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Aortic Dissection and Severe Renal Failure 6 Years After Kidney Transplantation

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Abstract: We report the case of a patient with long-term history of hypertension, presenting with transient neurological disorders and severe graft failure several years after kidney transplantation. Cause of end-stage renal disease was hypertensive nephrosclerosis. Chronic hemodialysis lasted for 1 year. After transplantation and throughout follow-up, serum creatinine ranged from 200 to 230 $\mu\text{mol/L}$ and maintenance immunosuppression included sirolimus and low-dose steroids. Six years after transplantation, the patient presented with right hip pain radiating to the lower back, transient aphasia, confusion, and hemiparesis. Surprisingly, progressive anuria was established requiring dialysis. After numerous nonconclusive investigations including renal histology, a contrast computed tomography scan discovered a Stanford B aortic dissection from the left common carotid artery and left subclavian artery to bilateral internal and external iliac arteries, including the right femoral artery. No surgical treatment was opted and hemodialysis, tight control of blood pressure and oral anticoagulation were established. Immunosuppression was lightened to low-dose steroids alone. After 8 months, chronic dialysis was stopped, and today, 22 months after the diagnosis of aortic dissection, the patient is doing well with a still functioning graft (creatinine, 377 $\mu\text{mol/L}$; modification of diet in renal disease-glomerular filtration rate, 15 mL/min), and without any other immunosuppression than low-dose steroids.

(*Transplantation Direct* 2017;3: e202; doi: 10.1097/TXD.0000000000000723. Published online 9 August, 2017.)

Cardiovascular complications are frequent after kidney transplantation and represent the main cause of death.¹ Hypertension is commonly associated. Causes of hypertension among the kidney transplant population are numerous including impaired graft function and the immunosuppressive therapy used.^{1,2} Aortic dissection is a rare and infrequent reported event.^{3,4} We report a case of aortic dissection

revealed by severe graft failure several years after kidney transplantation.

CASE REPORT

A 63-year-old Ghanaian man underwent first kidney transplantation in February, 2008. Chronic hemodialysis was started 1 year before due to end-stage renal failure probably secondary to hypertensive nephrosclerosis. Pretransplant Doppler ultrasound (US) (1 month before transplantation) and computed tomography (CT) angiography showed minimal arterial calcification in lower limbs. No history of smoking or alcohol abuse was noted. The donor was a 61-year-old Caucasian male without any known history of disease. Reason of death was hemorrhagic stroke. The right kidney was implanted in the right iliac fossa after 22 hours of cold ischemia time. No surgical complication was encountered. Induction immunosuppression consisted of Basiliximab. Delayed graft function occurred related to tacrolimus nephrotoxicity proven on histology. Seven hemodialysis sessions were performed, and tacrolimus was switched to sirolimus in addition to low-dose steroids and mycophenolic acid. Serum creatinine stabilized and remained around 2.3 mg/dL (200 $\mu\text{mol/L}$; estimated GFR [e-GFR], 35.5 mL/min) throughout follow-up. Antihypertensive treatment included amlodipine, 10 mg; perindopril, 5 mg; bisoprolol, 1.25 mg; urapidil, 180 mg; and furosemide, 40 mg. Despite a claimed good compliance, normal blood pressure levels were rarely achieved. Follow-up was done regularly every 3 to 4 months.

Received 17 March 2017. Revision requested 7 July 2017.

Accepted 14 July 2017.

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The authors declare no funding or conflict of interest.

A.D. participated in writing and translating the article, bibliographic research and clinical care of the patient. A.L.F. participated in writing the article, and clinical care of the patient. D.C. participated in writing and translating the article, and clinical care of the patient during the follow-up.

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000000723

Six years after transplantation, the patient presented with right hip pain radiating to the lower back, primarily diagnosed as sciatica. Few days later, a transient ischemic attack with aphasia, confusion, and left hemiparesis occurred. Oligo-anuria was observed after 48 hours. Blood pressure was 157/95 mm Hg (similar in both arms), and pulse rate was 93 beats per minute regular. He had a grade II systolic murmur related to a known mitral insufficiency. There were no carotid bruits. The electrocardiogram showed normal sinus rhythm. The kidney graft remained painless, without any murmur. A noncontrast cerebral CT scan was normal (no ischemic and no hemorrhagic stroke). Blood tests revealed a creatinine of 4.76 mg/dL (419 μ mol/L), urinary test strip showed 3 crosses of protein and 2 crosses of blood. The graft US did not reveal neither hydronephrosis nor graft arterial stenosis. The resistance index was 0.87 on pedicular artery and 0.81 on the hilum (comparable to previous US examinations), and cortical perfusion was normal. Sirolimus trough level was 7.5 ng/mL. Comprehensive pulmonary, cardiac, infectious, and immunological evaluations were all negative, including donor-specific anti-HLA antibodies (DSA) (HD Luminex test) and polymerase chain reactions for cytomegalovirus, Epstein-Barr virus, and BK virus. The patient had no fever, but C-reactive protein (CRP) was elevated (18 mg/dL) without any growth in repeated blood and urine cultures. LDH was also elevated (1800 U/L). Two days later, serum creatinine level increased to 10.41 mg/dL (916 μ mol/L), and the patient became anuric. Blood pressure was still high, around 160/90 mm Hg. Hemodialysis was started, and a graft biopsy was performed, searching for graft rejection. Histology showed severe ischemic acute tubular necrosis, associated with multifocal fibrosis and interstitial infiltration. No complement component 4d fixation was observed and DSA remained negative. Based on histology findings and persistent anuria, sirolimus was discontinued. To clarify the persistent inflammatory state (elevated CRP and LDH), a total body contrast CT scan was performed on day 7 after first symptoms appeared.

Interestingly, a Stanford B aortic dissection was discovered, which extended from the left common carotid artery and left subclavian artery to bilateral internal and external iliac arteries, including the right femoral artery (Figure 1). The tunica intima was thickened, suggestive of a recent dissection. The



FIGURE 1. Scanographic axial view of the thorax showing the aortic dissection, with true lumen (black arrow) and false lumen (white arrow).



FIGURE 2. Scanographic axial view of the pelvis, after division of the iliac arteries. The kidney graft is in the right iliac fossa and presents delayed contrast enhancement.

kidney graft artery was in the true lumen, the graft showed a delayed contrast enhancement, though it was well differentiated (Figure 2). The right vertebral artery, the celiac artery, the right renal artery, the superior mesenteric artery, and inferior mesenteric artery originate from the true lumen (Figure 3). In fact, possible mechanism of kidney graft failure was a transient ischemia due to intimal flap obstructing the graft artery.

The patient was referred for cardiovascular evaluation. The echocardiogram showed that the aorta was not dilated, and apart from left ventricular hypertrophy, no other disorder was noted. Although kidney graft failure was almost certainly caused by hemodynamic consequences of the aortic dissection, it was decided neither to fenestrate the abdominal aorta nor to place a stent. Because no surgical intervention was indicated for this type of aortic dissection, medical management was

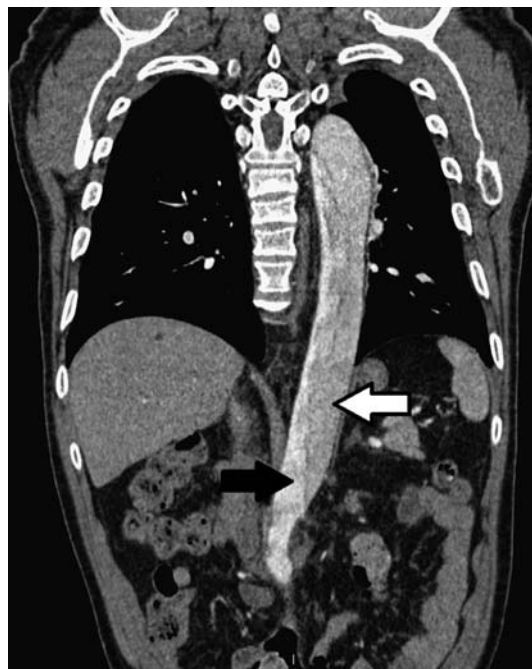


FIGURE 3. Scanographic frontal view of the thorax and abdomen showing the aortic dissection, with true lumen (black arrow) and false lumen (white arrow).

intensified as recommended for a Stanford B dissection. Blood pressure control required intravenous nicardipin followed by oral triple therapy with bisoprolol (5 mg twice a day), urapidil (60 mg thrice a day), and nicardipin (50 mg twice a day). Oral anticoagulation consisted of warfarine. The patient was finally discharged on chronic hemodialysis 3 times a week without any neurological sequelae. CRP decreased to 30 mg/L after 1 week and was less than 5 mg/L 1 month later. Repeated contrast CT scan revealed no sign of evolution and a well-vascularized graft (without argument for a fenestration between lumens). Mycophenolic acid was stopped 2 months later in the absence of renal function recovery. Low-dose steroids were maintained. Unexpectedly, after 8 months of chronic hemodialysis, urine output gradually increased, and hemodialysis was discontinued. On the last follow-up visit on December 2016 (14 months after dialysis discontinuation), serum creatinine was 377 $\mu\text{mol/L}$, and e-GFR was 15 mL/min. Blood pressure was within normal ranges. A DSA anti-DQ2 was recognized for the first time 6 months after hemodialysis withdrawal. Because of advanced chronic renal failure and the presence of DSA, it was decided not to introduce any new immunosuppressant and avoid histology control. The patient was informed of a probable close return to chronic hemodialysis.

DISCUSSION

Our clinical observation illustrates the diagnostic challenge of a severe graft failure occurring several years after kidney transplantation secondary to an aortic dissection. Retrospectively, some clinical findings could dictate toward the diagnosis in our case. Graft failure occurred within days or concomitantly to a cerebral transient ischemic attack, and in fact, these episodes were certainly related to the aortic dissection. Neurological symptoms were probably induced by a diminished carotid blood flow (because CT scan revealed no extension of the dissection to the carotid arteries). Transient neurological symptoms in kidney transplant recipients are somewhat frequent and usually associated to hypertension and cardiovascular complications, such as carotid atherosclerotic disease.⁵ The patient noted some clinical signs of severe atherosclerotic disease during previous medical visits. For example, he was complaining of erectile dysfunction and occasional leg pain. Although the patient was referred for specialist's advice, no definitive conclusions were drawn.

As stated before, blood pressure was indeed never well controlled since transplantation despite intense therapy, absence of calcineurin inhibitor treatment and dietary advices. In the general population, the strongest risk factors for aortic dissection are cardiac surgery, male sex, and hypertension.^{6,7} Hypertension is common after transplantation, especially in recipients with impaired graft function. This was the case in our patient with nonsatisfactory blood pressure and low e-GFR throughout follow-up. Even if well managed and controlled, hypertension remains a strong negative predictor of patient and graft survival.⁸ Our observation highlights the importance of strict blood pressure control after kidney transplantation. Guidelines for management of posttransplant hypertension recommend systematic measuring of blood pressure, with objectives less than 130/80 mm Hg.^{9,10}

The aortic dissection in our patient rapidly induced anuria probably due to hemodynamic hypoperfusion. Initial

Doppler US examination remained, nevertheless, normal. In fact, graft ischemia was due to a transient obstruction of the graft artery by intimal flap. One may hypothesize that his aorta could have been damaged by long-term hypertension and by turbulent flow induced by the arteriovenous fistula, which may have induced weakness of the media layer.¹¹ However, the latter is very unlikely because only a single case has been reported to date.¹²

In nontransplanted patients, renal symptoms are among the less frequent in case of aortic dissection.⁶ A longitudinal epidemiology study among 66 hospitalized patients with aortic dissection found only 15.5% with hematuria and 6% with oligoanuria.⁷ Acute renal failure is mostly related either to hemodynamic disorders or to the birth of both renal arteries from the false lumen. In these rare cases, reversal of end-stage renal disease mostly requires urgent endovascular treatment to avoid irreversible injury.¹³ Treatment of Stanford B aortic dissection includes primarily medical approach and/or aorta fenestration or stenting. Endovascular aortic repair showed superiority on survival rate only at long term.^{13,14}

Another atypical observation was the increased levels of CRP and LDH. As reported in the general population, aortic dissection *per se* may induce an inflammatory state.¹⁵ Our patient had unexplained and persistent inflammatory markers that motivated the CT scan prescription which confirmed the unexpected diagnosis of aortic dissection.

There are few published observations of aortic dissection. None of these observations were associated to severe renal dysfunction and were only focused on new techniques as well as anaesthesia management approaches for an urgent surgery.^{3,4}

CONCLUSIONS

Severe aortic dissection can be responsible of atypical graft failure with anuria and dialysis requirement several years after kidney transplantation. This diagnosis should be considered mostly in patients with uncontrolled blood pressure, vague and transient neurological disorders, and biological positivity of inflammatory markers. Contrast CT scan is the best procedure for the diagnosis and discussion of therapeutic approach. Renal function may partially recover, even several months later, if blood pressure is well controlled, under efficient anticoagulant therapy and without endovascular treatment.

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