Charcot neuroarthropathy (CN) is considered a major complication in diabetes mellitus (DM) (1), and it is estimated that 1% of diabetic patients may develop this complication (2). CN typically features two phases: (a) an acute active phase and (b) a stable chronic phase. The acute phase is characterized by erythema and unilateral oedema. A temperature difference of at least 2°C more is detected in the feet (1). The local inflammatory response is considered as the main characteristic expression of the acute phase (3).

Simultaneous kidney–pancreas transplantation (SKPT) is one of the most effective therapies for patients with type 1 DM and end-stage diabetic nephropathy (4–6). Some cases with a Charcot-modified clinical presentation during the postoperative convalescence period after SKPT have been described (7), and our goal of this article was to report on two case presentations of neuropathic arthropathy with rapid progression in the short term after SKPT.

Case report 1
The first patient was a 31-year-old woman with a type 1 DM diagnosed at the age of 7. Patient’s medical history consisted of hepatitis C (treated with pegylated interferon) in February 2010, diabetic retinopathy (amaurosis of the right eye; loss of visual acuity in the left eye), recurrent urinary tract infections, amputations from the third to the fifth rays of the right foot, and end-stage renal disease (ESRD) on haemodialysis leading to SKPT in April 2010. Post-transplant relevant clinical analytical data showed glycaemic levels of 106–136 mg % and creatinine levels of 1.4–2.1 mg % while the most routinely used post-transplant immunosuppressants included mycophenolate mofetil (1.4–1.5 g/day), tacrolimus (1–3 mg/day, adjusted according to blood tacrolimus levels), and glucocorticoids such as methylprednisolone for the last 8 months. During the post-transplant follow-up, the patient did not require insulin, had an episode of acute rejection, and was treated with metabolic control, diet, and with a transient correction of immunosuppressants.

The patient was being managed with topical negative pressure wound therapy treatment for ulcers in her right heel (posterior, non-weight bearing area) when she had a low-energy trauma in the lateral aspect of her heel due to a fall. At that time, plain radiographs (November
2009) did not reveal any structural bone changes (Fig. 1). One month later, due to persistent pain during the heel contact phase, a magnetic resonance imaging (MRI) was performed, which showed a complete short oblique fracture from the medial aspect of the calcaneus without displacement associated with bone oedema (Fig. 2). The topography of neuroarthropathy involvement was type 5 according to the Sanders and Frykberg classification (8).

Non-weight bearing and immobilization with a plaster cast for 8 weeks was then initiated and followed with new plain radiographs and computed tomography scan after the final cast removal. The studies revealed that reabsorption patterns and bone collapse in the anterior and medial tuberosity of the calcaneus as well as proximal displacement of the posterior tuberosity were evidenced due to traction of the Achilles tendon (Figs. 3 and 4). Stabilisation with rigid osteosynthesis using 3.5-mm screws and a T-shaped plate was then performed. Focus consolidation was observed 3 months after the surgery (Figs. 5 and 6).

**Case report 2**
The second patient was a 32-year-old woman with a medical history of type 1 DM, sedentarism, hypertension, ESRD without haemodialysis since January 1993, retinopathy and retinal detachment in the right eye, renal
and perinephric abscess (2002, left perirenal abscess requiring surgical treatment). Also presents antecedent of SKPT (3 years and 10 months ago) and the donor was an 18-year-old female, who died due to traumatic brain injury after a motor vehicle accident with negative cytomegalovirus serostatus and blood group O+. The patient also underwent a laparoscopic cholecystectomy 6 months after her SKPT for gallbladder lithiasis.

Post-transplant relevant clinical analytical data showed glycaemic levels of 83–85 mg % and creatinine levels of 0.6–0.8 mg %, while the most routinely post-transplant immunosuppressants included mycophenolate mofetil (500 mg–2 g/day), tacrolimus (2–6 mg/day, adjusted according to blood tacrolimus levels), and glucocorticoids such as methylprednisolone for the last 8 months.

In July 2008, the patient consulted our service for pain and deformity in her left foot. On physical examination, a widening of the hindfoot and an apparent length discrepancy due to shortening without any signs of local swelling (neither hyperthermia nor erythema) were seen. The patient also had paraesthesia sensations and preserved sensitivity in the Semmes–Weinstein monofilament testing. The patient stated that she had not had local swelling for the last 6 months but confirmed significant progression of both pain and deformity. Vascular examination using arterial echo Doppler of the lower limbs evidenced the following: mild obstruction (<20%) of the common femoral artery and bilateral superficial artery due to the presence of fibre-lipid plaques. The popliteal, posterior, and anterior tibial arteries depicted smooth walls with normal flow. Bilateral ankle/brachial index was >1 (within normal values).

The imaging protocol included plain radiographs and MRI that revealed complete reabsorption of the head and neck of the talus, talar body collapse and displacement in plantar flexion (type 4 Sanders and Frykberg classification) (8), and partial reabsorption of the navicular and cuboid (Figs. 7 and 8). Stabilisation was performed by osteosynthesis using 4.5- and 6.5-mm double-threaded screws (Fig. 9). The outcome was unfavourable due to mechanical assembly failure and reabsorption progression (Figs. 10 and 11). Revisional surgery was then
carried out with tibio-C1 talar-calcanal arthrodesis by retrograde intramedullary nailing (Panta†) (Fig. 12).

Discussion

A higher incidence of diabetic foot pathology has been observed in patients with concomitant renal disease, and the outcome is in general suboptimal due to the complications (amputations, mortality) (9). Several specific risk factors in all renal disease categories have been described including ESRD not requiring transplantation (stages 3 and 4) (10); renal disease managed with continuous ambulatory peritoneal dialysis (11); and renal disease managed with kidney transplant and renal disease in patients with type I DM managed with SKPT (12, 13).

In the cases studied, only the stable chronic stage of CN (1) was identified clearly. The pathogenesis of such an evolutive pattern is still unknown; at present the hypothesis of the role of immunosuppression still prevails, according to some authors (7). In both cases, destruction was ‘rapid and fulminant, without a leading infectious pattern’ (14), with well-defined disintegration models (15, 16). According to Caldara et al., for patients already affected by severe diabetic complications, tight metabolic control achieved with pancreas transplantation does not prevent the development of CN (17).

The MRI is a significant diagnostic implement when plain radiographs are negative and in the presence of a clinical suspicion of CN. However, MRI demonstrated bone marrow oedema in midfoot and hindfoot areas in 30% of the patients with neuropathic diabetic ulceration and did not predict future CN or osteomyelitis; this type of bone marrow oedema was more common in ESRD (7, 18). According to Valabhji and our brief experience, clinicians should be aware that Charcot can present post-transplantation without the cardinal clinical signs but still lead to deformity (7).

Patients undergoing SKPT are at risk for the development of CN de novo as a comorbidity. The dose of glucocorticoids is the main pathogenic factor, and this correlation could be observed in this series (4). According to Rangel et al., foot examination and orthopaedic assessment should be routinely performed even more when risk factors are identified. Immunosuppression regimen based on glucocorticoid minimisation or avoidance should also be considered (4).

The cases described use the ‘foot-at-risk’ concept characterised by baseline comorbidities (DM, severe peripheral vasculopathy, prolonged steroid therapy, etc.). The clinical substrate may condition severe destructive lesions, and good practices include systematic follow-up. Based on the cases described, SKPT is one more entity that might lead to neurogenic arthropathy.

Acknowledgements

The authors thank Claudia Tarazona and Gabriela Franke for their assistance in translating this article.

Conflict of interest and funding

The authors have not received any funding or benefits from the industry to conduct this study.
References

1. Petrova NL, Edmonds ME. Charcot neuro-osteoarthropathy – current standards. Diabetes Metab Res Rev 2008; 24(Suppl 1): S58–61.
2. Frykberg RG, Belczyk R. Epidemiology of the Charcot foot. Clin Pediatr Med Surg 2008; 25: 17–28.
3. Jeffcoate WJ. Charcot neuro-osteoarthropathy. Diabetes Metab Res Rev 2008; 24(Suppl 1): S62–5.
4. Rangel E´ B, Sa´ JR, Gomes SA, Carvalho AB, Melaragno CS, Gonzalez AM, et al. Charcot neuroarthropathy after simulta-
neous pancreas-kidney transplant. Transplantation 2012; 94: 642–5.
5. Drognitz O, Benz S, Pfeffer F, Fischer C, Makowiec F, Schareck W, et al. Long-term follow-up of 78 simultaneous pancreas-kidney transplants at a single-center institution in Europe. Transplantation 2004; 78: 1802–8.
6. Smets YF, Westendorp RG, van der Pijl JW, de Charro FT, Ringers J, de Fijter JW, et al. Effect of simultaneous pancreas-kidney transplantation on mortality of patients with type-I diabetes mellitus and end-stage renal failure. Lancet 1999; 353: 1915–9.
7. Valabhji J. Immunosuppression therapy posttransplantation can be associated with a different clinical phenotype for diabetic Charcot foot neuroarthropathy. Diabetes Care 2011; 34: e135.
8. Sanders LJ, Mrdjenovich D. Diabetic neuropathic osteoarthropathy: an analysis of 28 cases. In: Frykberg RG, ed. The high risk foot in diabetes mellitus. New York: Churchill Livingstone; 1991.
9. Ndip A, Lavery LA, Boulton AJ. Diabetic foot disease in people with advanced nephropathy and those on renal dialysis. Curr Diab Rep 2010; 10: 283–90.
10. Margolis DJ, Hofstad O, Feldman Hl. Association between renal failure and foot ulcer or lower-extremity amputation in patients with diabetes. Diabetes Care 2008; 31: 1331–6.
11. Ndip A, Rutten MK, Vileikyte L, Vardhan A, Asari A, Jameel M, et al. Dialysis treatment is an independent risk factor for foot ulceration in patients with diabetes and stage 4 or 5 chronic kidney disease. Diabetes Care 2010; 33: 1811–6.
12. Matricali GA, Bammens B, Kuypers D, Flour M, Mathieu C. High rate of Charcot foot attacks early after simultaneous pancreas-kidney transplantation. Transplantation 2007; 83: 245–6.
13. Valabhji J. Foot problems in patients with diabetes and chronic kidney disease. J Ren Care 2012; 38(Suppl 1): 99–108.
14. Charosky C, Volij W, Gallardo H. Demolicion fulminante del pie neuropático. Sociedad Argentina de Medicina y Cirugía del Pie 1989; 1: 27–9.
15. Harris JR, Brand PW. Patterns of disintegration of the tarsus in the anaesthetic foot. J Bone Joint Surg Br 1966; 48: 4–16.
16. Mamano RO, Zordán LA. Modelos de desintegración del pie neuropático. Sociedad Argentina de Medicina y Cirugía del Pie 1988; 1: 103–6.
17. Caldara R, Grispigni C, La Rocca E, Maffi P, Orsenigo E, Socci C, et al. Acute Charcot’s arthropathy despite 11 years of normoglycemia after successful kidney and pancreas transplantation. Diabetes Care 2001; 24: 1690.
18. Thorning C, Gedroyc WM, Tyler PA, Dick EA, Hui E, Valabhji J. Midfoot and hindfoot bone marrow edema identified by magnetic resonance imaging in feet of subjects with diabetes and neuropathic ulceration is common but of unknown clinical significance. Diabetes Care 2010; 33: 1602–3.

*Jorge Javier del Vecchio
Foot and Ankle Section
Department of Orthopaedic and Traumatology
Favaloro Foundation
146 Solis Street
CABA 1078
Argentina
Email: javierdv@mac.com