Pulmonary toxicity associated with sirolimus following kidney transplantation: computed tomography findings

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Dear Editor,

We read with great interest the letter by Calle et al. describing the case of a patient who underwent a kidney transplant and developed a pneumonitis caused by sirolimus. They related that there are, until now, only seven cases reported of recovery from pneumonitis caused by sirolimus.

We would like to describe the case of a 27-year-old woman with a two-year history of haemodialysis for end-stage renal disease underwent a haplo-identical, living kidney, donor transplantation. Following the procedure, she began immunosuppressive therapy with tacrolimus, mycophenolate mofetil, and steroid. Her renal function was stable and she was discharged with normal serum creatinine levels.

Two months after beginning immunosuppressive therapy she presented with diarrhoea of unknown aetiology. After recovery from the diarrhoea, the patient was discharged while using mycophenolate sodium and metronidazol. Six months later, she was admitted with another episode of diarrhoea and the tacrolymus was switched to sirolimus.

Ten months after initiation of the sirolimus treatment, the patient was admitted with fever, shortness of breath, and dehydration. Chest X-rays and high-resolution CT of the chest demonstrated bilateral areas of non-homogeneous air space consolidation, mainly in the left upper lobe and lower lobes (Figure 1A). Bronchoalveolar lavage revealed hypercellularity with lymphocytosis, and the microbiological evaluation was negative for bacteria, fungi, and viruses. Serological tests for cytomegalovirus were negative. The patient began an empirical, anti-infection treatment with intravenous azithromycin and ciprofloxacin, with no response. The fever persisted with antibiotic treatment and sirolimus was thought to be the cause of the symptoms. When sirolimus was switched to azathioprine symptoms improved within 10 days, and were resolved in 30 days. On the follow-up chest X-ray and high-resolution CT, 30 days after sirolimus discontinuation, the parenchymal abnormalities had improved, with accentuated reduction of the air-space consolidation pattern. There were persisting residual areas of bilateral ground-glass opacities on the high-resolution CT (Figure 1B).

Sirolimus (rapamycin) is a potent immunosuppressive drug that has been successfully used in solid organ transplant recipients as an alternative to calcineurin inhibitor therapy. The most common side effects associated with this drug are dose-dependent hyperlipidemia, and thrombocytopenia. Unlike calcineurin inhibitors, sirolimus does not induce acute or chronic nephrotoxicity. However, in very rare cases, patients treated with sirolimus may exhibit severe pulmonary toxicity.

The symptoms of pulmonary toxicity related to sirolimus are generally non-specific, and may include a dry cough, dyspnea, fatigue, and fever, frequently leading to the initial diagnosis of pulmonary infection. Some reports have described histopathological patterns as a result of sirolimus pulmonary toxicity, but these findings are usually non-specific, consisting of bronchiolitis obliterans with organizing pneumonia,

Figure 1. High-resolution CT at the level of the lower lobes (A) (obtained at the time of clinical presentation when respiratory symptoms were evident) demonstrates areas of non-homogeneous air space consolidation in the lower lobes, and mild ground-glass opacities. Follow-up scan (B), taken in the same plain as A, and 30 days after discontinuation of sirolimus, showed a reduction in the air-space consolidation pattern, with bilateral areas of residual ground-glass attenuation. The expiratory scans did not show air trapping.
interstitial pneumonitis, and non-necrotizing granulomas. For this reason, a lung biopsy is not essential, and the diagnosis of this condition must fulfill the following criteria: presence of lung disease on imaging tests, exclusion of pulmonary infection or other lung disease, and clinical improvement after drug withdrawal, independent of the pulmonary biopsy. All these criteria were fulfilled in the patient presented here, who showed significant imaging and clinical improvement after withdrawal of sirolimus.

Due to the increased use of sirolimus, radiologists interpreting imaging studies of transplant patients using this drug should be aware of the imaging features associated with this potentially treatable complication. Although some previous authors reported the use of CT, to our knowledge, there are no reports illustrating and discussing the high-resolution CT findings of pulmonary toxicity due to sirolimus.


Dear Editor,

Guillain-Barré syndrome (GBS) is the most frequent cause of acute polyneuropathy in adults. It manifests with progressive symmetrical motor weakness in the limbs and areflexia. Its most severe complication is acute respiratory failure, which has a mortality rate of 15 to 30% if it requires mechanical ventilation.

It may be associated with respiratory or gastrointestinal infection (cytomegalovirus [CMV], Campylobacter jejuni) in two thirds of all cases. It has been described in bone marrow transplants, but it is very rare in solid organ transplants. It has also been associated with neurotoxicity caused by calcineurin inhibitors. We present two cases of GBS in patients undergoing kidney transplants.

The first case is that of a woman who underwent a kidney transplant at age 22 with chronic renal failure (CRF) secondary to neurogenic bladder. She received steroids, tacrolimus and mycophenolate mofetil in addition to prophylactic treatment against CMV, hyperimmune gamma-globulin (recipient IgG negative/donor IgG positive). Evolution of renal function was excellent. Five weeks after the transplant, the patient became ill with CMV (severe leucopenia, hypertransaminasaemia, gastritis, AgP65 positive). She received intravenous gancyclovir during 15 days and made satisfactory progress. She was readmitted three weeks later due to progressive, symmetrical weakness of the lower limbs, paraesthesia and dysphagia, and in the next few hours she developed acute respiratory failure requiring mechanical ventilation.

The second case is that of a 62 year old man with unexplained chronic renal failure who underwent renal transplantation. He was treated with steroids, tacrolimus and mycophenolate mofetil. His renal function progressed very well. However, 2.5 months after the transplant he was admitted for severe paralysis of the lower limbs which quickly progressed to tetraparesis. His AgP65 was checked and found positive, and he was treated with IV gancyclovir during 18 days. He did not require mechanical ventilation, but did need prolonged physical therapy.

In both patients, the cerebrospinal fluid (CSF) and the electromyography offered a diagnosis of GBS (demyelinating sensory-motor polyneuropathy; CSF at normal pressure, proteins elevated, without pleocytosis).

The first patient received four cycles of plasmapheresis and five doses of hyperimmune gamma-globulin (0.4g/kg/day) and the second, five doses of hyperimmune gamma-globulin (0.4g/kg/day). The first transplant patient underwent a full recovery and was extubated after seven days. After eight years of follow-up, she remains asymptomatic and has no neurological consequences. Six months