

Ischemic reperfusion injury of renal transplant mimics acute rejection on renal scintigraphy in early post-operative period

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ABSTRACT

Renal scintigraphy of a renal graft is a non-invasive imaging used to evaluate renal graft dysfunction in relay postoperative period. We presented the case of a 42-year-old man when underwent renal transplantation and developed anuria with severe renal impairment. Renal scintigraphy yielded no visualization of the renal graft. Subsequently, the patient underwent an exploratory laparotomy. The graft was found to have normal perfusion, and a surgical biopsy suggestive of an acute perfusion injury and mild tubular necrosis. The patient recovered with conservative therapy. This case highlights a common limitation of renal scintigraphy in a post-renal-transplantation patient with severe renal impairment.

Introduction

Renal scintigraphy is a widely available test that provides information about the morphology and function of the kidney by utilizing non-nephrotoxic radiopharmaceuticals with high renal clearance. Post-renal scintigraphy is usually used to evaluate graft dysfunction in the first few days after surgery. This form of scintigraphy can be helpful for distinguishing patients with acute surgical conditions versus patients with medical conditions.¹

Knowledge of the surgical approach that was used and the severity of renal impairment is important in the interpretation of scintigraphic studies of renal transplants. Non-visualization of the transplant not necessary indicates acute surgical emergency such as acute renal vein or renal artery thrombosis, but it could be related to poor radiotracer uptake and/or excretion due to severe renal dysfunction, acute tubular necrosis, acute ischemia perfusion injury, or acute rejection.² It is essential to understand the pitfalls and limitations of renal scintigraphy in this clinical setting in order to avoid unnecessary intervention and/or futile surgery.

Case presentation

A 42-year-old man with end-stage renal disease of unknown etiology had been on regular dialysis for 11 years, with mild left ventricular systolic dysfunction, and secondary hyperparathyroidism. This patient underwent a living related donor renal transplant; this operation was

uneventful, and the patient was transferred to the intensive care unit (ICU). Later, he developed anuria, poor renal function, a serum creatinine level of 1100 $\mu\text{mol/L}$, and an estimated glomerular filtration rate of 4 mL/min/1.73m^2 . A renal doppler ultrasound demonstrated normal blood flow to the transplant with normal systolic and diastolic flow, and a color power image showed normal perfusion of the transplant (Fig. 1 A & B).

Due to the patient's persistent anuria and progressively worsening renal function, renal scintigraphy was requested on the second post-operative day to assess the blood flow of the transplant. Renal scintigraphy with technetium-99 m diethylenetriamine pentatectate acid (^{99m}Tc DTPA) revealed that perfusion to the transplant was completely absent consistent with that of a non-functioning graft (Fig. 2 A & B). Subsequently, the patient underwent an exploratory laparotomy to assess graft perfusion and exclude other major complications such as vascular compromise. The graft was found to be healthy with good perfusion. A surgical biopsy showed no evidence of acute cellular rejection, morphological changes suggestive of perfusion injury, and mild acute tubular injury.

Overall, these findings were suggestive of a perfusion injury rather than acute rejection. The patient was readmitted to the ICU on intermittent hemodialysis with an induction treatment of methylprednisolone and anti-thymocyte globulin. Two days after the patient was transferred to the floor, his urine output had improved and his serum creatinine level had dropped from 1100 $\mu\text{mol/L}$ to 420 $\mu\text{mol/L}$. Several days later, he was discharged in good condition.

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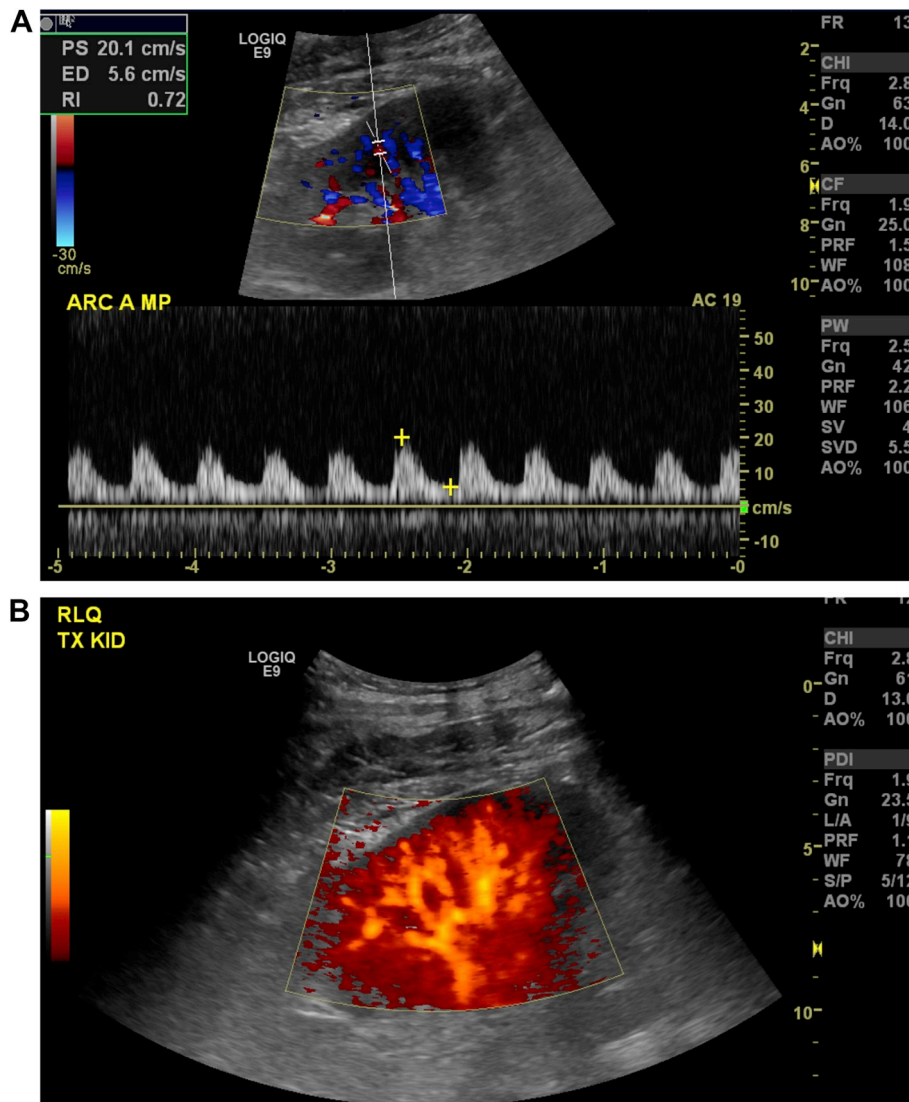


Fig. 1. Spectral doppler waveforms ultrasound and color power image of the transplant.

A. A spectral doppler waveforms ultrasound image of the arcuate artery demonstrates normal systolic and diastolic flow.

B. A color power image of the transplant demonstrates normal perfusion of the transplant.

Discussion

This case highlights an important limitation and pitfall of renal scintigraphy in early post-transplant evaluation. If renal dysfunction is severe and the serum creatinine level is greater than 530 $\mu\text{mol/L}$ (6 mg/dL), the value of renal scintigraphy may be limited because of poor radiotracer uptake and/or excretion. $^{99\text{m}}\text{Tc}$ Mertiatide (MAG 3) is the preferred radiopharmaceutical for renal transplants because it is secreted by renal tubules and its uptake occurs even in the setting of an impaired GFR, unlike $^{99\text{m}}\text{Tc}$ Pentetic acids such as $^{99\text{m}}\text{Tc}$ DTPA, which depends on the GFR and is likely to decrease if the serum creatinine level is greater than 220 $\mu\text{mol/L}$ (2.5 mg/L).³

Knowledge of the transplant function and severity of renal impairment is important in interpreting scintigraphic studies of renal transplantation. In the early postoperative period, absent or severely reduced graft perfusion is nonspecific and can occur due to arterial thrombosis, acute parenchymal failure such as acute severe tubular necrosis (ATN), acute ischemia reperfusion injury (IRI), or urinary obstruction. Because of the nonspecific, nondiagnostic capability of renal scintigraphy for post-transplant patients with severe impaired renal function, clinical correlation is extremely important. Ultrasound-guided needle biopsy

remains the gold standard for confirmatory diagnosis of ATN and acute rejection.⁴

Ideally, all new transplants should be scanned within 24–48 hours of surgery to provide a baseline for future comparison when problems develop. Post-transplant renal scintigraphy is particularly valuable in certain clinical scenarios, such as in cases of suspected ischemia. Renal scintigraphy can also be used to select the optimal time for biopsy in cases of delayed graft function (DGF), as serial studies at frequent intervals (every 2–3 days) are needed to distinguish between ATN and rejection by identifying the decline in tracer accumulation that indicates rejection. In ATN with relatively preserved renal function, renal scintigraphy typically shows good perfusion during the angiographic phase and progressive tracer accumulation during the parenchymal phase, with minimal excretion of the tracer into the collecting system and the urinary bladder, but poor parenchymal uptake, and high background activity in acute rejection.

In this patient, a surgical biopsy of the transplant revealed mild ATN and an overall pattern suggestive of a perfusion injury. Ischemia reperfusion injury (IRI) is an inevitable event in renal transplantation. The pathophysiology of IRI can be classified into two paradigms: the hemodynamic paradigm and the immune paradigm. The hemodynamic

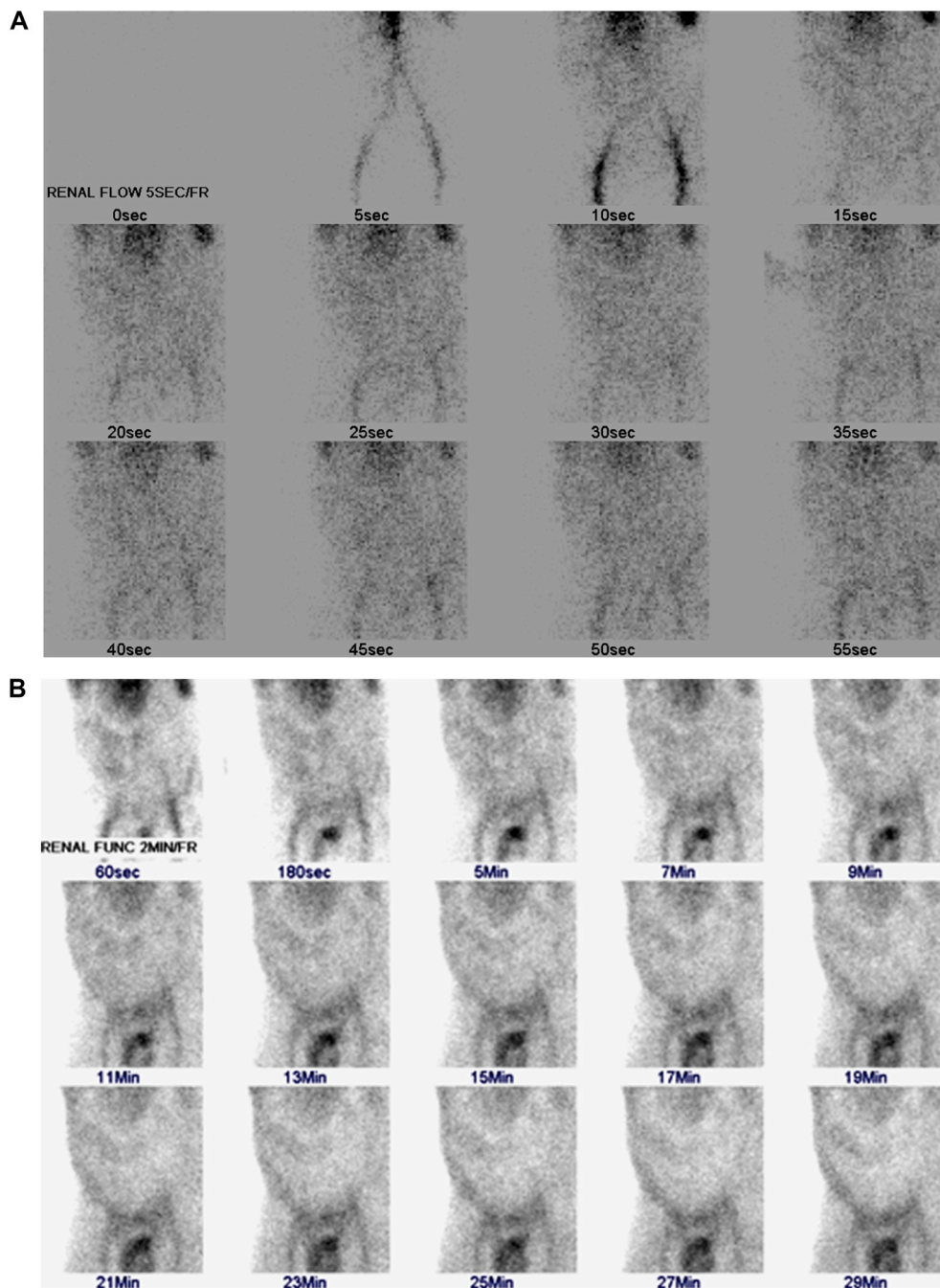


Fig. 2. Post-transplant ^{99m}Tc DTPA renal scintigraphy images.

A. Sequential angiographic-phase images demonstrate normal flow in the aorta and great vessels with no identified flow to transplanted kidney.

B. Sequential 2-minute renographic-phase images demonstrate excessive background activity with no tracer accumulation in the transplanted kidney.

paradigm has been described as the reduction of oxygen delivery due to blood flow interruption, involving many hormonal systems as well as the oxygen-free radicals produced after reperfusion.⁵

This case highlighted an important limitation of the use of renal scintigraphy in the early post-renal-transplantation period for patients with severe renal failure (if serum creatinine greater than 6 mg/dL), the diagnostic value of renal scintigraphy is limited due to poor tracer uptake and/or excretion. Failure to visualize the renal graft in the early post-transplantation period is nonspecific and has various medical such as ATN, IRI, and, acute rejection, and surgical etiologies such as renal vein or renal artery thrombosis. Therefore, clinical correlation is important. Other imaging modalities such as doppler ultrasound and ultrasound-guided needle biopsy are the gold-standard tests for the

confirmation of ATN or acute rejection. Knowledge the limitation of the renal scintigraphy in patient with severe renal impairment in immediate post-operative period is essential to avoid unnecessary high-risk interventions or futile surgeries.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.urocr.2020.101122>.

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