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# Sirolimus-associated chronic pyogenic periungual infection

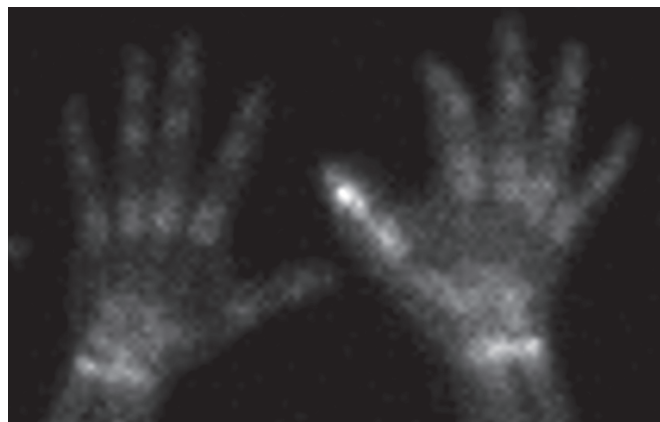
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**Figure 1** | Photograph of the patient's left thumb. Left panel: Periungual infection, suppurative ulceration, and diffuse swelling of the left thumb at presentation. Right panel: Six weeks after surgical wound debridement, nail removal, and withdrawal of sirolimus. Swelling and diffuse erythema have resolved, and regrowth of nail and (pink) tissue is demonstrated.



**Figure 2** | Gallium scan, 48-hour view of both hands, demonstrating increased signal activity of the left thumb with a focus in the distal phalanx, indicative of soft tissue cellulitis or tenosynovitis.

An 18-year-old man presented to the emergency room with fever and chills of 1 day's duration. He complained of increasing pain and swelling of his left thumb and part of the hand. He had received a deceased-donor kidney 3 years before this presentation. There was a patent arteriovenous fistula in his left forearm, which had been previously used for hemodialysis access. The patient's maintenance immunosuppression consisted of 5 mg tacrolimus twice a day, and 7.5 mg prednisone and 5 mg sirolimus daily. He had stable graft function with a serum creatinine of 115  $\mu$ mol per liter (1.3 mg per dl). On examination, his left hand was diffusely swollen and the first digit warm, erythematous, and exquisitely tender. A periungual suppurative ulceration was evident (Figure 1, left panel), and the patient was unable to flex or extend his thumb. He had been diagnosed with paronychia several months earlier and had been treated unsuccessfully with three courses of oral antibiotics until 2 weeks before presentation. A culture of the drained pus from the periungual ulcer grew 3+ *Staphylococcus aureus*, 3+ *Peptostreptococcus anaerobius*, and 1+ *Streptococcus milleri*. It was negative for acid-fast bacilli and herpes simplex virus. Serum C-reactive protein (18 mg per liter) and sedimentation rate (20 mm per hour) were moderately elevated. A bone

scan revealed increased signal activity of the left first digit with a focus in the distal phalanx, indicative of soft tissue cellulitis or tenosynovitis (Figure 2). A radiograph demonstrated an early periosteal reaction of the anterolateral aspect of the distal shaft of the proximal phalanx, which was corroborated by a second radiograph 2 weeks later. Surgical debridement of the thumb was performed, and treatment with intravenous antibiotics (ticarcillin-clavulanate) was initiated. Sirolimus was weaned and replaced by mycophenolate mofetil. The transplant function remained stable. The erythema and swelling of the patient's thumb gradually improved over 1–2 weeks as the ulcerations healed (Figure 1, right panel), although pain resolution appeared to be more protracted. After 4 weeks, antibiotic treatment was switched to oral moxifloxacin with continued dressings with silver-coated mesh.

Sirolimus is known to have several adverse cutaneous effects, including onycholysis and periungual disease, mainly pyogenic granulomas, presumably by reducing plasma and tissue levels of epidermal and vascular growth factors, which may compromise normal tissue healing. A similar mechanism may have contributed to the protracted course of the infection and the lack of response to previous antibiotic treatments.