Abstract

Objective

To report a case of a man who developed bilateral Charcot neuroarthropathic feet 11 years after a simultaneous pancreas kidney (SPK) transplantation for type 1 diabetes following which he had remained normoglycaemic

Methods

Retrospective review of case notes and serial imaging

Results

We describe the case of a man who had developed dense peripheral diabetic neuropathy due to poor glycaemic control. His biochemical markers of diabetes all normalised following SPK transplantation, and he was discharged by his primary and secondary care diabetes services. 11 years later he developed Charcot neuropathy in one foot and within a month, the other foot as well.

Conclusion

Individuals with diabetes who had pre-operative end organ diabetes related damage who biochemically into remission after SPK transplantation should never be discharged from specialist diabetes services and need continued education about foot care

Keywords: Diabetes; Charcot neuroarthopathy; simultaneous kidney pancreas transplant

Abbreviations

CN – Charcot neuroarthopathy

HbA1c - glycated haemoglobin

MR – Magnetic resonance

SPK - Simultaneous pancreas kidney

Introduction

Charcot neuroarthopathy (CN) is an uncommon but devastating complication that occurs in approximately 1 in 200 people with diabetes, but can result from any cause of peripheral neuropathy (1,2). Despite its disabling impact on patients, it is often overlooked, leading to a delay in diagnosis and subsequent mismanagement. A timely diagnosis is key to the management of CN (3). Once a diagnosis is established, initial treatment focuses on off-loading the affected limb to protect the skeleton until remission is achieved.

Simultaneous pancreas and kidney (SPK) transplantation is currently one of the management options for people with type 1 diabetes with end stage renal failure. Results have shown patients have a better quality or life and longer life expectancy. In individuals who may have had long standing poorly controlled diabetes, end organ complications may have occurred prior to SPK transplantation. However, after transplantation eye, gut, nerve and vascular disease have been shown to stabilise or improve as glycaemic control returns to the non-diabetic range (4).

One diabetes related complication that does not usually improve, however, is peripheral neuropathy. Charcot neuroarthopathy has been recognized to occur following SPK transplantation, but usually within the first post-operative year (5-8). There are reports of CN occurring several years after SPK transplantation (9). We present a case of bilateral simultaneous CN developing 11 years following SPK transplantation in a patient with diabetes with pre-existing peripheral neuropathy. To

our knowledge, this is the first documentation of a bilateral Charcot late occurrence, after SPK transplantation.

Case Report

A 55 year old self-employed builder had been diagnosed with type 1 diabetes mellitus aged 15, and was managed with insulin until the age of 44. He had several years of poor glycaemic control, and had developed proliferative diabetic retinopathy, and end-stage renal failure. He had developed a dense bilateral peripheral neuropathy for which all other potential causes had been excluded. In particular, he has no history of leprosy, spinal cord defects, syphilis, alcohol misuse, trauma, amyloidosis, or other autoimmune conditions. His vitamin B_{12} concentrations were within the reference range. As a result, he underwent SPK transplantation.

Following transplantation, he was commenced on a regimen of corticosteroids and calcineurin inhibitors for immunosuppression. The operation resolved the need for continued insulin therapy and reduced his blood glucose and glycated haemoglobin (HbA1c) concentrations to the 'non-diabetic' ranges. Because he biochemically no longer had diabetes, he was discharged from his local specialist diabetes services.

Approximately 11 years later, the patient presented to his general practitioner with a two-month history of increased temperature and swelling in his left foot. He was initially diagnosed with gout and commenced on treatment, which failed to resolve his symptoms. Subsequently a radiograph was requested, which identified features of a CN with midfoot fractures, consolidation and a loss of the medial longitudinal arch (Figures 1a and 1b).

The overall duration of treatment was 4 months during which he was successfully treated in a total contact cast until he was in remission followed by a below knee removable walking boot.

Unfortunately 1 month later, whilst under review he presented with features consistent with a contralateral right CN. The diagnosis was confirmed by radiographs (Figures 2a and 2b), and an MR scan (Figures 3a and 3b) of his right foot.

Once a CN of the right foot was diagnosed, a similar management strategy ensued, which was off-loading his affected foot. He is currently stable under regular review.

Discussion

We have described the unusual case of a man who presented with bilateral Charcot neuroarthropathic feet 11 years after SPK transplantation. Prior to transplantation he had poor control of his diabetes, and had evidence of end organ damage, including dense bilateral peripheral neuropathy. The CN occurred despite him having glucose concentrations in the non-diabetic range following his SPK transplant. All other causes of peripheral neuropathy had been excluded prior to his transplant and subsequently, after he had developed his CN.

Previous work has looked at CN following a SPK transplant (5-9). In two reviews, it was reported that the development of a CN commonly occurred within the first year, with the latest occurrence at 5 years post transplantation (5,6). Whilst one previous

case report has reported a case of CN 11 years after SPK transplantation (9), to our knowledge this is the first report detailing the development of bilateral CN a similar time after an SPK transplant.

We have previously described a similar case series of people developing CN after attaining normoglycaemia after bariatric surgery (10). This patient was lost to follow up when his SPK transplantation put his diabetes into remission and there was no longer a need for dialysis. He did not receive regular foot care after that. His pre-existing peripheral neuropathy and subsequent use of calcineurin inhibitors used as part of the immunosuppressive regimen may have also contributed because of the direct effects on bone metabolism, or a directly neurotoxic effect (5,11).

Barrado's retrospective review of 100 patients identified 9 patients who developed a CN (5). Almost half developed this within the first year, while the remaining 5 developed the condition within the next 5 years. In their analysis, the authors state that patients who developed a CN had a higher mortality and graft failure rate. They identified that patients with high pre-transplant HbA1c values and use of high corticosteroid doses as risk factors for developing an acute CN.

Matricali et al's, retrospective analysis of 66 patients, demonstrated a higher incidence of development of CN at 12% (6). Their conclusions were similar to Barrado et al, with a high pre-transplant HbA1c as a significant risk factor for developing a CN post SPK transplant and a higher rate of mortality and graft rejection in the CN group. They also suggested their results were due to the small cohort of patients.

In the review by Rangel et al, 130 patients without any history of CN were analysed retrospectively (7). Six patients developed de novo CN during the first year. They also suggested that high doses of glucocorticoids were the main risk factor leading to bone resorption and myofibril proteolysis. As a result of these reports and their own 2 cases, del Vecchio et al emphasized the importance of regular systematic follow up of patients with diabetes undergoing SPK transplantation with a pre-existing peripheral neuropathy (8).

In summary, this is the second reported presentation of a CN occuring 11 years following an SPK transplantation. However, our case is different to the one reported because it is bilateral. As this case demonstrates, there is no clear defined time period beyond which we can assume a patient is not at risk of developing a de novo CN following SPK transplantation. Therefore, despite normal glycaemic control following transplantation, these patients should remain under lifelong regular specialist diabetes review. Patients and health care clinicians should maintain a high degree of clinical suspicion when presented with a hot swollen foot with a concurrent peripheral neuropathy.

Written patient consent was obtained for this case report

Conflict of Interest Statement

None

References

1 Jeffcoate WJ, Game FL, Cavanagh PR. The role of proinflammatory cytokines in the cause of neuropathic osteoarthropathy (acute Charcot foot) in diabetes. *Lancet* 2005;366:2058-2061.

2 Dhatariya K, Gooday C, Murchison R, Bullen B, Hutchinson R. Pedal neuroarthropathy in a nondiabetic patient as a result of long-term amiodarone use. *J Foot Ankle Surg* 2009;48:362-364.

3 Jeffcoate WJ. Charcot foot syndrome. *Diabetic Med* 2015; 32(6):760-770.

4 Redfield RR, Scalea JR, Odorico JS. Simultaneous pancreas and kidney transplantation: current trends and future directions. *Curr Opin Organ Tran* 2018;20:94-102.

5 Garcia Barrado F, Kuypers DR, Matricali GA. Charcot neuroarthropathy after simultaneous pancreas-kidney transplantation: risk factors, prevalence, and outcome. *Clin Transplant* 2015;29:712-719.

6 Matricali GA, Bammens B, Kuypers D, Flour M, Mathieu C. High rate of Charcot foot attacks early after simultaneous pancreas-Kidney Transplantation. *Transplantation* 2007;83:245-246.

7 Rangel EB, Sa JR, Gomes SA et al. Charcot neuroarthropathy after simultaneous pancreas-kidney transplant. *Transplantation* 2012;94:642-645.

8 del Vecchio JJ, Raimondi N, Rivarola H, Autorino C. Charcot neuroarthropathy in simultaneous kidney-pancreas transplantation: report of two cases. *Diabetic Foot & Ankle* 2013;4:21819.

9 Caldara R, Grispigni C, la Rocca E et al. Acute Charcot's arthopathy despite 11 years of normoglycemia after successful kidney and pancreas transplantation. *Diabetes Care* 2001;24:1690.

10 Murchison R, Gooday C, Dhatariya K. The development of a Charcot foot after significant weight loss in people with diabetes. *J Am Podiatr Med Assoc* 2014;104:522-525.

11 Bechstein WO. Neurotoxicity of calcineurin inhibitors: impact and clinical management. *Transpl Int* 2000;13:313-326.

Legends to Figures

Figure 1a and 1b – Left foot AP and lateral radiograph demonstrating midfoot collapse, widening of the 1st and 2nd MT interspace.

Figure 2a and 2b – Right foot AP and lateral radiograph demonstrating erosive arthopathic changes of the tarsometatarsal joints – in particular the first– with reduction in joint space and sclerosis (solid arrow). In addition, there are ununited fractures at the base of the third and fourth metatarsals (striped arrows).

Figure 3a and 3b – Left foot MRI T1 sagittal and axial views demonstrating a destructive arthropathy of the common tarsometatarsal joint resulting in pes planus (solid arrow). There is marrow edema and severe erosive changes in the midfoot consistent with a Charcot neuroarthropathic joint. There is also collapse of the second metatarsal head.

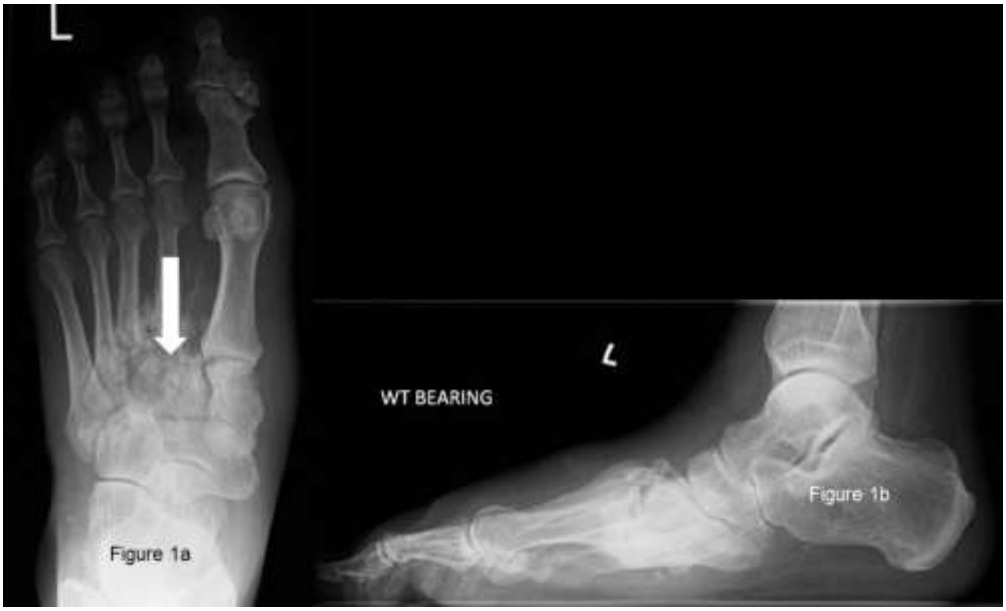

Figure 1a and 1b – Left foot AP and lateral radiograph demonstrating midfoot collapse, widening of the 1st and 2nd MT interspace.

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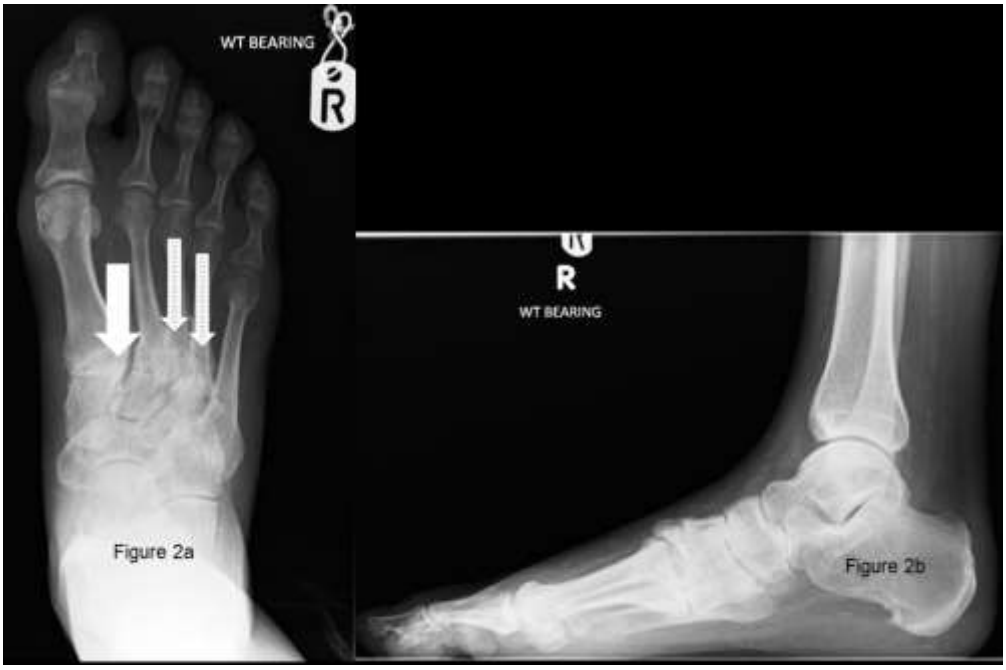

Figure 2a and 2b – Right foot AP and lateral radiograph demonstrating erosive arthopathic changes of the tarsometatarsal joints – in particular the first– with reduction in joint space and sclerosis(solid arrow). In addition, there are ununited fractures at the base of the third and fourth metatarsals (striped arrows)."

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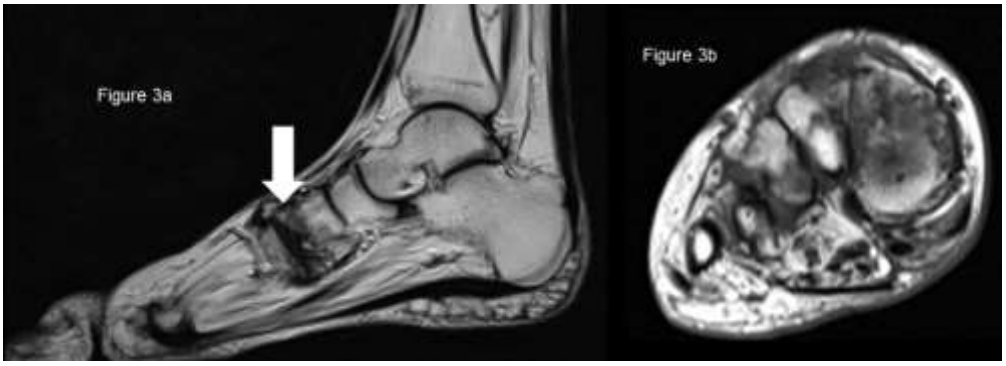

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