Renal Replacement Therapy

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Percutaneous transluminal angioplasty with carbon dioxide for peripheral arterial disease after kidney transplantation: a case report with literature review

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Abstract

Background: Arteriosclerosis may progress and lead to peripheral arterial disease (PAD) during the waiting period until kidney transplantation in end-stage kidney disease (ESKD) patients. Additionally, contrast-induced nephropathy (CIN) of a kidney allograft after the examination and treatment for PAD is problematic. Here, we report the case of a kidney transplant recipient with PAD in the lower extremities who underwent percutaneous transluminal angioplasty (PTA) with carbon dioxide to prevent CIN incidence.

Case presentation: A 57-year-old woman underwent a cadaveric kidney transplant when she was 49 years old. Immunosuppression was maintained with tacrolimus, methylprednisolone, and mycophenolate mofetil. Her post-transplant course was uneventful, and serum creatinine level was maintained at 1.1–1.3 mg/dL. Intermittent claudication of the lower legs began 3 years after transplantation. Under saline intravenous rehydration, computed tomographic angiographies were performed, and the patient was diagnosed with PAD in the bilateral lower extremities. Total PTA was performed thrice for PAD in the lower extremities via a combination of carbon dioxide and iodinated contrast medium to prevent CIN incidence at 3, 4, and 7 years after kidney transplantation. The patient's recoveries were uneventful. One year later, the serum creatinine level was maintained at 0.9–1.1 mg/dL, and since then, the patient has shown no evidence of recurrence.

Conclusions: In a kidney transplant recipient with PAD, PTA with carbon dioxide was effective to minimize the volumes of iodinated contrast medium and prevent CIN incidence.

Keywords: Arteriosclerosis obliterans, Carbon dioxide, Contrast-induced nephropathy, Kidney transplantation, Percutaneous transluminal angioplasty, Peripheral arterial disease

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Background

Arteriosclerosis may progress and lead to peripheral arterial disease (PAD) during the waiting period until kidney transplantation in end-stage kidney disease (ESKD) patients, and the symptoms of PAD may be noticed after kidney transplantation. Moreover, PAD is associated with cardiovascular events and mortality [1–4].

Kidney transplant recipients are highly susceptible to chronic kidney disease (CKD) [5]. CKD is the most common risk factor for contrast-induced nephropathy (CIN) [6]. Therefore, CIN due to iodinated contrast medium after the examination and treatment for PAD is problematic for kidney transplant patients [7, 8].

Here, we report the case of a kidney transplant recipient with PAD in the lower extremities who underwent percutaneous transluminal angioplasty (PTA) with carbon dioxide to prevent CIN incidence. Written informed consent for the use of personal information was obtained from the patient.

Case presentation

A 57-year-old woman received a cadaveric kidney transplant (left kidney graft) for ESKD due to lupus nephritis when she was 49 years old. Immunosuppression was induced with tacrolimus, methylprednisolone, mycophenolate mofetil, and basiliximab for 20 days and maintained with tacrolimus (1.5 mg/day), methylprednisolone (4 mg/day), and mycophenolate mofetil (750 mg/day). Her post-transplant course was uneventful, and serum creatinine level and body weight were maintained within the ranges of 1.1–1.3 mg/dL and 46–49 kg, respectively. However, 3 years post-transplantation, intermittent claudication of the lower extremities was observed. Under saline intravenous rehydration before and after (each 500 mL), computed tomographic angiographies (CTAs) were performed thrice with iohexol with an iodine concentration of 300 mg/ml (Ioverin 300; Teva Takeda Pharma Ltd., Nagoya, Japan): the amount of the administered iodinated contrast medium was 100 mL for each CTA, and the patient was diagnosed with PAD in the bilateral lower extremities at 3, 4, and 7 years after kidney transplantation (Fig. 1a–c). PTAs were performed thrice for PAD in the lower extremities via a combination of carbon dioxide (SODA CARTRIDGE; NIPPON TANSAN GAS CO., LTD., Tochigi, Japan; 200 mL for each PTA) for all lesions and iodixanol with an iodine concentration of 320 mg/ml (Visipaque 320; Daiichi Sankyo, Tokyo, Japan) for only below-the-knee arterial stenotic lesions to prevent the incidence of CIN at 3, 4, and 7 years after kidney transplantation (Fig. 1d–f); the amounts of the administered iodinated contrast medium at these PTAs were 15 mL, 30 mL, and 20 mL, respectively. We used the iodinated contrast medium in addition to carbon dioxide for below-the-knee arterial stenotic lesions in the patient due to the defocused image of the below-the-knee arterial stenotic lesions produced by carbon dioxide. The patient had leg pain for 2 weeks only after the first PTA but did not have any major complications after these PTAs. One year later, the serum creatinine level was maintained at 0.9–1.1 mg/dL (Fig. 2), and the patient has shown no evidence of recurrence.

Discussion

CIN is a common cause of hospital-acquired acute kidney injury [9]. Neyra et al. reported that CIN was associated with adverse in-hospital and long-term outcomes in both CKD and non-CKD patients [10]. Moreover, several studies demonstrated that CIN was associated with the development of CKD [11–13].

Kidney transplant recipients require calcineurin inhibitors for immunosuppressive treatment to prevent graft rejection, but kidney allograft function is mostly reduced as a result of this usage due to the nephrotoxicity of the calcineurin inhibitor and non-immunosuppressive burden [5]. Ahuja et al. reported that 21.2% of kidney transplant patients had CIN [7]. In a report by Light et al., CIN was more common and severe in patients with kidney allograft dysfunction than those without [14].

Cigarroa et al. advocated a guideline to limit iodinated contrast medium to significantly reduce the incidence of CIN: 5 mL of iodinated contrast medium per kilogram body weight/serum creatinine (mg/dL) with a maximum dose of 300 mL [15]. According to a cohort study by Gruberg et al. regarding CKD patients (baseline serum creatinine ≥ 1.8 mg/dL) undergoing percutaneous coronary intervention (PCI), the amount of iodinated contrast medium was significantly higher in patients who developed CIN compared with those who did not develop CIN (261 ± 148 mL vs 214 ± 98 mL) [16]. In a study regarding CKD patients (serum creatinine > 1.2 mg/dL and/or estimated creatinine clearance (CrCl) < 70 mL/min) undergoing elective coronary and/or peripheral angiography and/or angioplasty, Briguori et al. identified a volume of iodinated contrast medium ≥ 140 mL as the best cutoff value to predict the occurrence of CIN (sensitivity 89%, specificity 55%) [17]. In a report by Laskey et al. regarding patients undergoing PCI, the amount of iodinated contrast medium tended to be higher in patients who developed CIN compared with those who did not develop CIN (255 ± 124 mL vs 224 ± 112 mL), and the authors concluded that a ratio of the volume of iodinated contrast medium to the CrCl (V/CrCl) > 3.7 was a significant and independent predictor of developing CIN after PCI in the unselected patient population including both CKD and non-CKD patients [18]. Nevertheless, clinicians should minimize the volumes of

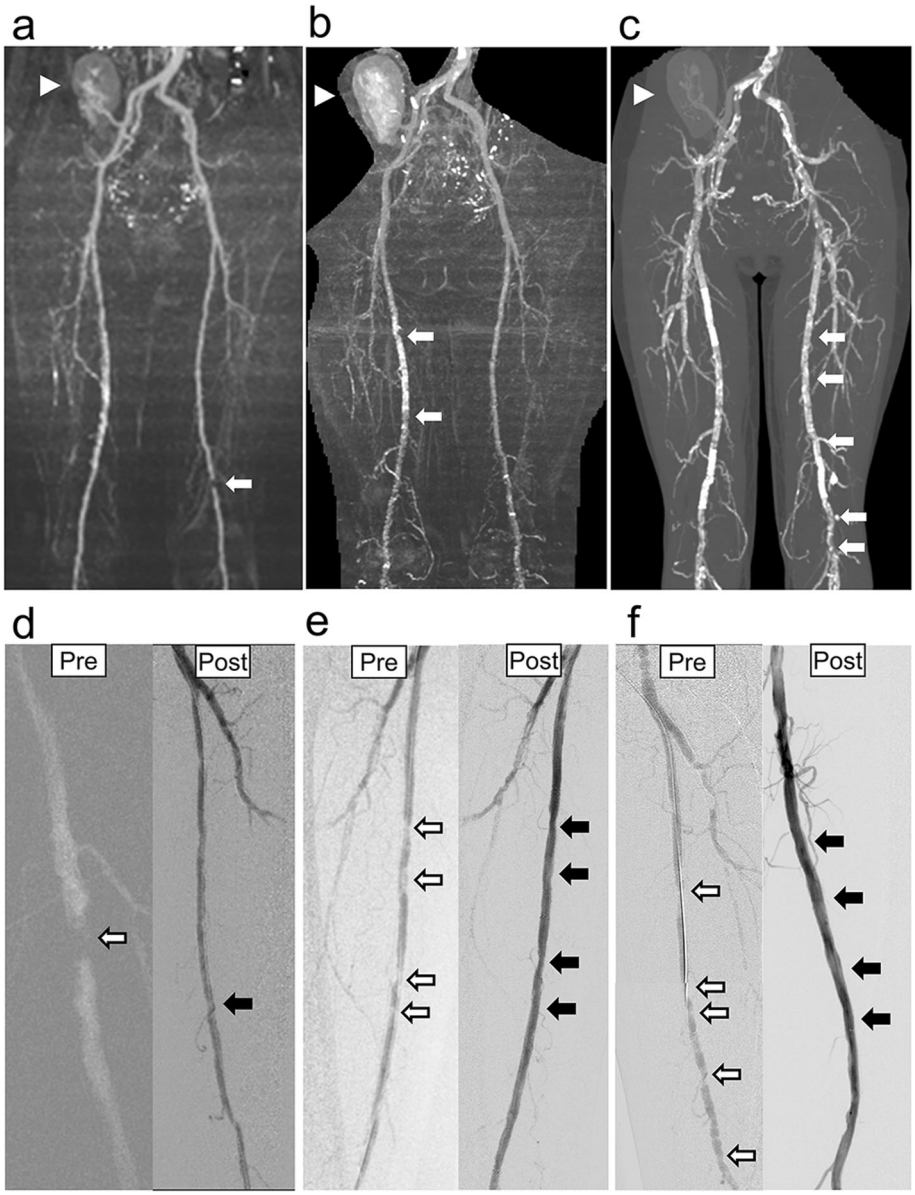

Fig. 1 Computed tomographic angiography (CTA) and percutaneous transluminal angioplasty (PTA) for peripheral arterial disease in a kidney transplant recipient. CTA revealing arterial stenotic lesions in the left or right femoral artery (*white arrows*) and the kidney graft in the right retroperitoneal space (*white arrow heads*): **a** first, **b** second, and **c** third CTA. Angiography with carbon dioxide or iodinated contrast medium revealing stenotic lesions before and after PTA: **d** first PTA by carbon dioxide, **e** second PTA by iodinated contrast medium, and **f** third PTA by carbon dioxide at pre-PTA and iodinated contrast medium at post-PTA (pre-PTA, *white arrows*; post-PTA, *black arrows*)

iodinated contrast medium at the time of examination and treatment for PAD in kidney transplant recipients.

Carbon dioxide is safely transported to the lungs, where it is eliminated by exhalation as a result of its 20-fold greater solubility in blood compared with oxygen and its ability to combine with blood buffers [19]. In guidelines on the use of iodinated contrast medium in patients with kidney disease which were developed in collaboration with the Japanese Society of Nephrology, the Japan Radiological Society, and the Japanese Circulation Society [20], the use of carbon dioxide was not mentioned to prevent CIN in patients with kidney disease. However, carbon dioxide has been used as an intra-arterial contrast medium during angiography-guided interventions in patients with PAD and kidney dysfunction because of its status as a non-allergen, affordability, and the absence of nephrotoxicity [21]. Moreover, the quality of angiography with carbon dioxide has improved due to the development of radiographic technology [22].

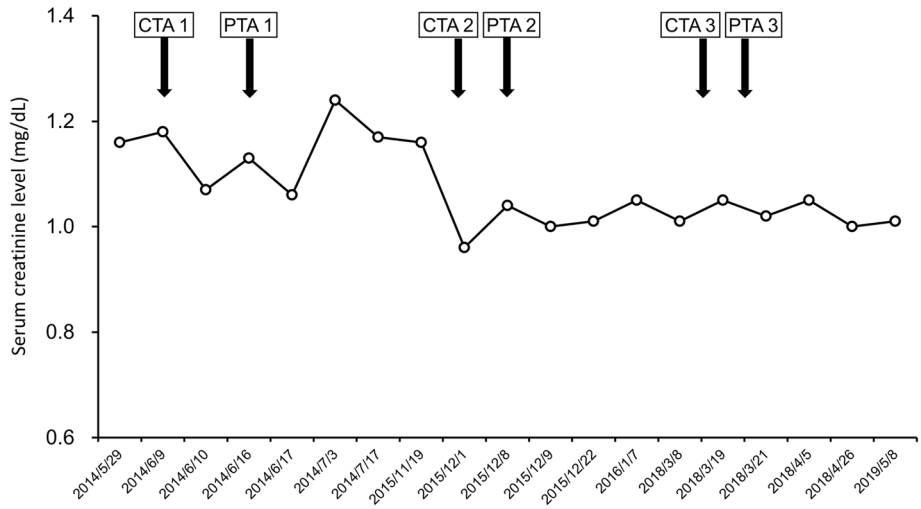

Fig. 2 Transition of serum creatinine level after computed tomographic angiography and percutaneous transluminal angioplasty for peripheral arterial disease in a kidney transplant recipient. CTA, computed tomographic angiography; PTA, percutaneous transluminal angioplasty

In a prospective study for patients with CKD undergoing peripheral angioplasty procedures, the incidence of CIN was significantly higher in the iodinated contrast medium group (29%) compared with the carbon dioxide group (14%) [23]. In a single-center study of carbon dioxide angiography for guiding kidney-related interventions in CKD (serum creatinine ≥ 3.0 mg/dL) patients with Takayasu arteritis, the incidence of CIN was higher in the iodinated contrast medium group (50%, 1 of 2 patients) compared with the carbon dioxide group (0%, 0 of 4 patients) [21]. In the single-center study, some patients felt mild transient abdominal discomfort immediately after carbon dioxide injection; however, none had nausea, vomiting, hypotension, narcosis, air contamination-related complications, or late complications related to carbon dioxide angiography. In a prospective multicenter trial of carbon dioxide angiography for PAD in CKD patients, the average doses of carbon dioxide and iodinated contrast medium were 281.4 ± 155.8 mL and 15.0 ± 18.1 mL, respectively, and the incidence of CIN was 5.1% [24]. In the multicenter trial, carbon dioxide-related complications occurred in 17.3% of the patients as well as leg pain (8.1%), abdominal pain (6.1%), diarrhea (1.0%), and non-occlusive mesenteric ischemia (2.0%).

In our case, we used the iodinated contrast medium in addition to carbon dioxide for below-the-knee arterial stenotic lesions in the kidney transplant patient due to the defocused image of below-the-knee stenotic lesions produced by carbon dioxide. Total PTAs with carbon dioxide (200 mL per each PTA) were performed 3 times for PAD in the lower extremities and minimized the volumes of iodinated contrast medium (15–30 mL) after kidney transplantation. The patient had leg pain for 2 weeks only after the first PTA but did not have any major complications after these PTAs. One year later, the serum creatinine level was maintained, and the patient has shown no evidence of recurrence.

Conclusions

In a kidney transplant recipient with PAD, PTA with carbon dioxide was effective to minimize the volumes of iodinated contrast medium and prevent CIN incidence.

Literature review

There are 7 reports on intra-arterial treatment with carbon dioxide for PADs in kidney transplant recipients (Table 1) [25–31]. In 5 out of 7 reports, PTA with carbon dioxide for the stenosis of kidney transplant graft artery or iliac artery was performed [25–29]. In the remaining 2 reports, embolization with carbon dioxide for arteriovenous fistula occurring in kidney transplant graft after biopsy was performed [30, 31]. In these reports, mean volumes of carbon dioxide, iodinated, and gadolinium contrast medium were 20–114.6, 0–18.3, and 4–44 mL, respectively. In 4 out of 7 reports, the mean serum creatinine levels were maintained after intra-arterial treatment [25, 28, 29, 31]. In the only 1 report, the mean serum creatinine level elevated after intra-arterial treatment [26]. In the remaining 2 reports, there were no data for the mean serum creatinine levels before or after intra-arterial treatment [27, 30]. There were no descriptions of adverse events (except for kidney function) after intra-arterial treatment with carbon dioxide in all 7 reports. There are no reports on PTA with carbon dioxide for PAD in lower extremity after kidney transplantation.

Table 1 Previous reports on intra-arterial treatment with carbon dioxide for peripheral arterial diseases in kidney transplant recipients

Author	Pt number (M/F), and mean age (range)	Mean duration (range) after KT	Type of peripheral arterial diseases	Type of treatment	Mean volumes of CO_2/IC (mL)	Mean s-Cr before treatment (mg/dL)	Mean s-Cr after treatment (mg/dL)	Complications after treatment
Koratala et al. [25]	1 (1/0), 43	0.25	Stenosis of KT graft artery	Balloon AG	n/a	3.1	1.5	None
Caridi et al. [26]	21 (13/8), n/a (22–81)	n/a	Stenosis of KT graft artery	Balloon AG	114.6/8.5*	1.2	2.3	None
Moresco et al. [27]	6 (3/3), 41 (33–53)	5.25 (0.30–13)	Stenosis of KT graft artery	Balloon AG	20/18.3	n/a	n/a	s-Cr elevated in one patient
Spinosa et al. [28]	4 (4/0), 50 (36–64)	n/a	Stenosis of KT graft artery or iliac artery	Balloon AG or stent insertion	40/44**	2.9	3.0	Acute kidney injury occurred in one patient
Kuo et al. [29]	1 (0/1), 44	1	Stenosis of KT graft artery	Balloon AG	n/a/0	2.8	2.1	None
Cheng et al. [30]	1 (0/1), 38	0.25	AVF of KT graft after biopsy	Embolization of AVF	30/9	2.7	n/a	None
Nicolini et al. [31]	3 (0/3), 35 (10–58)	6.19 (2.79–10)	AVF of KT graft after biopsy	Embolization of AVF	20/4**	4.2	3.5	None

AG angioplasty, *AVF* arteriovenous fistula, CO_2 carbon dioxide, *IC* iodinated contrast medium, *KT* kidney transplantation, *M/F* male/female, *n/a* not available, *Pt* patient, *PTA* percutaneous transluminal angioplasty, *s-Cr* serum creatinine

*Iodinated contrast medium was used in six patients

**Gadolinium contrast medium

Authors' contributions
MB designed and wrote the manuscript. SM, SS, TS, MM, ST, HO, and HK provided intellectual content of critical importance to the work described. All authors read and approved the final manuscript.

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Availability of data and materials
All data supporting our findings are contained within the manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patients to publish this case report and any accompanying images. A copy of the written consent form is available for review by the editor of this journal.

Competing interests
The authors declare that they have no competing interests.

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