Transplant International

Transplant International ISSN 0934-0874

CASE REPORT

Isolated left-sided pulmonary edema caused by alemtuzumab (Campath®) during kidney transplantation

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Keywords
alemtuzumab, campath, complication, pulmonary edema, renal transplantation.

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Received: 20 January 2010
Revision requested: 15 February 2010
Accepted: 22 February 2010
Published online: 16 March 2010

doi:10.1111/j.1432-2277.2010.01077.x

Summary

Alemtuzumab is a novel anti-CD-52 monoclonal antibody for immunosuppression. Although cost effective and efficacious, alemtuzumab is not without risk. Interestingly, intraoperative complications caused by alemtuzumab have rarely been reported. We describe a case of intraoperative pulmonary edema following administration of alemtuzumab. A 22-year-old man underwent kidney transplantation and received alemtuzumab intraoperatively. To provide better surgical exposure for transplantation, the operation table was tilted to the right. At the end of 3.5-h uneventful procedure, a sudden oxygen desaturation was noted after the bed was flattened. The postoperative chest X-ray showed opacification of the entire left lung field. After 4 days of bi-level positive airway pressure treatment, the lung field was cleared. This case is unique in that pulmonary edema developed during surgery after administration of alemtuzumab, and that the edema developed only in the nondependent lung. Transplant anesthesiologists should be aware of the risk of this complication with these novel anti-CD-52 monoclonal antibodies.

Introduction

Alemtuzumab (Campath®; Genzyme Corporation, Geel, Belgium) is a novel anti-CD-52 monoclonal antibody that has been used for both the induction and maintenance of immunosuppression in organ transplantation to minimize calcineurin inhibitor and steroid therapy [1–5]. Although cost effective [5] and efficacious [6], alemtuzumab therapy is not without risk [7]. Interestingly, intraoperative complications caused by alemtuzumab have been rarely reported. We describe a case of intraoperative pulmonary edema that only affected one side of the lung field following administration of alemtuzumab for renal transplantation.

Case report

A 22-year-old man (165 cm in height and 57 kg in weight) with end-stage renal disease secondary to polycystic kidney disease was admitted for repeat kidney transplantation. He had an initial kidney transplant 12 years ago, but returned to hemodialysis for the last 7 years. He had never received anti-CD-52 monoclonal antibodies. Preoperatively, he was afebrile and without distress. He was a nonsmoker without any known history of cardiopulmonary dysfunction or pneumonia. The chest auscultation was normal. His electrolytes were: sodium 143 mEq/l, potassium 4.8 mEq/l, chloride 87 mEq/l, bicarbonate 24 mEq/l, blood urea nitrogen 24 mg/dl, and creatinine 7.5 mg/dl. The complete blood count and coagulation studies were within normal limits. The last hemodialysis was performed 1 day prior to surgery. His home medications included clonidine, lisinopril, and amlodipine. The donor was a 24-year-old woman in the same hospital with brain death following head trauma. On biopsy, the donor kidney showed minimum glomerulosclerosis, interstitial fibrosis, and arterial atherosclerosis; however, it was accepted by both the recipient and the transplant team.

Preoperatively, the patient received methylprednisolone 1 g intravenously (i.v.), diphenhydramine 50 mg i.v., famotidine 20 mg i.v., and acetaminophen 650 mg orally

as premedications for alemtuzumab. After induction of general anesthesia, an endotracheal tube was placed without problems and secured at a depth of 22 cm at the frontal teeth. A 20-gauge arterial catheter was placed in the right radial artery and a 7 French double lumen central venous catheter was placed in the right internal jugular vein without difficulty. The patient was positioned supine with the table tilted 20° to the right to facilitate implantation of the renal graft. Initial arterial blood gas (ABG) was: pH 7.52, $PaCO_2$ 35 mmHg, PaO_2 197 mmHg, and HCO_3^- 29 mEq/l with F_IO_2 0.36. The peak inspiratory airway pressure (PIP) was 22 cm H_2O with a tidal volume of 600 ml.

After induction of general anesthesia, alemtuzumab 30 mg was administered i.v. over 2 h. The systolic blood pressure decreased from 120 mmHg to 85 mmHg in 45 min after the initiation of alemtuzumab infusion, but returned to the baseline with a dopamine infusion (3 μg/kg/min). The core temperature increased from 36.7 °C to 38.8 °C. The PIP was 26 cm H_2O with the same tidal volume.

Methylprednisolone 1 g i.v., furosemide 60 mg i.v., and mannitol 60 g i.v. were administered as the kidney graft was reperfused without any hemodynamic derangement. Throughout the procedure, the central venous pressure was maintained at 10–12 mmHg and systemic blood pressure was around 100/60 mmHg with dopamine infusion (2–5 μg/kg/min). Hemostasis was easily achieved with a total estimated blood loss of 250 ml. No blood transfusion was required. A total of 2000 ml of crystalloid and 2000 ml of colloid were administered intraoperatively. Total urine output was 2000 ml. The total fluid balance was 1750 ml positive. An ABG at 1 h prior to the completion of surgery showed pH 7.47, $PaCO_2$ 33 mmHg, PaO_2 160 mmHg, HCO_3^- 23 mEq/l with F_IO_2 of 0.33. The PIP was stable at 26 cm H_2O with the same tidal volume.

At the end of the 3.5-h transplantation procedure, the operation table was returned to a flattened position. Decreased oxygen saturation was noted on pulse oximetry from 99% to 90% with F_IO_2 of 0.33. After F_IO_2 was increased to 1.0, the oxygen saturation improved to 97%. The bilateral anterior chest auscultation remained normal. The decision was made to remove the endotracheal tube in the operation room. A chest X-ray was not taken prior to the removal of the endotracheal tube. No upper airway obstruction was noted.

The patient's vital signs at the time of arrival in the postanesthesia care unit (PACU) were: blood pressure of 127/52 mmHg, pulse at 112/min, and respiratory rate at 30/min with SaO_2 of 98% with 8 l/min of oxygen via a face mask. Unexpectedly, the patient was noted to have isolated left-sided pulmonary opacification on a routine chest X-ray at 1 h after the arrival to the PACU (Fig. 1).

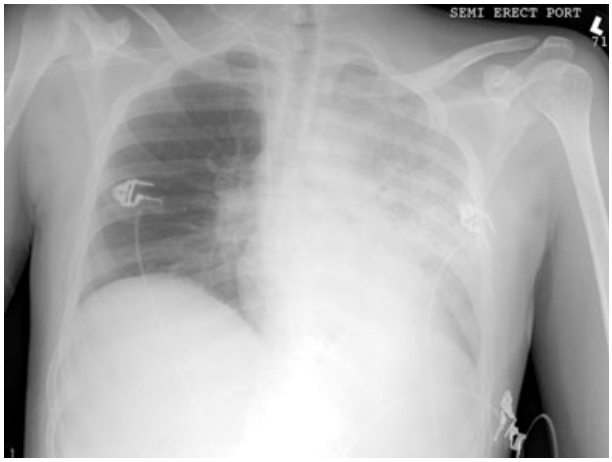

Figure 1 A portable chest X-ray 1 h postoperatively. A complete opacification of the entire left lung field without loss of the lung volume was noted.

The ABG revealed pH 7.42, $PaCO_2$ 42 mmHg, PaO_2 70 mmHg, HCO_3^- 25 mEq/l with 10 l/min O_2 via face mask. He was transferred to the intensive care unit (ICU) and was maintained on bi-level positive airway pressure (BiPAP) ventilation with settings of 10/5 cm H_2O and an oxygen flow rate of 15 l/min. Subsequent alemtuzumab was withheld.

Over the postoperative days 1 and 2, the patient underwent hemodialysis for reasons of delayed graft function with a total negative fluid balance of 3000 ml. A repeat chest X-ray showed no change, despite clinical improvement in respiratory status. On postoperative day 3, the patient was discharged from the ICU to a floor. On postoperative day 4, the chest X-ray showed complete resolution of the left-sided opacification (Fig. 2).

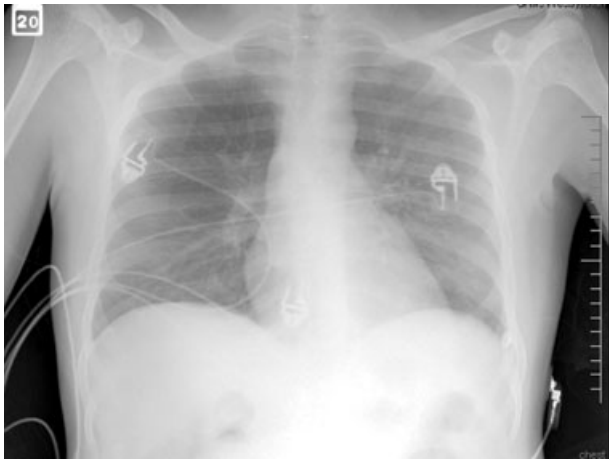

Figure 2 A chest X-ray on the day 4 after transplantation. The left lung field was completely normal.

Discussion

Although the Food and Drug Administration reports pulmonary edema as one of the side effects of alemtuzumab [8], perioperative pulmonary edema caused by almtuzumab has been rarely reported. In a large series of 100 pancreas transplantation patients, Muthusamy *et al.* [7] reported pulmonary edema caused by alemtuzumab in two patients, but did not report any details of the cases. A case of diffuse alveolar hemorrhage was also reported in association with alemtuzumab [9]; however, in this case the complication developed 2 days after the administration of alemtuzumab.

The diagnosis of pulmonary edema related to alemtuzumab is a diagnosis of exclusion. The differential diagnoses included pulmonary edema secondary to cardiogenic and noncardiogenic causes. In this patient, cardiogenic pulmonary edema is unlikely, given that the patient had normal cardiac function, that the edema was isolated, and that the affected lung was nondependent. The fluid balance was only 1750 ml positive during the surgery, and there were no signs of extreme hypertension. Noncardiogenic causes which could be relevant to this patient include adult respiratory distress syndrome, aspiration pneumonitis, neurogenic pulmonary edema, negative-pressure pulmonary edema, infection, transfusion-related issues, electrolyte imbalance, pulmonary embolism, and atelectasis. Adult respiratory distress syndrome seemed unlikely given the clinical scenario and the single lung nature of the edema. There was no evidence of aspiration during the operation, nor was there any evidence postoperatively of neurologic dysfunction or stroke. Negative pressure pulmonary edema should be considered as a potential cause; however, no airway suctioning was performed via the endotracheal tube and no upper airway obstruction was noticed after the removal of the endotracheal tube. There was no evidence of preoperative pneumonia, and the patient had no past history of pneumonia. Blood transfusion was not performed intraoperatively and there was no evidence of hyponatremia or other electrolyte abnormality. Pulmonary embolism was unlikely, given the relatively stable hemodynamics without any significant changes in E_TCO_2 monitoring during the procedure. Intubation of the right main-stem bronchus during the surgery could be a conceivable cause; however, it was unlikely because Trendelenberg position was not used during the surgery, the endotracheal tube was secured with tape at 22 cm at the incisor teeth for the patient (height of 165 cm), and bilateral anterior chest auscultation was confirmed normal. Taken together, the most likely cause of this case of isolated pulmonary edema was alemtuzumab-related pneumonitis.

Onset of the pulmonary edema likely occurred toward the end of surgery, i.e. 1 h prior to the completion of the procedure, when the arterial gas showed PaO_2 of 160 mmHg with F_IO_2 of 0.33. The postoperative chest X-ray (Fig. 1) was performed at 1 h after the arrival in PACU.

Our case was unique in that pulmonary edema developed only in the left side of the lung, which was the nondependent side during the surgery. The exact mechanism of the isolated lung pulmonary edema remains unclear. Alemtuzumab-induced pulmonary edema is a manifestation of chemical pneumonitis and this pathology should affect both lungs. We hypothesize that the larger mechanical stretch and oxygen content in the lung tissue by preferential ventilation of the nondependent lung might exacerbate production of oxygen free radicals and result in capillary leakage and edema. It might have been interesting to be able to follow the changes of cytokines in the peripheral blood samples in a case like this one.

Pulmonary edema secondary to alemtuzumab responded well to a conservative therapy, including BiPAP. Steroids given as an immunosuppressant for the transplantation might also contribute to the recovery. The opacification of the left lung was completely resolved in 4 days after the surgery.

In terms of the timing of the administration of the initial dosage of alemtuzumab, immediate post-transplantation period may be an alternative to initiate this agent, as was advocated by Ku *et al.* [10]. Potential side effects associated with alemtuzumab could be handled in a more stable environment.

In summary, we report a patient who developed isolated left-sided pulmonary edema resulting from the administration of a novel immunosuppressive agent, alemtuzumab, during kidney transplantation. Anesthesiologists should be aware of the risk of this complication during the use of these novel anti-CD-52 monoclonal antibodies.

Authorship

TS: designed study. TS, BG: performed study. TS, BG: collected data. TS, BG: wrote paper.

Funding

Support was received solely from the above institutional and departmental sources. No conflict of interest.

Acknowledgements

The authors thank Shannon M. Barnes, MS (Scientific Writer, Department of Anesthesiology, University of

Pittsburgh Medical Center, University of Pittsburgh, Pittsburgh, PA, USA) for her editorial assistance with the manuscript.

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