Tacrolimus-induced near-fatal interstitial pneumonitis and ARDS in a case of liver transplantation

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Introduction:

Tacrolimus(TAC) is an immunosuppressant medication usually given after organ transplants which were approved in 1994. It is also used as a disease-modifying antirheumatic drug (DMARD) for the treatment of several rheumatologic diseases. TAC is well known to cause hypertension, diabetes mellitus, seizure, confusion, kidney problems however, only a few cases of severe lung injury related to TAC administration have been reported in the current literature.

Here, we describe a case of interstitial pneumonitis and near-fatal acute respiratory distress syndrome (ARDS) case related to TAC toxicity.

Case Presentation:

The patient is a 58-year-old Hispanic male with a past medical history of liver cirrhosis, chronic hepatitis C infection, liver transplantation in 1999, diabetes mellitus type 2, chronic kidney disease stage 4, hypertension, and hypothyroidism was admitted for altered mental status, fever and respiratory distress. The patient was being on treatment with TAC 1 mg twice a day for liver transplantation. Chest X-ray showed diffuse bilateral infiltrates suspicious for pneumonia. The patient was intubated due to acute hypoxic respiratory failure and antibiotherapy with Azytromycin 500 mg, Ceftriaxone 2 gram, and Zyvox 3.375 gram twice a day treatment initiated. Urine legionella and streptococcus antigen were negative. In the meanwhile patient also has developed thrombocytopenia and acute kidney injury with leukocytosis and anemia. Liver enzymes were normal, peripheral blood smear did not show schistocyte to suggest acute hemolysis and Thrombotic Thrombocytopenic Purpura (TTP) was ruled out. The patient was on TAC treatment for a long time then had stopped in July 2018 and restarted it a few months ago.

High-resolution CT of the chest without contrast revealed new extensive bilateral ground-glass and consolidative opacification compatible with multifocal pneumonia or severe ARDS with FiO2/PaO2 78. Due to worsening of respiratory failure and rising of LDH from 103 U/L to 1590 U/L, we started Bactrim treatment for possible Pneumocystis Pneumonia (PCP), later on, PCP was ruled out by bronchoscopy and Fungitell Glucan Assay test which was 32 pg/mL (Normal<80). Bronchoalveolar (BAL) cytology and culture were negative. All the blood culture samples were negative. The patient developed oliguric acute tubular necrosis and non-anion gap metabolic acidosis compatible with TAC induced nephropathy, treated with 3 sessions of hemodialysis. Blood pressure was well controlled with amlodipine 10 mg daily, hydralazine 50 mg three times a day and Lopressor 50 mg twice a day. Losartan was discontinued due to the acute worsening of kidney function. Despite the aggressive treatment of ARDS with mechanical ventilatory support and antibiotherapies, his respiratory status couldn't improve. On the day of twelve of admission, the TAC level was at the therapeutic level which was 4.2 ng/mL (Normal:2-20). TAC was discontinued due to possible TAC-induced interstitial pneumonitis and ARDS and the treatment with 60 mg intravenous methylprednisolone twice a day treatment initiated. Respiratory status dramatically improved within a few days, we were able to successfully extubate the patient. After

the day of eighteen, we switched intravenous methylprednisolone to per-oral prednisone 30 mg daily treatment and tapered gradually within 10 days. On the day of twenty of admission, we were able to discharge the patient with a complete resolution. These findings suggested that TAC-induced lung injury is mainly reversible.

Discussion:

In conclusion, here we reported the case of TAC-induced severe ARDS and interstitial pneumonia presented with near-fatal respiratory failure. Until now, there have been only a few reports of TAC-induced severe lung injury. Considering the catastrophic complication of respiratory failure and reversibility of nature, it is important to consider the dose reduction or cessation of TAC if severe ARDS and interstitial pneumonitis are detected during the administration of this agent.