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## Everolimus induced pulmonary thromboembolism after kidney transplantation; a case report

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### ABSTRACT

Choice of maintenance immunosuppressive therapy after renal transplantation is important for graft survival. However, complication may also occur. Venous thromboembolic event with the mTOR inhibitor (mTORi) everolimus is a rare but life-threatening complication. Here we describe a renal transplant recipient who developed pulmonary thromboembolism.

*Keywords:* Renal transplant, Everolimus, Pulmonary thromboembolisms

### *Implication for health policy/practice/research/medical education:*

Paying attention to the major side effects of immunosuppressive drugs can be effective in selecting and preventing bad events.

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### Introduction

During maintenance, immunosuppressive therapy after renal transplantation the occurrence of major complications can affect the graft survival. One of these rare but important complications is venous thromboembolic events with the mTOR inhibitor (mTORi) everolimus. Here we describe a renal transplant recipient who developed pulmonary thromboembolism (1).

### Case Presentation

A 48-year-old male presented with right lower extremity edema associated with dyspnea, his past medical history was, kidney transplantation since 18 years ago from a deceased donor and chronic gout since 10 years ago. On admission, his vital signs were as follows: PR = 98/min, RR=20/min, BP=120/85 mm Hg, T 37.2C. Rales and rhonchus on lung auscultation were noted and his heart sounds were normal except for tachycardia and II/VI murmur on mitral valve. Jugular venous pressure was normal and in abdominal examination had no organomegaly. Right lower extremity edema was noted. All pulses were unremarkable. His drug history was everolimus (Certican) 0.75 mg twice daily, tacrolimus (Prograf) 4 mg/d, prednisolone 10 mg daily.

Lab data revealed serum creatinine = 2.9 mg/dL, uric acid = 7.8 mg/dL, Hg = 5 g/dL, WBC =  $4.8 \times 10^9/L$ , PLT =  $100 \times 10^9/L$ . Viral serology for HBV, HCV, BKV, CMV was negative. Color Doppler revealed deep vein thrombosis on popliteal and femoral veins.

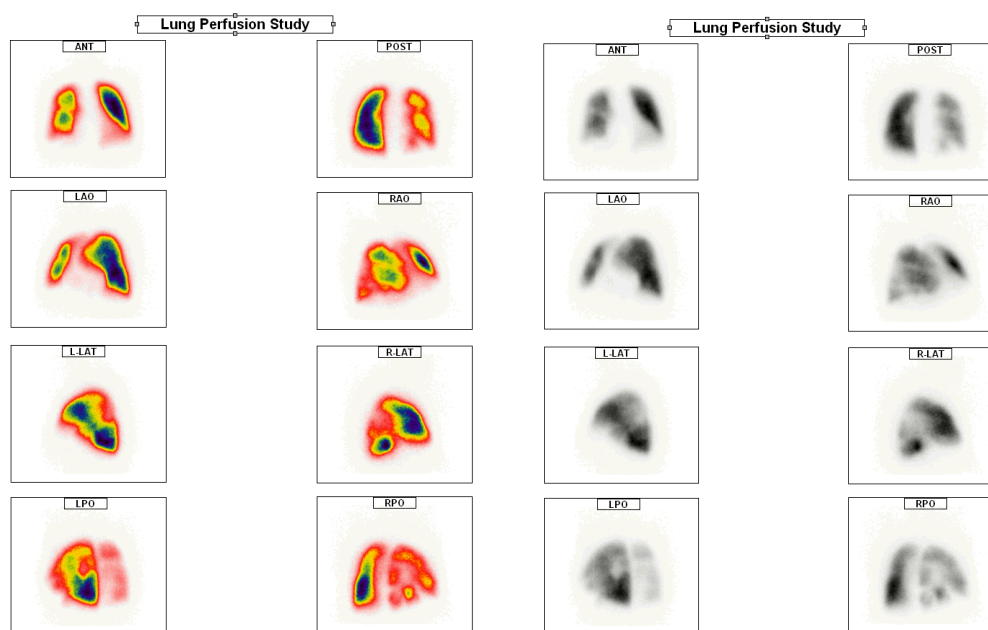
He underwent lung perfusion scan by Tc-MAA and the image showed multiple segmental and sub-segmental perfusion defects in the right lung (Figure 1).

For evaluation of the PTE etiology, we performed pro-coagulant studies including anticardiolipin IgG and IgM; results were 1.7 GPL (immunoglobulin G [IgG] phospholipid units) and 2.3 MPL (immunoglobulin M [IgM] phospholipid units) respectively, indicating normal ranges. Protein C and S levels were 72 IU/dL and 134 IU/dL respectively which were in the normal ranges. The serum levels for antiphospholipid IgM and IgG were negative, 1.3 APL and 3.7 APL respectively, and antithrombin activities 96% (normal range 80-130%).

The patient was treated with anticoagulant therapies and IVC filter inserted during hospitalization.

We found that the only reason for his PTE event was immunosuppressive medication everolimus (Certican). The mTOR inhibitor was discontinued and the patient was discharged in a good condition.

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**Figure 1.** Lung perfusion scintigraphy by  $^{99m}\text{Tc}$ -MAA perfusion- multiple segmental and sub segmental perfusion defects in the right lung.

## Discussion

The modality of choice for end-stage kidney disease is renal transplantation. Since novel immunosuppression emergence, the overall survival of patients and graft are increasing significantly. Despite improvement in patient's survival, its complications such as infection, malignancy, bone disease, and cardiovascular disease remains during years after transplantation. Patient's quality of life has been changed because of these unwanted complications. Calcineurin inhibitor (CNI) based therapy is a routine immunosuppression treatment after kidney transplantation but in some patients the adverse effect of these agents on renal function are severe and sometimes is irreversible (1). Combination of an mTOR inhibitor with calcineurin inhibitor for decreasing the CNI dosage is the best way for preserving the graft function and reducing the CNI nephrotoxicity. From 1999 sirolimus – a mTOR inhibitor – approved by Food and Drug Administration for the prevention of allograft rejection after kidney transplantation (2) in order to decrease acute rejections and increased graft survival. One of the main complication of these drugs is a significantly increased risk of venous thromboembolism (VTE), although the occurrence of VTE is high immediately after lung, kidney, and liver transplantation (3). The existence of PTE 18 years after kidney transplantation is rare. In our patient, we excluded the major causes of VTE (4) and our patient did not have recent major surgery or trauma, sedentary life or prolonged bed rest, we ruled out malignancy, thrombophilia. We concluded that mTOR inhibitor (Certican) was the cause of his VTE event.

## Conclusion

Procoagulant state associated with everolimus can cause VTE events and nephrologists should be aware of this complication.

## Authors' contribution

FS was the main investigator of the study. MHF revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

## Conflicts of interest

The authors declare that they have no competing interests.

## Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient gave informed consent for publication as a case report.

## Funding/Support

None.

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