Transplant Renal Artery Stenosis: A Case Report and Literature Review

Nasser Simforoosh*, Amirhossein Nayebzade, Meisam Ghaedi

Transplant renal artery stenosis is the most common vascular complication that occurs following kidney transplantation and can lead to graft dysfunction and even its loss. The present report describes A patient with end-stage renal disease who underwent living related renal transplantation. He had oliguria and creatinine rise in the post-operative course but all doppler ultrasonography (DUS) during the 2 months post-operation for the renal graft showed a normal mean resistive index in the graft renal artery. Hemodialysis treatment started and continued for 4.5 months. On post-operative day 137, because of the patient's anuria and resistant hypertension, another DUS carried out and reported evidence that suggested arterial stenosis. A computed tomographic (CT) renal angiogram showed a small filling defect in the proximal graft artery that was highly suggestive for transplant renal artery stenosis (TRAS). Following angiography revealed a short linear stenosis. Endovascular intervention and stent placement were performed successfully for the patient on post-operative day 139. This case was initially diagnosed as ongoing acute rejection for which he received antirejection therapy without any significant improvement. After percutaneous transluminal angioplasty (PTA), serum creatinine trended down and urine output improved within 12 h, and they were stable at one-year follow up with a good renal function. It was noteworthy that, despite after a 4.5-month delay in diagnosis and maintenance need for dialysis, the patient responded to endovascular treatment and the graft function became normalized. Our case demonstrates that graft can be saved even if renal artery stenosis is diagnosed after several months of dialysis and diagnosis of end stage renal disease post transplantation.

Keywords: renal transplantation; stent implantation; transluminal treatment; transplant renal artery stenosis; kidney transplant

INTRODUCTION

Transplant renal artery stenosis (TRAS), characterized by narrowing or impediment of the renal supply route, is a serious vascular complication that turns out regularly within the first 6 months following kidney transplantation[1]. The prevalence reported in the literature ranges from 1% to 23%, mainly because of screening and diagnostic criteria variation in different studies[2]. The known predisposing factors for TRAS include elderly recipients, atherosclerosis, Diabetes Mellitus and delayed graft function. This condition is mostly attributed to surgical procedures, but atheroma, immune-mediated vascular damage and mechanical renal artery kinking are considered as rare causes[2, 3,4,5,6]. Clinical findings can indicate this complication, but they are subtle and nonspecific. Its main

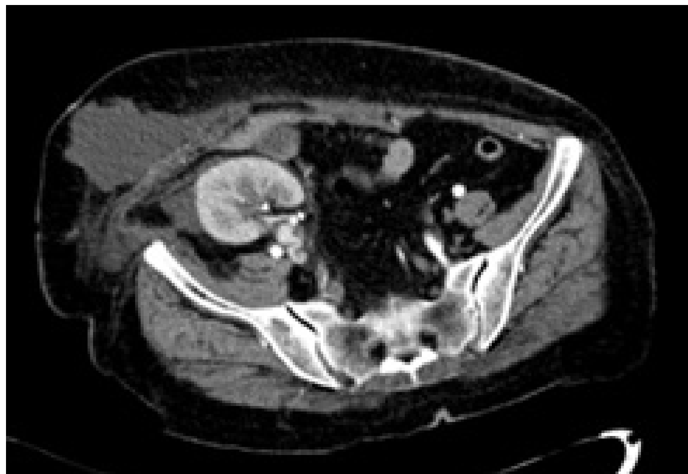

Figure 1. Image from computed tomographic angiogram.

Department of Urology and Renal Transplantation, Urology and Nephrology Research Center, Shahid Labbafinejad Hospital, Center of Excellence in Urology, Shahid Beheshti University of Medical Science, 9th St., Pasdaran Ave, PO Box 1666679951, Tehran, Iran.
*Correspondence: Department of Urology and Renal Transplantation, Urology and Nephrology Research Center, Shahid Labbafinejad Hospital, Center of Excellence in Urology, Shahid Beheshti University of Medical Science, 9th St., Pasdaran Ave, PO Box 1666679951, Tehran, Iran.E mail: simforoosh@iurtc.org.ir
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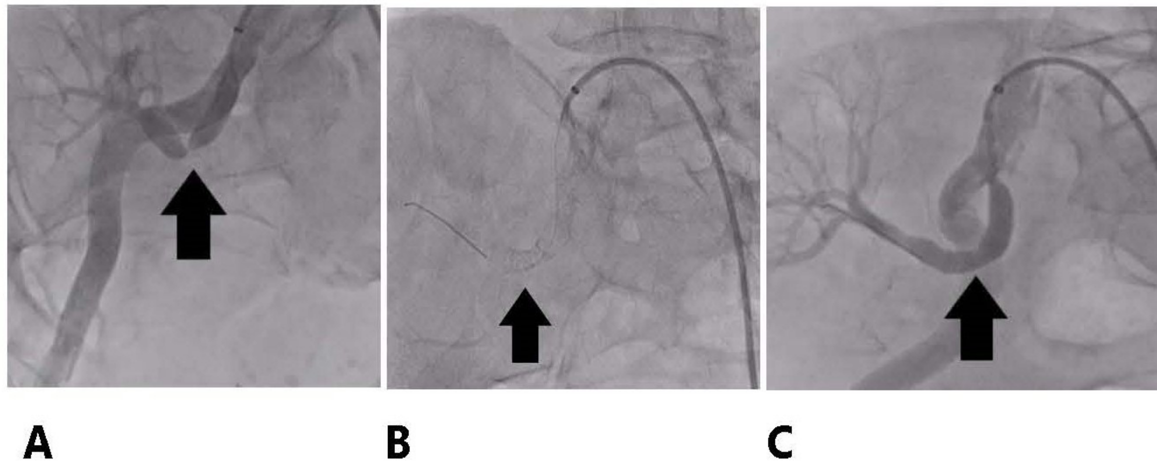

Figure 2. Angiography revealing >70% stenosis in the renal artery and post stenotic dilatation **(A).** The arrow shows the stent at the place of renal artery stenosis **(B)**. Percutaneous transluminal angioplasty (PTA) image of the renal artery after successful angioplasty and stenting **(C)**

manifestations are high blood pressure, swelling, and creatinine rise. The clinical suspicion can be supported by a Doppler Ultrasonography and ultimately contrast-enhanced angiograms confirm the diagnosis[4,6]. In cases of extreme stenosis or graft dysfunction, endovascular interventions, percutaneous transluminal angioplasty with or without stenting, have risen as successful treatment options such that restenosis has been reported just in 15 – 28% of cases[7,8]. This report contributes to the existing body of knowledge on TRAS by providing valuable insights into its diagnosis and management. We aim to shed light on the importance of early recognition and appropriate intervention in optimizing patient outcomes.

CASE PRESENTATION

A 67-year-old male patient of end-stage renal disease due to type 2 diabetes mellitus (DM2) underwent a living related renal transplantation on 08/2021. He had been anuric and on maintenance hemodialysis for several years. The kidney was transplanted into his right iliac fossa and the graft renal vessels were anastomosed end to side to internal iliac artery and external iliac vein. Pre-transplant creatinine was 5.09 mg/dl. Post-transplant creatinine was 4.13 mg/dl on day one and decreased to 2.86 mg/dl at the time of discharge on the 15th day after the operation. On the post-operation course, Doppler ultrasonography (DUS) showed normal vascular flow velocity. The DTPA scan showed moderate to severely reduced perfusion and function of the renal graft and the patient had been treated with pulse steroids and anti-thymocyte globulin with a presumed diagnosis of acute rejection.

Following discharge, serum creatinine rose, and the patient was readmitted 14 days later with a creatinine level of 4.65 mg/dl, so hemodialysis treatment started. The transplant biopsy in this time showed a normal pattern and the IHC study was negative for CD4 deposition. There were two more hospitalizations for the patient because of weakness and lethargy, nausea and vomiting, and increased creatinine. During these hospitalizations, blood pressure increased intermittently despite receiving antihypertensive drugs. Three times a week hemodialysis has also been performed during

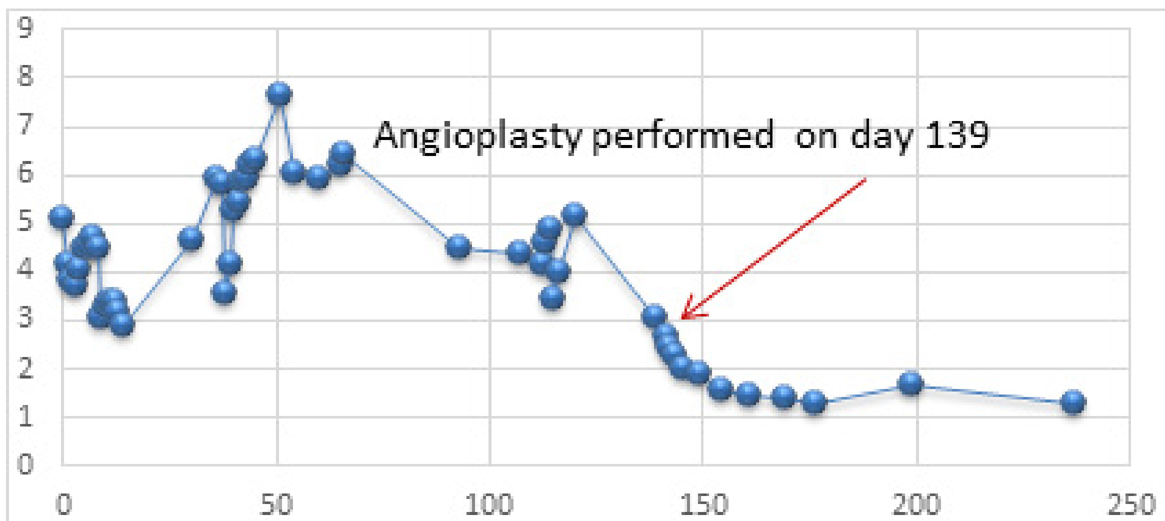

Figure 3. Trend in creatinine following kidney transplantation. The PTA was performed on day 139.

this period. However, all repeated DUS during the 2 months post-operation for the renal graft were similar to the previous ones and showed a mean resistive index of 0.55-0.65 in the graft renal artery.
On post-operative day 137, because of patient's anuria and resistant hypertension, another DUS carried out and reported increased acceleration time (>70msec) in intrarenal arteries, increased peak systolic velocity (400 cm/s) and decreased mean resistive index (0.32) in the graft renal artery, suggesting arterial stenosis. Follow up, a computed tomographic renal angiogram showed a small filling defect in the proximal graft artery, consistent with the assumed diagnosis (Fig.1). Subsequently, a scintigram was performed in angiographic and function phases after IV injection of 4 mci Tc-EC and showed decreased perfusion, diminished and non-homogenous initial cortical uptake and impaired excretory function. Finally, renal angiography revealed a short, linear stenosis in the anastomosis (**Fig.2.A**). Hence, invasive balloon angioplasty and stent placement in the graft renal artery anastomosis was performed on the 139th day after the operation. This led to an improvement of intrarenal perfusion (**Fig.2.C**) and a drop in creatinine from 3.04 mg/dl pre-procedure to 1.55 at discharge 15 days later (**Fig.3**). post-procedure renal transplant scan with Tc-EC, showed acceptable perfusion, mildly decreased initial cortical uptake and excretory function with good drainage after Lasix injection. In a one-year follow up with DUS and lab tests, the patient had an improved serum creatinine control of around 1.3 mg/dL and his clinical condition was stable and in 2.5 years follow up, the serum creatinine was 1.5 mg/dL.

DISCUSSION

According to different definitions and diagnostic approaches in distinct studies, the reported incidence of TRAS is generally inextensible. Most of these studies are retrospective and single center dependent, such as a large cohort at our center that noted only one case with renal arterial thrombosis among 1510 recipients [1,9]. The only study using a national sample of renal transplant recipients was Hurst et al, which showed an overall incidence rate of TRAS of 8.3 cases per 1000 patient-years[5]. They additionally offered factors in the recipients to be associated with TRAS such as the older age of recipients, HTN and DM2, as seen in our case. Also, there is some donors' characteristics, such as ischemic heart disease and age that were absent in our case. The chronic atherosclerotic process in the elderly and factors involved in metabolic syndrome can lead to Proximal TRAS, and explain the higher prevalence of this rare clinical condition in these patients[4].
Most commonly, TRAS is related to surgical complications and occurs close to the site of anastomosis. Some other underlying factors have been identified including atheroma in the donor artery, immune modulating vascular injury and intimal hyperplasia. These events may set the stage for changes in arterial caliber that are seen in diagnostic imaging, as in our case[2,3,5,7]. In rare conditions, mechanical kinking of the graft renal artery secondary to malposition leads to early graft dysfunction. In this situation, imaging may reveal a lesion that does not behave like a true stenosis. Due to the rarity of this entity, the precise incidence isn't clearly assessed. Soy et al retrospectively evaluated 2594 renal transplantation of one center for vascular complications and there were 7 (0.3%) of renal artery kinks[7,10].
TRAS may present at any time but often occurs between 3 months and 2 years after renal transplantation[2]. Clinical symptoms including worsening hypertension, fluid retention or graft dysfunction (rising creatinine, decreased urine output) usually occur when greater than 50 to 80% of the renal artery is occluded[4]. Although hypertension is very common following kidney transplantation, with a prevalence of 80% to 85%, TRAS accounts for only 1–5% of cases of post-transplant hypertension[6]. In this report, graft dysfunction happened alone 4 months after transplantation, which in the absence of any other causes was indicative of a critical renal artery stenosis. In patients with more severe TRAS, there may be hypertensive crisis and pulmonary edema develops, which is classically present with abrupt and unprovoked dyspnea[1].
Although invasive angiography is the gold-standard for diagnosis of TRAS, Doppler ultrasonography is commonly utilized as an initial tool to evaluate transplant dysfunction because of its availability and being safe. However, it is highly operator-dependent, so a single normal test may not be enough to exclude renal artery stenosis[11]. Our case initially received immunosuppressive therapy for assumed acute graft rejection, without any significant improvement. Similarly, two other studies also reported, the first negative doppler examinations led to delayed diagnosis[10,12]. We also performed renal scintigraphy with Tc-EC as a non-invasive diagnostic modality, to assess renal transplant related complications and especially to indicate renal perfusion. Although it was shown that radionuclide renography can be used for diagnosis in these settings[13], no special superiority was observed for it over other methods. In our case, all indirect values suggestive of renal artery stenosis in DUS, lower resistance indices (RI), increased peak systolic velocity (PSV) and slow acceleration have been investigated. CT angiography and MR angiography are the non-invasive tools that can confirm the diagnosis of TRAS without any significant accuracy differences, but they are not as essential as invasive angiography, which simultaneously allows treatment[14].
Early diagnosis and adjustment of TRAS are vital to avoiding graft morbidity or loss. In our case, consistently high levels of creatinine and positive results on a DUS test led to further investigation of graft blood perfusion, using a renal angiogram which confirmed the diagnosis. Different types of endovascular interventions (EVIs) such as percutaneous transluminal angioplasty (PTA) with or without stenting, are the preferred initial treatment option in more severe TRAS patients, as in our case[7]. The renal artery kink management is not clear right now. Some management approaches have been used successfully, ranging from endovascular intervention[15] to surgical repair[10,16,17,18,19,20,21] and even conservative care[22]. Based on the literature review, this complication is often resistant to EVI and requires instant surgical repair. However, 2 out of 14 cases reviewed, were treated with stenting, as was our case. Such artery kinks seem to be distal to the anastomosis and not due to significant graft misplacement[10,15,16,17,18,19,20,21].
After revascularization, a reliable tool for assessing effectiveness is the evaluation of PSV and RI with DUS, which have 100% sensitivity and specificity[6]. Our patient has been followed with DUS at three monthly

intervals for about 1 year after angioplasty and has normal PSV in the main graft renal artery and a mean RI of approximately 0.7. There is currently no randomized controlled trial examining the efficacy of EVIs over medical therapy alone. Patel et al, in a retrospective study, showed that 10-year transplant survival after revascularization for TRAS was the same as patients who had never had TRAS[23]. Ngo et al reviewed outcomes following PTA in 26 case series and 6 cohort studies including 884 cases, and showed that the majority of studies reported procedural success rates higher than 90% and clinical success rates (improvements in blood pressure or eGFR levels) were in the range 65.5-94%. Additionally, the complication rate was 9.9%, and the most frequently observed were vessel dissection, puncture site hematoma and vessel thrombosis respectively. In comparing treatment with PTA alone and treatment by means of stenting, Ngo et al reported a lower re-intervention rate in the stented group (9.1% vs. 18.9%) [24]. though a recent cohort study showed that event-free survival was significantly higher in the stented group at 1 year, but similar between groups at 10 years [25].

CONCLUSIONS

TRAS occurs potentially anytime post renal transplantation. Even late diagnosis and adjustment of TRAS can prevent graft morbidity or its loss. DUS is frequently used as the first-line imaging modality in TRAS, but it is highly operator dependent and may miss cases in early stages. Endovascular interventions (EVIs) such as percutaneous transluminal angioplasty (PTA) resulted in significant improvement in graft functions and lead to favorable outcomes. Our case demonstrates that graft can be saved even if renal artery stenosis is diagnosed after several months of dialysis and diagnosis of end stage renal disease post transplantation.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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