



Role of Tacrolimus in Return of Hand Function after Brachial Plexus Injury in a Lung Transplantation Patient: a Case Report

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Background

Tacrolimus (FK506) is a calcineurin inhibitor used for prevention of allograft rejection after solid organ transplantation (SOT).

The neuroregenerative properties of tacrolimus have received more attention in basic science animal studies.

Binding to the immunophilin, FK506-binding protein 52 (FKBP-52) receptor, is suggested to stimulate nerve regeneration.

FKPB-52 contains two binding domains, explaining the bimodal dose response of tacrolimus.

Only anecdotal data of two successful hand transplantations, treated with tacrolimus, demonstrated enhancement of axonal regeneration and sensation without confirmation by neurodiagnostic or clinical exams.

We report the functional outcomes of a patient with concomitant SOT and brachial plexus injury (BPI), treated with tacrolimus, with unusual recovery of hand function eighteen months after onset of the injury.

Case Presentation

The patient is a 46-year-old man diagnosed with interstitial lung disease and oxygen dependent idiopathic pulmonary fibrosis.

In November 2017, he underwent a successful bilateral pulmonary allotransplantation. Immediately following surgery, the patient described severe left arm and hand paralysis.

Complete loss of wrist function and intrinsic muscles of the left hand were reported, consistent with a complete lower trunk injury and partial middle trunk involvement, secondary to sternotomy.

The patient had diminished sensation over the ulnar aspect of the left elbow to hand with complete numbness in the C7-T1 distribution of his left hand, including digits II-V. No sudden onset of pain prior to the weakness was described.

No previous significant neurological or orthopedic problems of the left upper extremity or neck were reported.

Immunosuppressive Treatment

The patient was immunosuppressed with oral mycophenolate mofetil (MMF) 500 mg twice daily. After renal recovery, oral tacrolimus was commenced at 1.5 mg daily for his transplant.

Tacrolimus levels were closely followed to maintain trough levels between 6-10 ng/mL. Dose was maintained between 1.0 to 2.5 mg daily over 18 months.

Triple-drug immunosuppressive regiment (MMF, prednisone, tacrolimus) was maintained and he was treated with itraconazole to prevent invasive fungal infections post-lung transplantation. No severe side effects were reported.

Investigations

After 18 months, electromyogram reported reduced left median and ulnar compound muscle action potentials with slow nerve conduction velocities.

The left ulnar sensory response was reported to be absent. The left medial antebrachial cutaneous sensory nerve action potential amplitudes were reduced compared to the right side.

Magnetic resonance imaging (MRI) of the left brachial plexus reported moderate diffuse T2 hyperintensity of the lower elements of the brachial plexus.

Physical Examination

Eighteen months after onset, a positive Horner syndrome and neuropathic pain over the C8-T1 distribution were reported.

Clawing of his 4th and 5th left digits and a positive Wartenberg sign were reported. Tip to tip pinch was difficult. Sensory examination reported dense sensory loss in the 4th and 5th digits of his left hand with two point sensation of 10 mm.

Discussion

There are no previous cases reported with similar improvement of hand function after BPI, confirmed with physical examination over time.

Due to drug interactions, the patient's daily tacrolimus dose was low, but in the target therapeutic range for immunosuppression.

The neuroregenerative effects of tacrolimus are proven to be dose-dependent, with doses that are commonly sub-immunosuppressive.

This unique case report objectively demonstrates functional recovery, including grip strength, after clinically unrecoverable lower trunk BPI, most likely as a result of tacrolimus.

Table 1: Muscle Strength, 18 Months after Onset

Upper and middle trunk (C7), except for the muscles listed below:	mBMRC grade 5 (at onset grade 5)	All radial innervated muscles	mBMRC grade 5 (at onset grade 5)
Flexor digitorum profundus of digit II-IV, flexor digitorum superficialis	mBMRC grade 3 (at onset grade 0)	Besides the flexor carpi ulnaris, other distal ulnar innervated muscles reported weak, including the muscles listed below:	mBMRC grade 5 (at onset grade 5)
Flexor pollicis longus	mBMRC grade 3+ (at onset grade 0)	Adductor pollicis, dorsal interosseous I-IV	mBMRC grade 1 (at onset grade 0)
Flexor pollicis brevis, lumbricals I, II	mBMRC grade 3- (at onset grade 0)	Abductor digiti minimi, opponens digiti minimi, proximal interosseous I-III, lumbricals III, IV	mBMRC grade 0 (at onset grade 0)

Objective outcome measurements of muscle strength were assessed using the modified British Medical Research Council (mBMRC) motor grading.