High Blood Tacrolimus and Hyperkalemia in a Heart Transplant Patient

The Editor,

A 43-year-old female patient (weight 54 kg) underwent orthotopic heart transplantation (OHT) for dilated cardiomyopathy. Postoperative recovery was uneventful and her left ventricle (LV) function was 60% on two-dimensional echocardiography at the time of discharge. She was on immune suppressive therapy with tacrolimus 2 mg/twice daily, mycophenolate mofetil 500 mg/twice daily, and prednisolone 20 mg/twice daily. The other medications were trimethoprim/sulfamethoxazole (80/400)/once daily, voriconazole 200 mg/twice daily, valganciclovir 450 mg/twice daily, insulin, and frusemide 40 mg/once daily. She was readmitted on 68th postoperative day with type 1 respiratory failure. Prophylactic broad spectrum antibiotics (meropenem 1 g/intravenous [iv]/thrice daily and teicoplanin 400 mg/iv/once daily) were started, in addition to the above prophylaxis, after sending blood, urine, and sputum cultures. A complete hemogram, serum electrolytes, kidney function tests, liver function tests, and tacrolimus level were done. She was managed conservatively with noninvasive ventilation, dieresis (injection frusemide 20 mg/iv/twice daily), and bronchodilation (ipratropium bromide and asthalin nebulization/four times daily). Klebsiella pneumonae was isolated on sputum culture, and therapy was initiated with colistin (10 lac IU/iv/thrice daily). Echocardiography showed good LV function (50%) and mild right ventricle dysfunction. Other hematological investigations were unremarkable except for hyperkalemia (Na^+ = 128 meq/L, K^+ = 6.7). Twice repeated tests also yielded high K^+ 7.2 meq/L and 6.9 meq/L. Repeat blood urea nitrogen and creatinine were also normal (45 mg% and 1.0 mg/dl). Electrocardiogram did not show any sign of hyperkalemia. Tacrolimus level was 21.3 ng/dl much higher than the earlier report (10 days before) of 12.3 ng/dl. Tacrolimus was withheld, and treatment started for hyperkalemia with oral sodium polystyrene sulfonate, intravenous frusemide, calcium gluconate, sodium bicarbonate, and glucose-insulin infusion. Serum potassium (K^+) level decreased only up to 6.2 after 48 h [Figure 1]. On 3rd day, oral fludrocortisone 0.1 mg/day was added. On 4th day, the K^+ levels came within normal limits and blood tacrolimus levels decreased to 12.7 ng/dl. On 5th day, the serum K^+ decreased to 4.5 and fludrocortisone was continued for another 2 days. Tacrolimus was restarted at 1 mg/twice daily; other medications were continued. Sodium and potassium were monitored twice daily for the next 7 days and both remained within normal limits [Figures 1 and 2].

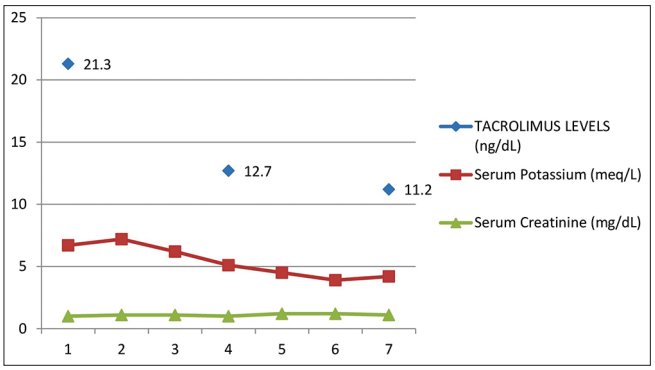

Figure 1: Blood tacrolimus levels every 3rd day, daily serum levels of potassium, and creatinine from day 1 of readmission (68th postoperative day)

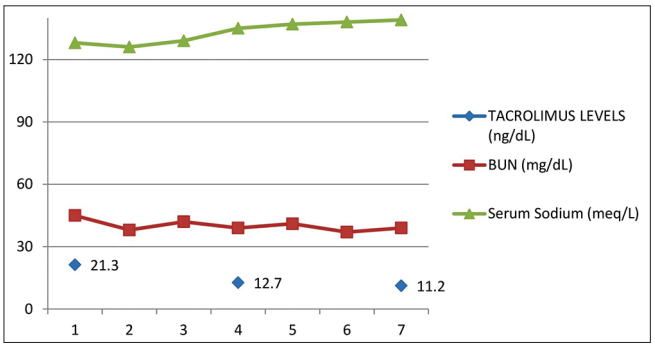

Figure 2: Blood tacrolimus levels every 3rd day, daily serum levels of sodium, and blood urea nitrogen from day 1 of readmission (68th postoperative day)

Tacrolimus-induced hyperkalemia has been reported earlier in liver and kidney transplant patients.[1,2] This is the first report of tacrolimus induced hyperkalemia in OHT recipients.

Calcineurin inhibitors (CNIs), tacrolimus, and cyclosporine are the mainstay of immunosuppressive therapy regimen for solid organ transplants including orthotopic heart transplants. Tacrolimus is known to cause electrolyte disturbances such as hyperkalemia and hyponatremia more than cyclosporine.[3] CNIs produce hyperkalemia by causing renal tubular acidosis (RTA) in distal convoluted tubule (DCT) of the nephron. This CNI-induced RTA occurs in the absence of renal insufficiency, due to decreased renal tubular hydrogen ion secretion. Hyperkalemia after heart transplantation can be because of acute kidney injury, low cardiac output syndrome, or drug-induced (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, trimethoprim/sulfamethoxazole, and CNIs). Fludrocortisone, a mineralocorticoid having effects such as aldosterone, was originally used for adrenocortical insufficiency in Addison's disease and salt losing

adrenogenital syndrome.[4] Fludrocortisone increases potassium reabsorption in the DCT and hastens its excretion in urine. Other side effects of fludrocortisone are hypernatremia, fluid retention, osteoporosis, hyperglycemia, and hypertension.[4] Fludrocortisone should be used as a last option in the treatment of hyperkalemia induced by CNIs.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Access this article online	
Quick Response Code:	Website: www.annals.in
	DOI: 10.4103/0971-9784.203933

How to cite this article: Sahu MK, Singh SP, Das A, Abraham A, Airan B, Alam I, *et al.* High blood tacrolimus and hyperkalemia in a heart transplant patient. Ann Card Anaesth 2017;20:270-1.

Received: August, 2016. **Accepted:** December, 2016.