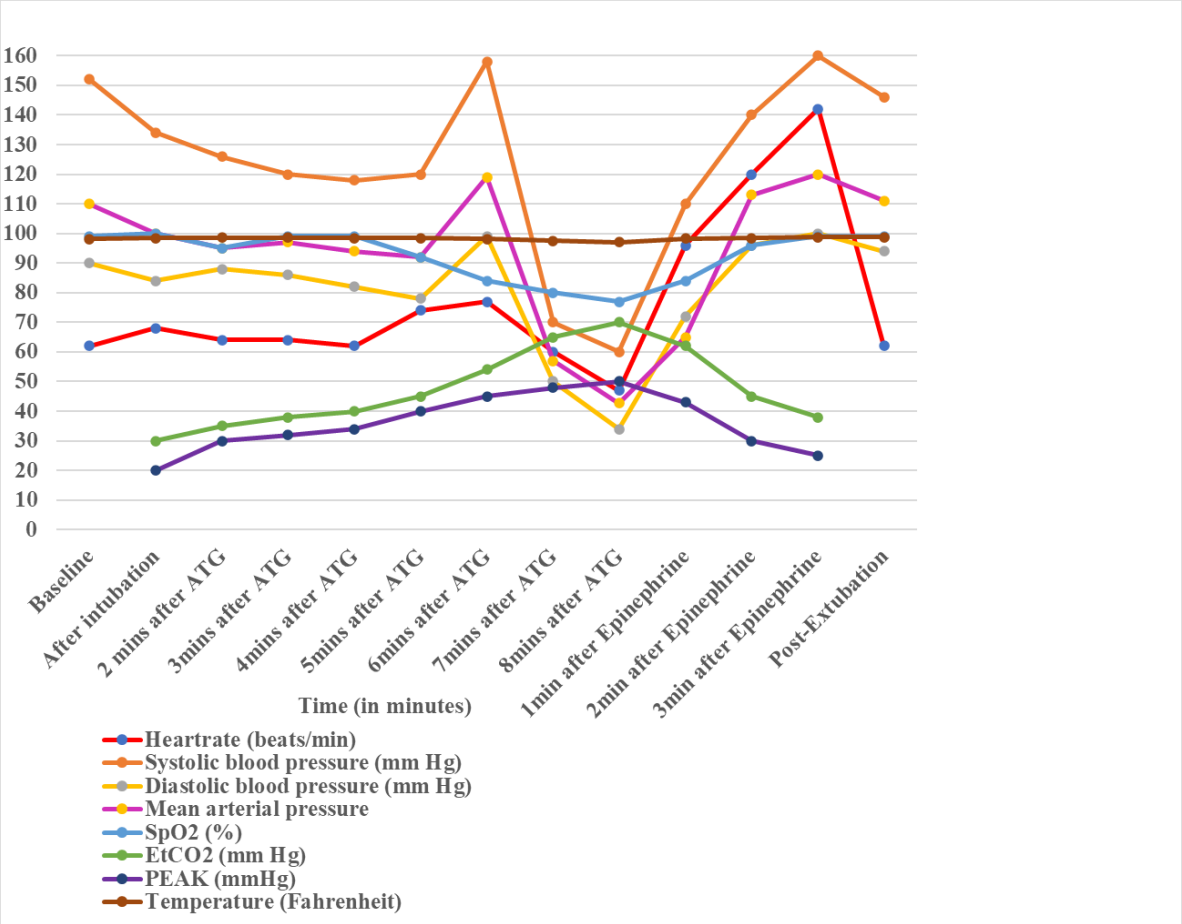

Figure 1. Vital signs, end Tidal CO_2 and peak airway pressures after iv ATG and Epinephrine

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