“De novo use of everolimus in renal transplant patients; Postoperative complications; everolimus toxicity masquerading AS pneumonia ? ”

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Introduction

- Renal transplant is now the best treatment for end-stage renal failure. To avoid rejection and prolong graft function, organ recipients need immunosuppressive therapy.
- The immunosuppressive combination most commonly used in *de novo* kidney transplantation comprises a calcineurin inhibitor (CNI), a mycophenolic acid derivative and steroids. This combination has reduced the incidence of acute rejection. However, a proportional improvement in long-term graft survival is still lacking.
- Minimisation or elimination of CNI while using m-TOR inhibitors like sirolimus or everolimus, which acts through mechanisms complementary to the CNIS, achieves a synergic immunosuppressive effect that is not nephrotoxic.
- This strategy allows for the reduction of CNIS during the early post-transplant period along with other advantages like reduction of tumour growth, reduction of viral infection etc.

Objective

- Different clinical trials support the use of everolimus as a standard immunosuppressive drug associated with reduced exposure to calcineurin inhibitors in renal transplant patients. Hence here we present a case of de novo use of everolimus in our patient and its 3 months outcome to support this practice.

Case presentation

- Our patient is 33 -years- old male with chronic kidney disease with graft dysfunction(first renal transplant in 2017) on maintenance hemodialysis who underwent a deceased donor renal transplant in October 2023 (ABOCompatible second transplant). Our patient was started with triple immunosuppressive drugs tacrolimus, mycophenolate mofetil and corticosteroid as per our institute protocol. Postoperatively patient underwent acute graft rejection. Considering humoral rejection patient underwent plasmapheresis and was given injection rituximab in post - operative period .
- I/V/O decreasing CNI exposure and to salvage graft function we added m-TOR inhibitor (Tab everolimus 0.5 mg BD) and discharged the patient on quadruple immunosuppressive drug regimen with creatinine 1.92 mg/dl.
- On follow up patient had stable renal graft function.

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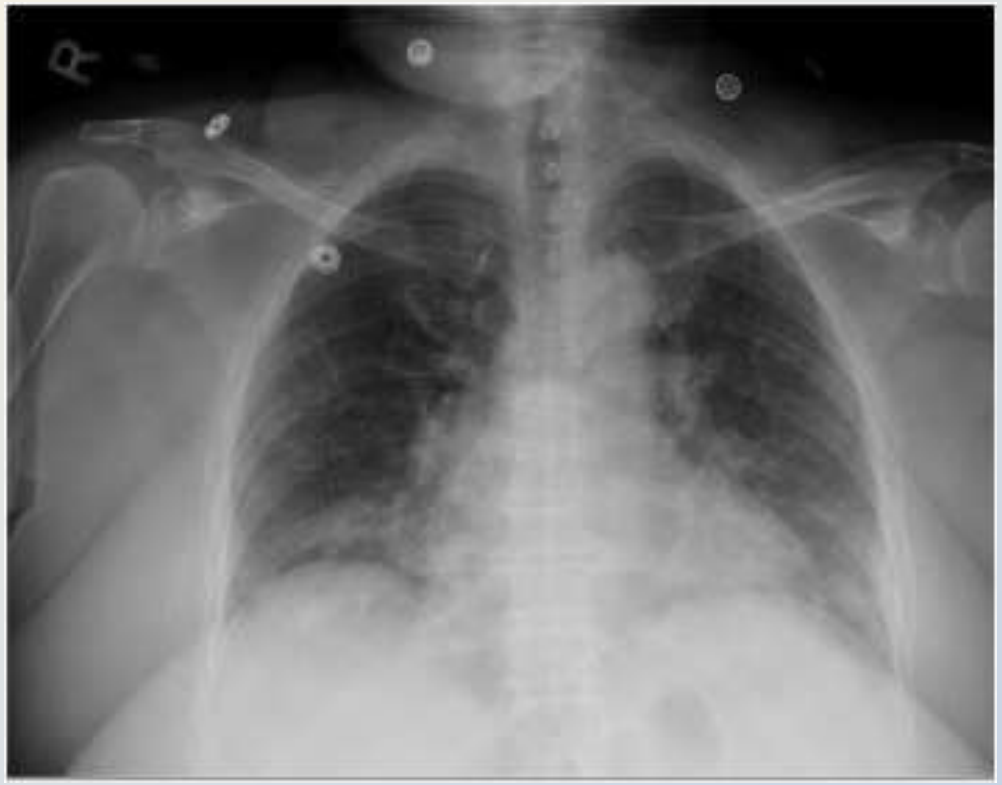
- Post-operatively (after 2 months of transplant) patient was admitted with fever, breathlessness and cough. On physical examination, he had a temperature of 100.8 F, initial oxygen saturation was 94% on room air, blood pressure of 130/80 mm hg and heart rate of 72 /min. Chest auscultation revealed diminished breath sounds in the basal area bilaterally. The rest of the physical examination was unremarkable. Along with this patient also developed c/o abdominal pain hence CT abdomen was done s/o lymphocele of around 220 cc along the left pelvic sidewall. (It was same as the previous study). Patient had a history of hospitalization with similar complaints during last 2 months also.

- In the setting of non-resolving symptoms, persistent lymphocele and negative diagnostic workup, drug-induced interstitial pneumonitis was considered. The association of everolimus with interstitial pneumonitis has been described in the literature, therefore everolimus was discontinued as a therapeutic intervention and patient was managed on triple immunosuppressants (T+P+M). (Investigation as follows)

- His symptoms gradually improved and at 3 months follow up, he had complete resolution of clinical symptoms along with stable graft function at present.



Chest x ray showing patchy bibasilar interstitial infiltrates.

No.	Lab Test	Value
1	Complete Blood Count	8.9/4600/22500
2	S. Creatinine Electrolytes	2.55 mg/dl Na 135.8/ K 3.9/ Bicarb 17.3
3	Urine, Blood and Sputum culture	Negative for growth
4	Everolimus level	7 ng/ml

Conclusion

- The exact pathogenesis of the lung toxicity cause by m-TOR inhibitors is not clear. A proposed mechanism includes interaction with the STAT1 (signal transducer and activator of transcription 1) gene, which may amplify cellular apoptosis and can increase lung injury.
- Clinical presentation includes cough, shortness of breath, fever and hypoxemic respiratory failure.
- Radiographic patterns vary from ground glass infiltrates to diffuse interstitial infiltrates. Treatment of everolimus induced pneumonitis is early discontinuation of the drug.
- The patient in our case had normal levels of everolimus. Our case highlights a rare case of interstitial pneumonitis associated with normal levels of everolimus in a renal transplant patient