

Neurotoxicity of Immunosuppressive Therapies in Heart Transplantation

Introduction:

Neurological complications are common after solid organ transplantation and are associated with significant morbidity. Neurotoxicity is a common and early complication related to immunosuppressive drugs, especially calcineurin inhibitors.

Case report:

Patient, female, 57 years old, with Chagas cardiomyopathy, was submitted to a heart transplant after two months hospitalized in INTERMACS 3. It was started immunosuppression regimen with corticosteroids, mycophenolate and tacrolimus.

The endomyocardial biopsy was performed 15 days after the heart transplant and a 2R result suggested a high dose of corticosteroid therapy for 3 days.

After 24 hours, the patient reported recent memory deficit and partial visual loss, but normal neurologic examination.

The findings were attributed to pulse therapy and the patient was placed in observation. She remained without clinical or laboratory abnormality of inflammatory markers, as well as the kidney and liver function. Serum levels of tacrolimus were in the therapeutic range. However, gradually it evolved with worsening of confusion state despite the gradual reduction of corticosteroids and early antipsychotic prescription. After 4 days of neurological symptoms onset, the evaluation of the neurological and psychiatric team was required. They reinforced the encephalopathy diagnosis. The CT and MRI performed and the normal cerebrospinal fluid were normal. Based on suspicion of neurotoxicity, we decided to conduct a therapeutic trial with the replacement of tacrolimus for cyclosporine. The patient presented partial neurological improvement in 24 and complete, in 48 hours. Still during the index hospitalization, a new pulse therapy was done. However, the patient did not present any neurological disorder, which reinforces the non-matching event with corticosteroids.

Summary:

The neurotoxicity associated with immunosuppressive drugs is the most common cause of neurological complication following solid organ transplantation.

Through a variety of mechanisms, calcineurin inhibitors can cause effects in central or peripheral nervous system with normal or supra-therapeutic levels. Symptoms such as tremors, visual impairment, headache and insomnia may occur. The toxic encephalopathy, PRES and seizures are more severe manifestations and can cause irreversible damage or death if not identified early.

Tests such as MRI assist in the diagnosis, however, the clinical suspicion is essential. Many diagnostics are done only based on drug therapeutic trial reduction or its replacement.