ultrasound clearly indicated a high systolic flow and a low acceleration index within the repaired artery (Fig. 1C-2) and a moderate depression of the resistance index downstream (Fig. 1C-3) of the repair. At 12 weeks after transplantation, the child was free of infection, normotensive with no antihypertensive drugs, and showed excellent graft function.

DISCUSSION

The survival of the patient described in this report was the result of a fortunate combination of circumstances. However, the technique used to repair the infection-induced artery fissure deserves attention. Infection-induced vascular damage is typically localized at the site of anastomosis. In our patient, subadventitial blood collecting at the site of future vascular wall melting (Fig. 1A, *green arrow*) indicated that the branch of the renal artery was ruptured, likely as a result of wound contamination. We decided to save the graft despite the suspected multidrug–resistant *Pseudomonas* infection because we had at our disposal both of the effective antibiotics: fosfomycin for systemic administration and polymyxin E for soaking the knitted tissue.

Of the few reports in the literature involving graft rescue in cases of infection-induced artery damage, most describe surgical treatment of the pseudoaneurysm. Saving the affected recipient's artery is often difficult to achieve. Tagavi et al. (*1*) reported good results after an 18-month follow-up in a case of artery repair involving a saphenous vein patch. Albano et al. (*2*) described two patients with aneurysms of the graft or iliac artery caused by *Candida* arteritis in which the graft was saved after arterial patching. Osman et al. (*3*) summarized the data for 24 patients with pseudoaneurysms related to kidney graft. The grafts were saved in only 5 of the patients (21%), and 9 of 17 transplantectomized patients lost the iliac or femoral artery, with or without subsequent bypass. Benson (*4*) was the first to describe wrapping of an aortic aneurysm with synthetic material. A similar technique can be used to successfully repair smaller vessels when bypass is not suitable because of infection-induced wall melting and when internal stenting may favor advance of the infection.

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Received 27 November 2012.
Accepted 20 December 2012.

ISSN: 0041-1337/13/9507-e48
DOI: 10.1097/TP.0b013e3182846029

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Effects of Oral Paricalcitol on Secondary Hyperparathyroidism and Proteinuria of Kidney Transplant Patients

Secondary hyperparathyroidism (SHPT) persists up to 15% to 50% of patients at 1 year of kidney transplantation (*1*). This persistent SHPT contributes to bone mass loss, a higher risk of fracture, hypercalcemia, hypophosphoremia, and vascular calcifications in transplanted patients. On the contrary, the magnitude of proteinuria is a factor of paramount importance for the rate of progression in many kidney diseases (*2, 3*). Several studies have clearly indicated that the same correlation can be observed in kidney transplant patients and that the sensitivity of transplanted kidney to the level of proteinuria could be even higher than that of native kidneys (*4–7*).

Paricalcitol is a selective activator of vitamin D receptor that has demonstrated a significant improvement of SHPT in patients with chronic kidney disease while inducing less hypercalcemia and hyperphosphoremia than other vitamin D analogues (*8*). Recent experimental and clinical studies have demonstrated a reduction in proteinuria and less structural damage after paricalcitol treatment in diabetic and nondiabetic nephropathies (*9, 10*). These renoprotective influences have been corroborated by the Vitamin D activation with Paricalcitol for Reduction of Albuminuria in Patients with Type 2 Diabetes Trial study, which demonstrated a significant reduction in albuminuria in type 2 diabetic patients treated with paricalcitol (*11*).

Information about paricalcitol treatment for SHPT after kidney transplantation is remarkably scarce. The aim of this study was to analyze our experience with paricalcitol in the treatment of transplanted patients with SHPT.

We included all the transplanted patients who had received paricalcitol treatment in the period 2009–2010. Criteria for paricalcitol treatment were the

presence of a SHPT, with serum intact parathyroid hormone (iPTH) ≥150 pg/mL along with serum calcium ≤10 mg/mL and serum phosphorus ≤4.5 mg/dL. Oral paricalcitol at a dose of 1 μg on alternate days was prescribed. When serum calcium increased to 10.5 to 10.9 mg/dL and serum phosphorus increased to ≥5 mg/dL, paricalcitol was reduced to two thirds of previous dose; when serum calcium increased above 11 mg/dL, paricalcitol was stopped. No patient received vitamin D supplements.

The main outcomes of the study were the reduction of serum iPTH ≥30% and changes in serum iPTH during follow-up. Secondary outcomes were the reduction in proteinuria ≥50% of the baseline values and changes in proteinuria during follow-up. Tertiary outcomes were changes in renal function, blood pressure, and changes in serum C-reactive protein (CRP) during follow-up. Mean and median of follow-up was 20.1 and 18 months, respectively.

Data are expressed as the mean±1 standard deviation. Remission ≥30% of iPTH and ≥50% of 24 hr proteinuria was calculated by univariate and multivariable logistic regression. We reported adjusted odds ratio (OR) with 95% confidence intervals (CI). For all tests, *P* values<0.05 were considered to be statistically significant.

Fifty-eight patients were included in the study. The mean age was 55.7±12.7 years and time since kidney transplantation was 74.2±45.4 months. A combination of corticosteroids, tacrolimus, and mycophenolate was the most commonly used immunosuppressive regimen. Mean serum creatinine at baseline was 2.1±0.7 mg/dL, and estimated glomerular filtration rate (eGFR) was 34.9±14.1 mL/min/1.73 m^2. Angiotensin-converting enzyme inhibitors (ACEI) were used in 28 (48.3%) patients and no patient received treatment with angiotensin II receptor antagonist. ACEI doses were not changed after paricalcitol introduction.

The levels of iPTH showed a rapid and sustained significant decrease after paricalcitol treatment, as shown in Table 1 and Figure 1. The percentage of patients who achieved a reduction of baseline PTH ≥30% increased gradually from 55% at month 3 up to 76% at the end of follow-up. By multivariable logistic regression, a baseline iPTH ≥500 pg/mL was the only clinical factor significantly associated with an iPTH reduction ≥30% (OR, 5.6; 95% CI, 1.3–24.6; *P*=0.022).

Changes in serum calcium, phosphorus, and 25(OH)D after paricalcitol treatment are shown in Table 1. A mild but significant increase in serum calcium and serum phosphorus was observed. Paricalcitol doses were reduced since the third month of treatment until the end of the follow-up (4.1±1.8–3.3±1.2 μg/week; *P*<0.05) to avoid higher increases in serum calcium and serum phosphorus.

Proteinuria showed a significant decrease after the introduction of paricalcitol, ranging from 29.2% to 42.1% (mean, 35.6%), as shown in Table 1 and Figure 1. This reduction was significant since the third month of treatment until the end of the follow-up (1.1±0.7 g/24 hr at baseline vs. 0.7±0.7 g/24 hr at last visit; *P*<0.05). No associations were found between the reduction in proteinuria and changes in renal function or blood pressure. The number of patients who achieved a reduction of proteinuria ≥50% increased gradually from 10.3% (6 of 58 patients) at month 3 up to 44.8% (26 of 58 patients) at the last visit (Table 1). Patients with or without ACEI treatment showed a similar proteinuria reduction after paricalcitol treatment. By multivariable logistic regression, the only baseline clinical factor independently associated to a proteinuria decrease ≥50% was a serum CRP <1.2 mg/dL (OR, 13.8; 95% CI, 2.0–95.1; *P*=0.008).

As shown in Table 1 and Figure 1, renal function remained stable after the onset of paricalcitol treatment. By contrast, eGFR had significantly decreased during the 2 years previous to paricalcitol treatment, from 39.9±14.7 mL/min/1.73 m^2 at −2 years to 34.9±14.1 mL/min/1.73 m^2 at baseline (*P*<0.01). A significant difference was found between the change in eGFR during the −2 year pre-paricalcitol period (−2.51 mL/min/1.73 m^2/yr) and the change after paricalcitol treatment (−1.21 mL/min/1.73 m^2/yr; *P*<0.001; Fig. 1).

Systemic inflammation, measured by CRP serum levels, showed a significant decline after paricalcitol therapy (Table 1). No significant changes in blood pressure were observed (Table 1). There were no changes in the number of antihypertensive drugs or in the percentage of patients treated with ACEI.

No clinical side effects attributable to paricalcitol were observed. Mild increases of serum calcium (10–10.5 mg/dL) or phosphorus (4–4.5 mg/dL) were detected in 4 (6.9%) and 7 (12.1%) patients, respectively, and they responded to reduction in paricalcitol doses. No episodes of more severe hypercalcemia (serum calcium >10.5 mg/dL) or hyperphosphoremia (serum phosphorus >5 mg/dL) were detected. No episodes of acute rejection or clinically significant worsening or renal function were observed during paricalcitol treatment. No patient required withdrawal, even temporary, of paricalcitol.

Our study is the first to report the effects of paricalcitol on SHPT in a cohort of kidney transplant patients with chronic kidney disease and vitamin D insufficiency several years after kidney transplantation. The rapid and significant decline of serum iPTH (76% of the patients had achieved >30% baseline iPTH decrease at the last visit) was accompanied by only a mild increase in the levels of serum calcium and phosphorus that, although statistically significant, maintained these parameters within normal limits in a majority of patients throughout paricalcitol therapy. Another finding of our study worth remarking is that these beneficial effects were achieved with relatively low paricalcitol doses (1 μg three to four times per week). It should be considered, however, that iPTH tends to decline over time after kidney transplantation and that dual-energy X-ray absorptiometry scans were not performed in our patients, thus precluding the demonstration of a beneficial effect of paricalcitol on bone disease.

There is a cumulative number of studies showing a close correlation between the presence of proteinuria in kidney transplant recipients patients and graft survival. The risk of graft loss is directly correlated with the amount of proteinuria and recent studies have shown that the presence of proteinuria >0.150 g per 24 hour at 1 year after transplantation significantly decreases graft survival (*4–7*). In this context, our finding that paricalcitol significantly decreases proteinuria in kidney transplant patients is novel and important. Mean proteinuria reduction from baseline was 36% and almost a half of the patients showed >50% baseline proteinuria decrease.

Another interesting finding of our study was the remarkable stability of eGFR throughout paricalcitol treatment, as shown in Table 1 and Figure 1.

TABLE 1. Evolution of mineral metabolism, blood pressure, and renal function parameters with paricalcitol therapy

	Months since the onset of paricalcitol therapy						
Variable	**0**	**3**	**6**	**9**	**12**	**18**	**Last visit**
No. patients	58	58	58	58	58	58	58
iPTH, pg/mL	333 (225)	195 (87)[a]	195 (93)[a]	197 (93)[a]	182 (82)[a]	181 (83)[a]	187 (88)[a]
PTH reduction ≥30%, n (%)	—	32 (55)	38 (65)[b]	40 (69)[b]	42 (72)[b]	44 (75)[b]	44 (75)[b]
25(OH)D, ng/mL	17.6 (3.3)	—	17.8 (3.9)	—	18.1 (2.8)	18.3 (2.9)[a]	18.1 (2.9)[a]
Serum calcium, mg/dL	9.3 (0.5)	9.6 (0.5)[a]	9.6 (0.5)[a]	9.6 (0.5)[a]	9.6 (0.4)[a]	9.6 (0.4)[a]	9.6 (0.4)[a]
Serum phosphorus, mg/dL	3.4 (0.5)	3.5 (0.5)[a]	3.5 (0.5)[a]	3.5 (0.5)[a]	3.5 (0.5)[a]	3.5 (0.5[a]	3.5 (0.5)[a]
Proteinuria, g/24 hr	1.1 (0.7)	1.0 (1.0)[a]	0.9 (0.8)[a]	0.8 (0.9)[a]	0.8 (0.8)[a]	0.7 (0.8)[a]	0.7 (0.7)[a]
Proteinuria remission ≥50%, n (%)	—	6 (10.3)	12 (20.7)[b]	16 (27.6)[b]	19 (32.8)[b]	26 (44.8)[b]	26 (44.8)[b]
SCr, mg/dL	2.1 (0.7)	2.0 (0.7)	2.0 (0.7)	2.0 (0.7)	2.0 (0.6)	2.0 (0.6)	2.1 (0.7)
GFR, mL/min/1.73 m^2	34.9 (14.1)	35.8 (14.6)	35.5 (14.3)	35.3 (14.3)	34.7 (14.1)	34.8 (14.3)	33.9 (14.0)
CRP, mg/dL	1.1 (0.3)	0.9 (0.2)[a]	0.9 (0.2)[a]	0.9 (0.2)[a]	0.8 (0.2)[a]	0.8 (0.2)[a]	0.8 (0.2)[a]
MBP, mm Hg	93.2 (5.9)	92.7 (5.2)	92.3 (4.9)	92.2 (4.9)	92.4 (5.3)	92.6 (5.4)	92.6 (5.5)
ACEI therapy, n (%)	28 (48.3)	26 (44.8)	26 (44.8)	26 (44.8)	27 (46.6)	27 (46.6)	28 (48.3)
Paricalcitol dose, mg/wk	4.1 (1.8)	3.3 (1.2)[a]	3.3 (1.2)[a]	3.3 (1.2)[a]	3.3 (1.2)[a]	3.4 (1.3)[a]	3.3 (1.2)[a]

[a] $P<0.01$ with respect to baseline determination (month 0).

[b] $P<0.01$ with respect to month 3.

ACEI, angiotensin-converting enzyme inhibitor; CRP, C-reactive protein; GFR, glomerular filtration rate; iPTH, intact parathyroid hormone; MBP, mean blood pressure; 25(OH)D, 25-hydroxyvitamin D3; PTH, parathyroid hormone; SCr, serum creatinine.

This eGFR stability contrasted with the −2 year period preceding paricalcitol treatment, in which a significant eGFR decline had been observed. Hypothetically, both the reduction in proteinuria and a possible immunomodulatory effect of paricalcitol (*12*) could have played a protective role in our patients. In a recent experimental study, paricalcitol attenuated cyclosporine-induced kidney damage by suppressing inflammatory, fibrotic, and apoptotic factors (*13*). Nevertheless,

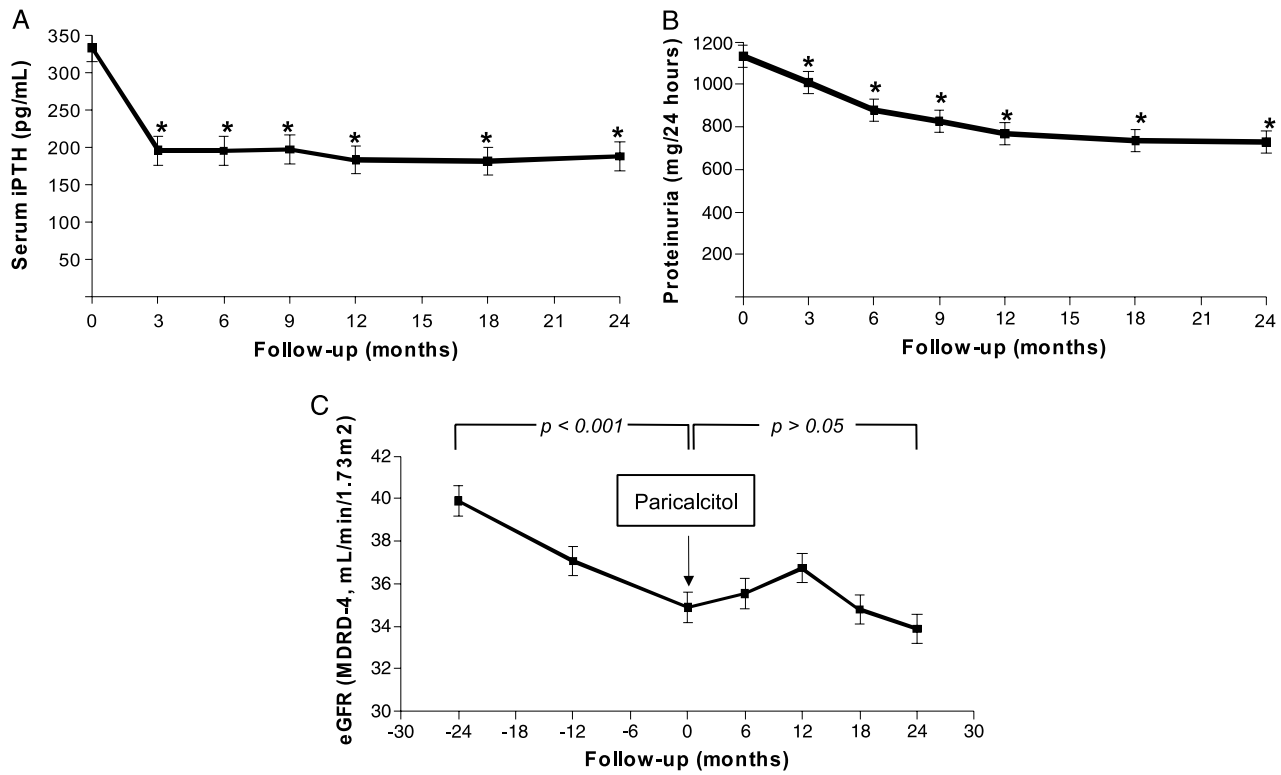

FIGURE 1. Evolution of serum iPTH (A), proteinuria (B), and eGFR (C) after paricalcitol treatment. *$P<0.05$, with respect to baseline. eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone.

it should be considered that our patients were stable kidney transplant recipients several years after the kidney graft and that renal function was evaluated by means of creatinine-based estimating equations, without a precise measurement of GFR. Finally, and confirming the anti-inflammatory properties of paricalcitol and other vitamin D analogues reported in previous studies (*14*), we found a significant decrease in serum CRP levels after paricalcitol treatment. In conclusion, oral paricalcitol at relatively low doses (1 μg three to four times per week) is a safe and efficacious treatment of SHPT in long-term kidney transplant patients. Paricalcitol treatment was accompanied by a significant and sustained reduction in proteinuria and stable renal function. In addition, a significant reduction in serum CRP was observed. These renoprotective and systemic beneficial effects of paricalcitol in the setting of kidney transplantation should be confirmed by means of randomized controlled trials.

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This study was funded by grants from the Fondo de Investigaciones Sanitarias (FIS10/02668) and Asociación para la Investigación y Tratamiento de la Enfermedad Renal.
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Received 18 December 2012.
Accepted 28 December 2012.

ISSN: 0041-1337/13/9507-e49
DOI: 10.1097/TP.0b013e3182855565

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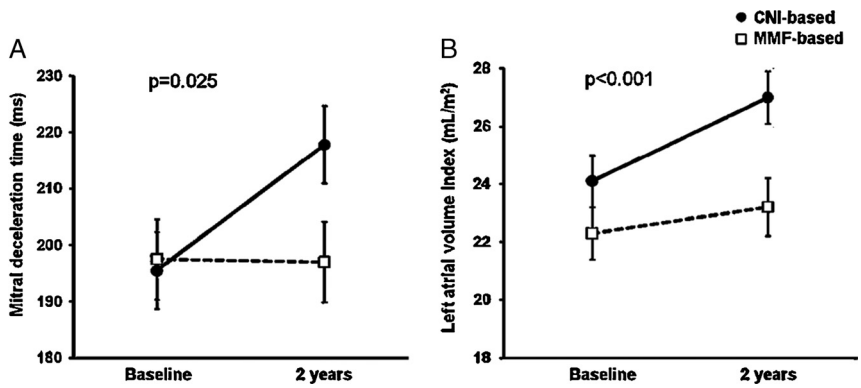
ERRATA

Late Calcineurin Inhibitor Withdrawal Prevents Progressive Left Ventricular Diastolic Dysfunction in Renal Transplant Recipients: Erratum

In the October 27, 2012 issue of *Transplantation* in the article by Mourer et al, "Late Calcineurin Inhibitor Withdrawal Prevents Progressive Left Ventricular Diastolic Dysfunction in Renal Transplant Recipients", the image for Figure 1 was incorrect. The correct figure is shown below.



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Mourer JS, Ewe SH, Mallat MJK, et al. Late calcineurin inhibitor withdrawal prevents progressive left ventricular diastolic dysfunction in renal transplant recipients. *Transplantation.* 2012; 94: 721.