

## **INTRAOPERATIVE REFRACTORY HYPOTENSION DURING A KIDNEY TRANSPLANT: A CASE REPORT AND REVIEW**

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### **Abstract:**

We present here a patient who received preoperative doses of the drugs amlodepin and atenolol [amlong - 4 hours prior to anaesthesia], basiliximab [Simulect], a chimeric human/mouse antibody specific to the interleukin II receptor expressed on activated T lymphocytes and epidural bupivacaine with adrenaline 3ml., all before induction of anaesthesia for a living related renal transplantation. Within half an hour of induction of anaesthesia he developed a refractory hypotension in-spite of maintaining a CVP of above 15cms of H<sub>2</sub>O. Since a direct causal relationship with basiliximab could not be proved, other aetiologies in the differential diagnosis of hypotension were also analyzed and reviewed.

**Key words:** Refractory hypotension, Basiliximab, Amlong

### **Case Report:**

A 45 yrs old man [62kg, 160cm] of end stage renal disease [ESRD] with native kidney output of 500-600 ml in 24hrs, a diabetic and hypertensive for the last 12 years with CAD, was taken up for a live donor renal allografting (recipient). He was on maintenance haemodialysis for eight months through an AV fistula in the left forearm prior to renal transplant. He received last haemodialysis two days prior to the proposed kidney transplant.

Pre operative work up showed a low Hb. [7.6 gm%, Hct 22.5] deranged KFT [Creatinine 6.3, BUN 35] and normal serum electrolytes [Sodium 132, Potassium 4.4,] LFT, IgG, IgM, Chest X-ray and Carotid Doppler studies.

There was ST depression in V 4,5,6 leads in 12 lead ECG. Two-dimensional Echo showed mild septal and posterior wall hypokinesia, fair LV systolic function and mild MR. Preoperative Stress Thallium revealed ischaemia in apex, apico anterior, anterior, anterolateral, lateral and inferior segments. Coronary angiography showed an evidence of distal and diffuse triple vessel disease.

The patient was on Tab. Amlong (amlodipin + atenolol), insulin by sliding scale, Cap. Tacrolimus, Tab Mycophenolate sodium and Cefoperazone-sulbactam till the day prior to surgery. On the morning of operation he received his usual antihypertensive medicines.

In OT the patient recorded a preoperative blood pressure of 140/87 mmHg. [MAP 104.6] and a heart rate of 86/min. ECG showed ST depression in lead II. Before induction of anaesthesia, Inj. Basiliximab 20 mg [monoclonal antibodies] diluted with 50 ml of normal saline was started [9.00 am] and infused in half an hour. In the mean time right radial artery was cannulated and a lumbar epidural catheter was introduced at the level of T12-L1 interspace. Epidural test dose was given with 3 cc of 2% lignocaine and adrenaline (1 in 2.00,000).

After premedication with IV Midazolam [1 mg] and Fentanyl 75 microgram, preoxygenation was done for five minutes followed by Thiopentone Sodium 100mg, Oxygen, Nitrous Oxide and Isoflurane 0.5%. Endotracheal intubation was facilitated with atracurium 30mg.

Triple lumen central venous catheter was placed in the right internal jugular vein, which showed a CVP reading of 14. Inj methyl prednisolone 500 mg infusion was also started according to the protocol.

One hour after the infusion of monoclonal antibodies, the operative procedure started. Blood pressure recorded at that time was 120/ 76 (MAP 90) mmHg after an infusion of one litre of normal saline. An intra-operative MAP of 100 mmHg was targeted. A low dose Dopamine infusion was started @ 5 microgram/kg/min. to meet that goal.

Fifteen minutes after skin incision the blood pressure was observed to gradually decrease to a systolic blood pressure of 90 mmHg [MAP 66 mmHg.]. Isoflurane was stopped and anaesthesia maintained with an additional dose of fentanyl 25 mcg and low dose ketamine 10 mg, oxygen and nitrous oxide. The resuscitative efforts included administration of intravascular fluids, and infusions of combination of vasopressors like dopamine, adrenaline and nor-adrenaline.

Inj. Dopamine infusion was increased to 10 microgram/kg/min and Albumin 5% started through the central line @ 50 ml/hr. Dobutamine was added @ 5 microgram/kg/min. but within five minutes the systolic BP showed a further fall to 86 mmHg with a heart rate of 130/min. Dobutamine infusion was stopped and Inj Adrenaline infusion was started @ 0.1 microgram/kg/min. Five minutes post adrenaline the heart rate became 110/min, but BP remained between 82 – 86 mmHg systolic.

Inj nor -adrenaline started @ 0.1 microgram/kg/min and an ABG was also sent. ABG showed a metabolic acidosis [pH of 7.238, PCO<sub>2</sub> 40.3, PO<sub>2</sub> 187, HCO<sub>3</sub> 16.6, BE -9.5, SO<sub>2</sub> 99.0%, Na<sup>+</sup> 129, K<sup>+</sup> 3.5, sugar 211 and Lactic acid 3.40]. Sodium bicarbonate 100 cc was slowly infused intravenously. Insulin infusion was also started @ 3 units/hr. BP remained between 82 – 86 mmHg systolic for the next one and a half hours with heart rate of 110-120/min, CVP was maintained at 18-20 with normal 5 lead ECG without any arrhythmias. Repeat ABG showed more metabolic acidosis with a pH of 7.222 and a base deficit of -11.6. An additional dose of 100 cc of Sodium bicarbonate was infused slowly.

After vascular anastomoses and clamp release, Frusemide in a dose of 120 mg was injected I.V. No urine output was recorded. Blood pressure remained at the systolic level of 85 mm Hg. Third ABG taken intraoperatively, after half an hour showed a persistent metabolic acidosis with a pH of 7.24 and a base deficit of -10.6. 3<sup>rd</sup> aliquot of 100 cc Sodium bicarbonate was infused.

The patient was shifted to ICU three hours after induction of anaesthesia on elective IPPV, and infusions of Dopamine @ 10 micrograms/kg/min, adrenaline @ 0.12 micrograms/kg/min, nor adrenaline @ 0.1 micrograms/kg/min, Insulin @ 2 units/hr with a positive intraoperative fluid balance of 1650 ml comprising of 1500 cc crystalloid, 100 cc albumin 20%, and one unit of packed RBC. Intraoperative blood loss was approximately 200 ml and the urine

output was 50 ml. In ICU, on IPPV, the patient's blood pressure was 86/47 mmHg [MAP 60], heart rate 122/min, SpO<sub>2</sub> 100%, CVP 15, and a normal sinus rhythm on ECG. Chest auscultation was normal with no basal crepts. Soda bicarbonate infusion was continued.

Postoperative echocardiography showed good LV contractility, left ventricular ejection fraction of 55%, no pericardial effusion and no significant regurgitation. Doppler of Transplant kidney showed normal perfusion and no perinephric collection.

One unit packed RBC was transfused. Blood gases were done hourly which consistently showed metabolic acidosis. ABG done 3 hours post operatively showed a pH of 7.271, PCO<sub>2</sub> of 35.5, PO<sub>2</sub> 174, K<sup>+</sup> 3.2, base deficit of -9.8. By this time the blood pressure had risen to 140/62 mmHg with the same inotropic support. But urine output was in the range of 10-15 ml/hr so haemodialysis was started.

One hour into dialysis the repeat ABG showed a pH of 7.359, PO<sub>2</sub> 144, PCO<sub>2</sub> 40.2, and base deficit of -2.5. Gradually the inotropes were tapered and nor adrenaline stopped two hours later followed by adrenaline an hour later. Patient started producing urine @ 70-100 ml/hr. Patient was extubated after observation for another two hours [11.30 pm]. Intravenous infusion of Frusemide @ 60 mg/hr and Epidural infusion with Bupivacaine 0.125% and fentanyl 2 microgram/ml @ 6 ml/hr started.

Nine hours later, Dopamine infusion was stopped. Patient maintained good haemodynamics with a urine output of 100 ml/hr. ABG by this time had become normal. [pH was 7.413, PCO<sub>2</sub> 42.4, PO<sub>2</sub> 103, K<sup>+</sup> 3.9, Lactate 1.3, Hb 9.6, Base excess 2.2. Laboratory reports revealed a serum creatinine level of 4.5, BUN 31.]

Patient remained haemodynamically stable and produced urine at an average rate of 100 ml/hr without Frusemide on the second day postoperatively. A repeat dose of Simulect was given on the fourth day after transplantation with no change in haemodynamics.

### **Discussion:**

When patients with chronic kidney disease undergo organ transplantation, their blood pressure regulation may worsen due to an increased incidence of autonomic dysfunction<sup>1</sup> and the systemic vasoconstriction induced by the immunosuppression medications<sup>2</sup>. This autonomic dysfunction is incompletely corrected by allograft transplantation and symptomatic orthostatic hypotension may

persist<sup>3,4</sup>. In order to provide better perfusion to the grafted kidney care is taken to avoid hypovolaemia. The fluid therapy protocol for the recipient is targeted to achieve an intraoperative mean arterial pressure [MAP] of 100mm Hg and a CVP above 15cm of water by intravenous infusions of normal saline, low dose dopamine and 5% human albumin @ 8-10ml/min. In spite of using 1.5 litres of fluid during the first hour of surgery and multiple vasopressors, the intra-operative MAP could not be raised beyond 66 mm Hg in our patient.

Hypotension can also occur during general anaesthesia due to myocardial depression and vasodilatation produced by the anaesthetic agents. Coupled with antihypertensive agents this hypotensive effect can become potentiated. Amlodipin, the calcium channel blocker, exhibits primary cardiac symptoms of hypotension and bradycardia if an overdose occurs. Our patient however had tachycardia, probably caused by dopamine.

Profound hypotension associated with labetalol-induced vasoplegia has been reported<sup>5</sup>. Could atenolol have contributed to the hypotensive effects in our case?

Hypotension was observed in the patient an hour after the infusion of the immunosuppressant drug basiliximab. On medline search the cardiovascular adverse events with the basiliximab [Simulect®] were reported to be 3 - 10% of the treated patients. These included abnormal heart sounds, aggravated hypertension, angina pectoris, cardiac failure and hypotension. Severe acute hypersensitivity reactions including anaphylaxis characterized by hypotension<sup>6</sup>, tachycardia, cardiac failure, dyspnoea, wheezing, bronchospasm, pulmonary oedema, respiratory symptoms and/or sneezing, as well as capillary leak syndrome and cytokine release syndrome, have also been reported during post-marketing experience with Simulect®. However, the second dose of basiliximab given to this patient four days later did not elicit a similar hypotensive response.

Hypermagnesemia is quite common in renal failure and can contribute to the refractory hypotension. Since the estimation of magnesium levels was not done in this patient so it is difficult to say whether it had a role to play in the aforementioned hypotension.

Should 8-Arginine vasopressin (AVP) be used in cases of refractory hypotension? The literature review recommends its use<sup>7</sup>.

### Conclusion:

We report the occurrence of refractory hypotension during renal transplantation. The factors suspected to have contributed to hypotension were the use of preoperative antihypertensives, hypersensitivity reaction to basiliximab or human albumin, autonomic dysfunction and perhaps hypermagnesemia.

	During induction	½hr post incision	1 & 1/2hr Post incision	2 hrs Post incision	5 hrs Post incision	13 hrs Post incision
<b>H.R./min</b>	86	130	110	122		
<b>B.P mmHg [MAP]</b>	140/87	120/76	90/[66]	86/	140/62	
<b>pH</b>		7.238	7.24	7.271	7.359,	7.413,
<b>PCO<sub>2</sub></b>		40.3		35.5,	40.2	42.4
<b>PO<sub>2</sub></b>		187,		174,	144	103
<b>HCO<sub>3</sub></b>		16.6				
<b>BE</b>		-9.5	-10.6	-9.8	-2.5	2.2
<b>Na/K<sup>+</sup></b>	132/4.4	130/3.5		3.2		3.9
<b>Lactate</b>		3.40				1.3
<b>Sugar</b>	101	211				
<b>Hb.</b>	7.6					9.6
<b>BUN</b>	35					31
<b>Cr.</b>	6.3					4.5

Table 1: Vital parameters and gasometry during renal transplant and postoperative period

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