Massive pleural effusion in a renal transplant recipient on tacrolimus

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ABSTRACT

Fluid and salt retention have been described as a side effect of tacrolimus therapy. We report a case of unexplained massive fluid retention with pleural effusion and ascites in the immediate post-transplant period. The patient recovered immediately on conversion from tacrolimus to sirolimus.

Key words: Fluid retention, sirolimus, tacrolimus

Introduction

Tacrolimus is the calcineurin inhibitor (CNI) of choice for maintenance immunosuppression in kidney transplant recipients. The major drawbacks of tacrolimus are its narrow therapeutic window, unpredictable bioavailability and nephrotoxicity. Fluid and sodium retention are reported rarely. Here, we report a patient who developed significant fluid retention including third space collection in the immediate post-transplant period and showed dramatic improvement on conversion to sirolimus.

Case Report

A 51-year-old female patient was admitted with rapidly progressive renal failure 3 years ago. She had proteinuria and microhematuria. Antinuclear antibodies were positive. Complement levels were normal and anti-double stranded deoxyribonucleic acid antibodies and antineutrophil cytoplasmic antibodies were negative. Hepatitis B surface antigen, hepatitis C virus (HCV) antibodies and enzyme-linked immunosorbent assay for human immunodeficiency virus were negative. Ultrasonogram showed normal kidney size. However kidney biopsy showed only chronic changes with fibrous crescents. She was started on maintenance hemodialysis and oral prednisolone for arthralgia. She was on hemodialysis for next 30 months along with alternate day prednisolone 5 mg/day. She became anti-HCV positive a year later. Liver functions were normal and there was no evidence of chronic liver disease and portal hypertension on ultrasonogram and upper gastrointestinal endoscopy. She was not considered for interferon therapy. She was euthyroid on thyroxine replacement (100 μg/day) at the time of transplantation. There was no edema prior to transplantation and she was at her dry weight on the day of transplantation. She was started on tacrolimus 0.1 mg/kg/day, mycophenolate mofetil 500 mg b.d. and prednisolone 20 mg/day. She had received pulse methyl prednisolone 1 g on day and 500 mg for the next 2 days. Induction antibodies were not given. Trough tacrolimus level on post-operative day 2 was 12.1 ng/ml. Graft started functioning immediately and creatinine had dropped to 1.6 mg/dl on day 2 and 1.4 mg/dl on day 4. Patient developed breathlessness (relieved on lying to the left side), pedal edema, abdominal distension and swelling of upper limbs (more on the left side) 4 days after transplantation. Urine output was 2 l/day. Creatinine stabilized between 1.4 and 1.7 mg/dl. There was no proteinuria and serum albumin was 3.2 g. Twenty four hour urine protein estimation done 2 days after the onset of symptoms was 300 mg/day. Echocardiography showed normal left ventricular

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function, mild pericardial effusion and there was no suggestion of pulmonary embolism. She remained euthyroid. Chest X-ray showed a massive left pleural effusion [Figure 1]. Computed tomography scan showed a massive left pleural effusion with complete collapse of left lung, moderate right pleural effusion and massive ascites. She was transfused two units of packed cells and 100 ml of 20% human albumin along with diuretics. She was maintained on a negative fluid balance. Anasarca persisted in spite of these measures. Urine output remained between 2 and 3 l/day and serum creatinine 10 days after transplantation was 1.4 mg/dl. Intercostal tube drainage of left pleural effusion was carried out. Pleural fluid was clear, transudative and pleural fluid adenosine deaminase was normal. Tacrolimus dose was reduced from 4.5 mg/day to 3.5 mg/day following which the trough level came down to 11.9 ng/ml. There was no improvement in fluid overload and right pleural effusion started worsening. A diagnosis of fluid retention secondary to tacrolimus was suspected and 6 days after the onset of fluid retention tacrolimus was stopped. She was started on sirolimus with a maintenance dose of 2 mg/day. Her trough sirolimus level was 6.54 ng/ml. Patient's edema started decreasing 48 h after stopping tacrolimus. Urine output improved to 3.5-4 l/day and creatinine stabilized around 1.4 mg/dl. Intercostal tube drainage was removed 3 days later and there was significant improvement in right pleural effusion and ascites also. Chest X-ray showed a complete resolution of pleural effusion [Figure 2]. Patient has not developed fluid retention during the 7 months of follow-up. At the last follow-up, patient's serum creatinine was 1.4 mg/dl and there was no proteinuria.

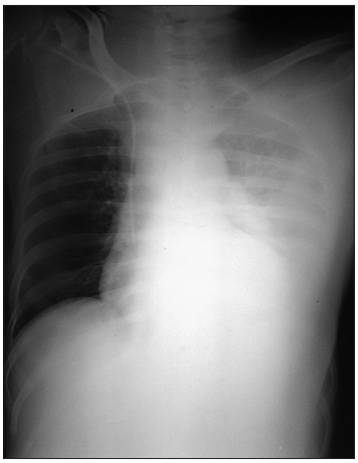

Figure 1: Chest X-ray on post-transplant day 5 showing a massive left pleural effusion

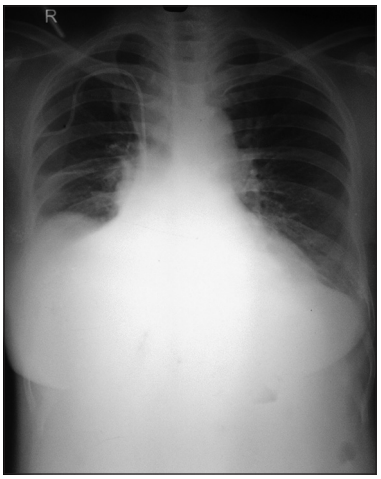

Figure 2: Chest X-ray 3 days after conversion to sirolimus

Discussion

Nephrotoxicity is the major limiting factor, with tacrolimus therapy often dictating the optimal dosage regime of the drug. Nephrotoxicity manifests in many ways such as oliguria, increased serum creatinine, hyperkalemia, fluid and salt retention.[1,2] Lowering the dosage of tacrolimus generally, but not always, reduces the toxic effects. However reduction in dosage is associated with risk of under immunosuppression and acute rejection. Fluid retention manifesting as peripheral edema, ascites and pleural effusion has been reported in 20-30% of patients receiving tacrolimus for liver transplant.[1,3] The incidence of peripheral edema and ascites was less than 15% and pleural effusion was 35% in the European FK 506 Multicenter Liver Study Group.[4] The incidence of fluid retention is similar for cyclosporine. There has not been any case report of significant pleural effusion, necessitating intercostal tube drainage, with tacrolimus. Most of the time fluid retention improves with dose reduction. However, our patient did not respond to reduction in dosage. Conversion from CNIs to sirolimus has been a standard practice for CNI nephrotoxicity. Hence in our patient, we considered the possibility of tacrolimus induced pleural effusion and shifted her to sirolimus and the patient showed immediate response.

In summary, we report a case of massive pleural effusion and ascites induced by tacrolimus in the immediate post-transplant period and which rapidly improved after conversion to sirolimus.

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