Olgu Sunumu

A Successful Renal Transplantation in A Diabetic Male Patient with Calciphylaxis

Kalsiflaksisi Olan Bir Diyabetik Erkek Hastada Başarılı Renal Transplantasyon

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ABSTRACT

Calcific uremic arteriolopathy also known as calciphlaxis is a fatal complication of chronic renal failure. It is characterised by medial calcification of subcutaneous small arterial vessels and necrosis of adipose and subcutaneous tissues resulting from ischemia. Data concerning renal transplantation in individuals with calciphlaxis is very scant. We report a diabetic male patient who underwent renal transplantation successfully after treatment of calciphylaxis with conservative methods and pamidronate.

A 31 year old "type 1 diabetic" male patient who was on hemodialysis treatment for six months was admitted with painful, ischemic lesion on his left hand's third finger's distal phalanx. We diagnosed calciphylaxis by clinical investigation, x-ray and whole body bone scintigraphy and treated with conservative methods and pamidronate for six months. Unfortunately, in the early phase of the treatment he underwent urgent distal phalanx amputation and histological examination of the amputated materials confirmed our diagnosis. New calciphylactic lesion didn't occur after the treatment with conservative methods and pamidronate. He underwent successful renal transplantation from a living donor one year after the calciphylaxis diagnosis. At the eighteenth month of post-transplantation period, he had a functional graft, furthermore, the regression of the vascular calcification was clearly seen. Renal transplantation can be a safe treatment option in patients with calciphylaxis if they are appropriately treated with conservative methods and a functional renal graft can accelerate the regression of vascular calcification.

Keywords: *calciphylaxis, renal transplantation*

ÖZET

Kalsifik üremik arteriolopati olarak da adlandırılan kalsiflaksi sıklıkla son dönem böbrek yetmezliğinin fatal bir komplikasyonudur. Subkutanöz dokunun küçük arterlerinin medial kalsifikasyonu ve yağ ve cilt nekrozuna yol açan subkutanöz iskemi ile karakterizedir. Bu hastalarda renal transplantasyon konusunda veriler oldukça azdır. Bu yazıda konservatif metodlar ve pamidronat ile kalsiflaksi tedavi edildikten sonra başarılı bir renal transplantasyon uygulanan bir diyabetik olguyu sunduk.

Altı aydır hemodializ tedavisinde olan 31 yaşında tip 1 diabetik erkek hasta sol el üçüncü parmak distal falanksta ağrılı, iskemik lezyonla müracaat etti. Klinik araştırma, düz grafi ve tüm vücut kemik sintigrafisi ile kalsiflaksi tanısı kondu ve 6 ay müddetle konservatif metotlar ve pamidronat ile tedavi edildi. Tedavinin erken döneminde distal falanks ampütasyonuna gitti ve ampute edilen materyalin histopatolojik incelemesi kalsiflaksi tanısını doğruladı. Tedavi ile yeni kalsiflaktik lezyon gelişmedi ve kalsiflaksi tanısından yaklaşık 1 yıl sonra canlı donörden renal transplantasyon uygulandı. Transplantasyon sonrası onsekizinci ayda greft fonksiyoneldi ve vasküler kalsifikasyonda gerileme gözlendi.

Konservatif metodlarla uygun bir şekilde tedavi edilen kalsiflaksi hastalarında renal transplantasyon güvenli bir tedavi seçeneği olabilir ve fonksiyonel renal greft vasküler kalsifikasyonda gerilemeye yol açabilir.

Anahtar Kelimeler: *kalsiflaksi, renal transplantasyon*

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INTRODUCTION

Calciphylaxis, also called calcific uremic arteriolopathy, is often a fatal complication of end-stage renal disease (ESRD). It is characterized by medial calcification of the small arteries and ischemia of the subcutaneous tissue, often leading to necrosis of subcutaneous fat and skin. Historically considered rare, calciphylaxis seems to occur more frequently than previously believed, with an incidence of 1% per year and a prevalence of 4% in dialysis patients (1).Non-ulcerating lesions represent early disease. A proximal distribution of the lesions and the presence of skin ulcers are associated with a very poor prognosis (1).The rate of mortality approaches up to 60% to 80% due to mainly sepsis and cardiovascular disease (1). Female gender, obesity, diabetes mellitus, peritoneal dialysis, high alkaline phosphatase level, hyperparathyroidism, usage of calcium (Ca)-containing phosphorus (P) binders and active vitamin D, high dialysate Ca content, hypercoagulative states such as protein C and S deficiency; usage of steroids, coumadin, low molecular weight heparin (LMWH), hypoalbuminemia, dialysis duration, changes in inhibitors of calcification and renal transplantation (Tx) are suggested as risk factors for calciphylaxis in patients with ESRD (2-5).

Data concerned with renal Tx in uremic patients with calciphylaxis are very scant. Here, we reported a diabetic male case who undergone successful renal Tx from a living donor one year after the calciphylaxis diagnosis.

CASE

A 31 year old diabetic male patient with lean body mass index who was on hemodialysis treatment for six months (for 4 hours/day, three days per week) was admitted with painful, ischemic lesion on his left hand's third finger's distal phalanx which began 10 days ago. He was being dialysed with Ca-containing dialysate of 1.5 mMol/L and LMWH before the calciphylaxis diagnosis. Medical history revealed that he had type 1 diabetes mellitus for 21 years and diabetic nephropathy was initially diagnosed 5 years ago. He was treated with intensive insulin therapy by preprandial short-acting insulin and bedtime long-acting insulin. He had proliferative retinopathy and a poor glycemic control with 8.6% HbA1c value. Also, medical history revealed that he had used Ca-containing P binders and active vitamin D for 2 years in pre-dialysis stage. The levels of protein-C, protein-S, anti-trombin-III, anti-cardiolipin IgG and IgM were normal. The levels of serum aluminum and ferritin were 12 µg/L and 275 ng/mL, respectively. Peripheral pulses were palpable and neurological examination was normal. Thrombosis and narrowness was eliminated by doppler ultrasonography. Echocardiography revealed diastolic dysfunction. Widespread vascular calcifications on interphalangial arteries (Figure 1) and abdominal aorta by x-ray and increased tracer accumulation in the subcutaneous tissues by Tc-99m whole body bone scintigraphy were seen.

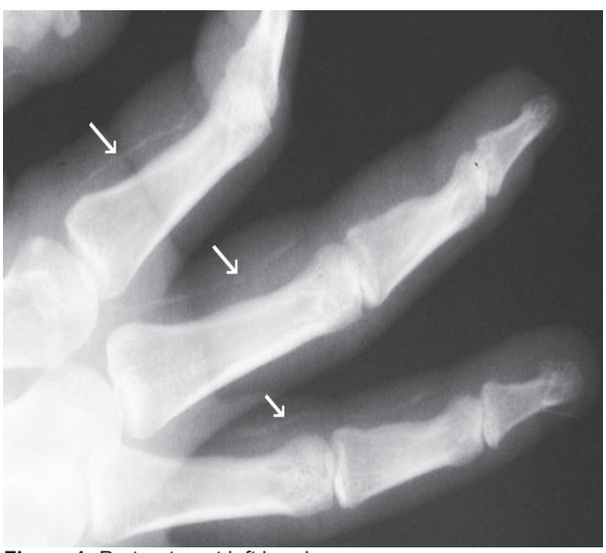

Figure 1: Pretreatment left hand x-ray.

Bone density was normal by Dual-Energy X-ray Absorptiometry. Calciphylaxis diagnosed by clinical investigation, x-ray and whole body bone scintigraphy. Dialysis regimen was rearranged as for 5 hours/day, two days per week by 1.25 mMol/L Ca-containing dialysate and high flux membrane, and online hemodiafiltration (HDF) for five hours per week was added for six months. Sevelamer instead of Ca-based P binder, hyperbaric oxygen, statin, acetylsalicylate, intensive insulin therapies were started. In addition, pamidronate was administered at doses of 45 mg/week for 8 weeks; afterwards, this treatment was continued for 6 months at doses of 90 mg/month. Before and after the sixth month of post-treatment levels of Ca, P, Ca x P product, iPTH, C-reactive protein (CRP) and single pool Kt/V (spKt/V) are shown in Table 1.

Table 1: Levels of some parameters before and after six months of treatment with conservative methods and pamidronate.

	Pre-treatment	After six months of treatment
Ca (mg/dL)	10.7	8.2
P (mg/dL)	7.6	4.8
CaXP product	81.3	39.4
spKt/V	1.1	1.4
iPTH (pg/mL)	92	102
CRP (mg/dL)	17.9	0.8

Unfortunately, he underwent urgent distal phalanx amputation in the early phase of treatment and AV fistula was closed for reducing the ischemia. Histological examination of the amputated materials confirmed the diagnosis of calciphylaxis. After treatments mentioned above, new calciphylactic lesion did not develop although vascular calcification persisted on control x-ray. He underwent successful renal Tx from a living donor one year after the calciphylaxis diagnosis. An oligo-anuria state was not seen in the post-Tx period. Immunosuppressive treatment was constituted with tacrolimus, mycophenelate mofetil, prednisolon; and additionally basiliximab 20 mg was administered 2 hours before operation and on the fourth day after Tx.

Rejection or infection did not occur in eighteen month period of post-Tx. He has still a functional graft. In addition, evident regression of vascular calcification was seen on control x-ray at the sixth month of post-Tx (Figure 2).

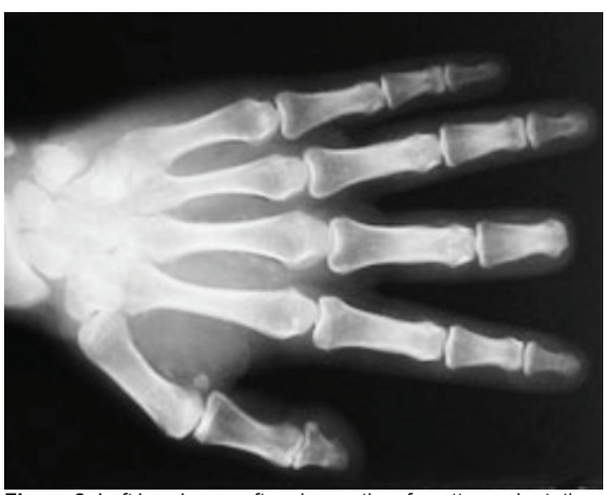

Figure 2: Left hand x-ray after six months of posttransplantation.

DISCUSSION

We report a diabetic male case who underwent successful renal Tx from a living donor after calciphylaxis was treated by conservative methods and pamidronate therapy.

The etiology of calciphylaxis remains unclear. The pathogenesis is not completely clear and also treatment of the calciphylaxis is equally unsatisfactory. In treatment of calciphylaxis, increase of dialysis dose, using of Ca-free P binders instead of Ca-containing P binders, P-restricted diet, usage of low Ca-containing dialysate, treatment of aluminum accumulation if exists, surgical parathyroidectomy of hyperparathyroidism, local debridement of wound and hyperbaric oxygen therapy have been reported in previous studies. There are some reports showing that calciphylaxis can be treated with bisphosphonates or sodium thiosulphate (6, 7). It has been reported that the inflammatory syndrome in calciphylaxis might result from the release of proinflammatory cytokines associated with the local activity of osteoclasts and that pamidronate had an anti-inflammatory effect (8). It has also been reported that lesion severity at the beginning of therapy appeared to best correlate with clinical course.

Therefore, earlier recognition of calciphylaxis is important for ameliorating the symptoms and preventing or retarding its progressive squeal. Our case had most of risk factors reported previously, e.g diabetes mellitus, high dialysate Ca content and Ca-P product, long-term usage of Ca-containing P binder in pre-dialysis stage and usage of LMWH in dialysis treatment. In addition to conservative treatments including intensified hemodialysis with low Ca-containing dialysate, lowering of Ca and P loads and hyperbaric oxygen we administered pamidronate therapy. Bisphosphonate therapy can lead to worsening of Adynamic Bone Disease (ABD) (9). Therefore, pamidronate therapy in this case was a critical decision due to high probability of ABD in patients with diabetic nephropathy and low PTH levels.

Although existence of normal bone mineral density and lack of bone pain can be a clue for absence of ABD, it cannot be excluded without bone biopsy in this case. We observed a slight increase in PTH level and moderate decrease at serum Ca level after pamidronate therapy, suggesting possibility of PTH suppression rather than ABD. It is possible that pamidronate therapy exerts an additional benefit in preventing the formation of new calciphylactic lesions. Our case represents less severe form of calciphylaxis with distal involvement but not early diagnosis. Despite all treatments, amputation is inevitable in some patients, particularly in those lately diagnosed.

On the other hand, although the development of calciphylaxis in renal Tx recipients with varying stages of renal dysfunction is relatively frequent and renal Tx itself had been suggested as a risk factor for calciphylaxis, data about the results of renal Tx in uremic patients who already have calciphylaxis are very scant (5, 10-14).

Meissner et al. reported a patient who had undergone a succesful renal Tx after the therapy of calciphylaxis with sodium thiosulphate (7). Asmundsson et al. reported a patient who had undergone renal Tx from a cadaver after

parathyroidectomy for calciphylaxis and died from complications related with calciphylaxis seven months after Tx (15). In previously reported cases where calciphylaxis developed after renal Tx, hyperparathyroidism occured before or after Tx and prolonged episode of acute tubular necrosis following the Tx had been suggested as a risk factor for calciphylaxis. It has also been suggested that early parathyroidectomy would lead to healing of calciphylaxis in patients receiving renal Tx. Therefore, in uremic patients with hyperparathyroidism renal Tx can be a risk factor for development of post-Tx calciphylaxis and extra attention will be required for such patients. Furthermore, it has been reported that calciphylaxis development may be seen as late as 20 years after renal Tx. For this reason, one must always be alert for development of calciphylaxis after renal Tx. In our case, a new calciphylactic lesion did not develop.

Moreover, in the sixth month of post-Tx, the striking regression of the vascular calcification was clearly observed. The lack of hyperparathyroidism and prolonged anuric period, associated with intensive preoperative treatment of calciphylaxis, may have a role in favorable outcome of this patient.

We think functional renal graft might have accelerated the regression of vascular calcification without decline of ongoing effect of the preceding conservative therapy. Existence of calciphylaxis in patients with renal failure is not a reason for depriving them from Tx.

CONCLUSION

Renal Tx can be a safe treatment option in patients with calciphylaxis if they are appropriately treated with conservative methods and pamidronate in preoperative period and functional renal graft can accelerate the regression of vascular calcification by improving uremic environment.

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