

## Clinical Image

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# A case of severe calcineurin inhibitor pain syndrome rescued with LCP-Tacrolimus

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### Description

We report a 30-year old male patient with a severe Calcineurin Inhibitor Pain Syndrome (CIPS) after deceased donor transplantation. The patient was transplanted on a Cyclosporine A-based immunosuppressive regimen. Three months after transplantation, he presented with subacute and debilitating oligo-articular pain projected to the metatarsal bones and knees of both legs. Clinical examination and blood tests didn't reveal particular abnormalities. Magnetic resonance imaging revealed diffuse bone marrow edema, highly suggestive for CIPS (Figure 1) [1]. In addition to intensive physiotherapy, the immunosuppressive regimen was changed to Extended-Release (ER) Tacrolimus (Advagraf®) without significant improvement. Consequently, the treatment was once again modified to LCP-Tacrolimus (Envarsus®) with progressive and substantial clinical improvement of CIPS.

### Discussion

CNIs represents the cornerstone in the immunosuppressive regimen after solid organ transplantation. Allograft and patient outcomes are greatly improved since their introduction, although they are burdened with many and often treatment limiting side effects [2]. The most common are nephrotoxicity, hypertension, diabetes mellitus, electrolytes abnormalities and

neurotoxicity (in particular tremors). CIPS is a rare and severe CNI-associated complication affecting the patient's quality of life [3]. Estimated frequency is 1.5-14% [1] and the pathogenesis is not fully elucidated. It has been postulated that CNIs are disturb bone microperfusion and permeability leading to intraosseous vasoconstriction [4]. The diagnosis is based on the exclusion of other severe causes of pain (insufficiency fracture, osteonecrosis, reflex sympathetic dystrophy, ischemic pain). Although there is no specific treatment, the prognosis is usually good. Calcium channel blockers and GABA-analogs have been tried [3]. Reduction of CNI exposition with gradual conversion to alterantive regimens be another useful strategy [4]. Recently, two novel Tacrolimus formulations, namely ER-Tacrolimus and LCP-Tacrolimus have been introduced [5]. Compared to immediate release-Tacrolimus (Prograf®), these substances have a longer half-live and allow once-daily dosing [6]. Therefore ER-Tacrolimus could reduce side effects, although definitive proof for this hypothesis remains elusive. At similar exposure, LCP-Tacrolimus provokes a delayed and reduced Tacrolimus-peak concentration. Langone et al. [6] compared neurotoxic side effects of ER- and LCP-Tacrolimus in a cross-over design and showed reduced intensity of tremor in the latter group. Here we report for the first time a case with superior control of severe CIPS with LCP-Tacrolimus.



**Figure 1:** (A) Conventional pa radiograph of right forefoot. Puctum maximum of pain was head of metatarsal bone I and V. (B,C) T2 weighed MRI of right forefoot in sagittal and coronal axis revealing medullary edema of affected bones. Inlays show respective scout images.

### Learning points and take home messages

- CIPS is a rare, severe and self-limiting complication in patients with solid organ transplantation under CNI-based regimens.
- Conversion of CNI-treatment LCP-Tacrolimus may be beneficial in patients with severe CIPS who need to remain on CNI-treatment.
- The clinical improvement may be attributed to the lower Tacrolimus-peak concentration of LCP-formulation.

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