



Case Report

Chronic Renal Failure in a Post-Kidney Transplant Patient with Kidney Graft Hydronephrosis and Renal Anemia

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ABSTRACT

A kidney transplant is the ideal option for End Stage Renal Disease (ESRD). A successful kidney transplant will improve the excretory function of the kidney so that it can return the quality of life for patients with Chronic Kidney Disease (CKD) to normal. However, in some cases of transplant recipients, the grafted kidney does not function optimally due to several complications. Post-kidney transplant complications may occur, which are classified into two groups, namely surgical and medical complications. Cases of obstruction characterized by hydronephrosis of the graft kidney, a post-transplant surgical complication. The most common location is where the ureter implants into the bladder, namely the distal 1/3 ureter. The most important medical or non-surgical complications are rejection or rejection reactions ranging from acute, hyperacute and chronic. Chronic rejection is the gradual loss of function of the transplanted organ over several months to years after the organ is functioning normally. Chronic rejection is difficult to treat where the use of immunosuppression is of little use because the damage has already occurred, so the patient again needs another renal replacement therapy, namely hemodialysis. The following is a case report of a patient after a kidney transplant six years ago, experienced decreased kidney function again and had to receive hemodialysis therapy due to a kidney graft/hydronephrosis graft.

INTRODUCTION

The 2018 Indonesia Renal Registry (IRR) noted that cases of End Stage Renal Disease (ESRD) were increasing every year, where 66,433 new cases had to undergo hemodialysis. ¹ Currently, kidney

transplantation is the most ideal choice for End Stage Renal Disease (ESRD) because it can improve quality of life compared to the two other main modalities of renal replacement therapy, namely hemodialysis and peritoneal dialysis. Apart from that, hemodialysis and

peritoneal dialysis are transitional therapies before the kidney transplant process is carried out.² The United States Renal Data System (USRDS) reported that between 1994-1998 and 1999-2003, the survival probability rate for kidney transplant patients was twice as high as for patients using dialysis methods.³

A successful kidney transplant not only improves kidney excretory function but also endocrine function, namely through restoring the synthesis of erythropoietin and vitamin D. However, in some cases of transplant recipients, the transplanted kidney (graft) does not function optimally with several complications occurring. After a kidney transplant, complications may occur, which can be classified into two groups, namely surgical and medical complications.⁴

Post-transplant surgical complications, in general, are urological and vascular complications that have a substantial influence on morbidity and mortality. Urological complications occur in 4-8% of patients, including urethral/ureteral obstruction and stenosis, urine leakage, and peritransplant fluid accumulation (hematoma, lymphocele, abscess, infection). Cases of obstruction characterized by hydronephrosis of the kidney graft occur in almost 2% of patients, usually within the first 6 months after transplantation. The most common location is at the site of implantation of the ureter into the bladder, where more than 90% of ureteral stenosis occurs in the distal 1/3 of the ureter. Abnormalities in the form of narrowing of the ureterovesical junction, which can be caused by scar tissue due to ischemia or rejection, technical errors in ureteroneocystostomy or kinking. Post-transplant vascular complications occur in 1-2%, including renal artery stenosis, infarction, arteriovenous fistula, pseudoaneurysm and renal vein thrombosis.⁴

The most important medical complications are rejection reactions ranging from acute, hyperacute and chronic. Chronic rejection is the loss of function of a transplanted organ that occurs slowly over several months to years after the organ

functions normally. Chronic rejection may have no visible symptoms, and kidney failure occurs slowly and progressively. Chronic rejection is also difficult to treat; immunosuppression is currently of little use as the damage has already been done, and the patient can return to dialysis. Apart from complications of rejection, anemia in post-transplant patients is also common. A cross-sectional analysis of transplant recipients found an anemia prevalence of 40%.^{2,4} The incidence of anemia increases by almost 26% in the 5 years after kidney transplantation.⁵

CASE REPORT

The male patient, Mr. HP, 43 years old, married, came complaining of discomfort in the waist and lower abdomen. The patient complained of left lower back pain that radiated to the front of the abdomen for the past 1 month. Pain is as if being pricked by a sharp object, but the pain comes and goes. There are no complaints of chest pain and heartburn and no complaints of cold sweat when pain occurs. There is no history of trauma or fever; sometimes, the patient feels nausea and bloating in the stomach. In January 2015, the patient was diagnosed with End Stage Renal Disease (PGTA) and underwent kidney replacement therapy in the form of hemodialysis. At that time, the patient often felt stomach ache and low back pain. This complaint has begun to decrease since the patient received kidney transplant therapy 6 years ago, and the pain only appears again when the patient is too tired or tense. The pain is not too bothersome and will go away on its own without treatment. But stomach pain often reappears.

The patient is routinely monitored to receive immunosuppressive therapy (prograf) and other drug therapy, namely, methylprednisolone, concept, herbesser. The patient is no longer undergoing hemodialysis kidney replacement therapy since the kidney transplant. Patients also routinely undergo laboratory tests, especially kidney function (urea, creatinine), and routine blood and tacrolimus levels. The patient experienced a

decrease in kidney function from the results of routine laboratory tests (urea 32, creatinine 2.02), a decrease in hemoglobin levels (Hb 8.6), impaired kidney function (urea 108, creatinine 5.13) and tacrolimus levels 11, 7 ng/mL. At that time, the patient's dose of immunosuppressive medication (prograf) was increased gradually to a dose of 5 mg (3 mg in the morning and 2 mg in the evening). The patient was also given an additional 30 mg darbopoetin alfa (NESP) injection therapy every 2 weeks. Because there was no improvement in hemoglobin levels, the NESP dose was increased by 40 mg every week. Patients complain of increasingly frequent low

back pain, nausea, weakness, and bloating and are often tired.

The patient had grade III hydronephrosis with hydro ureter proximal to the transplanted kidney without visible stones. On physical examination, it was found that the general condition was mildly ill, compos mentis consciousness, blood pressure (BP) 190/104, pulse 80x/minute with strong lift, respiratory rate 20x/minute, temperature afebrile, Body Mass Index (BMI) 29 (severe obesity), palpebral conjunctiva pale, sclera not icteric, no increase in JVP, heart and lung examination within normal limits, abdominal examination palpable kidneys palpable in the right lower quadrant, no tenderness.



Figure 1. Doppler ultrasound results

The patient had significant laboratory results: hemoglobin 6 g/dl, leukocytes 9.36 103/mm³, MCV 89.8 fL, MCH 28 Pg, MCHC 31 g/L, RDW-CV 15.90 %, ferritin 296.8 ng/ml, Fe 89 µg/ dL, TIBC 214 µg/dL, albumin 3.4 g/dl, urea 131 mg/dl, creatinine 7.45 mg/dl, uric acid 7.7 mg/dl. Based on Doppler ultrasound, it is known that the

kidney size is small according to the description of CKD. In the right iliac fossa, there is a renal transplant with the cortex appearing thickened and slightly hyperechoic. Moderate dilation of the Pelvic Calyceal System (PCS) was seen, and the Resistive Index (RI) of the renal arteries increased.

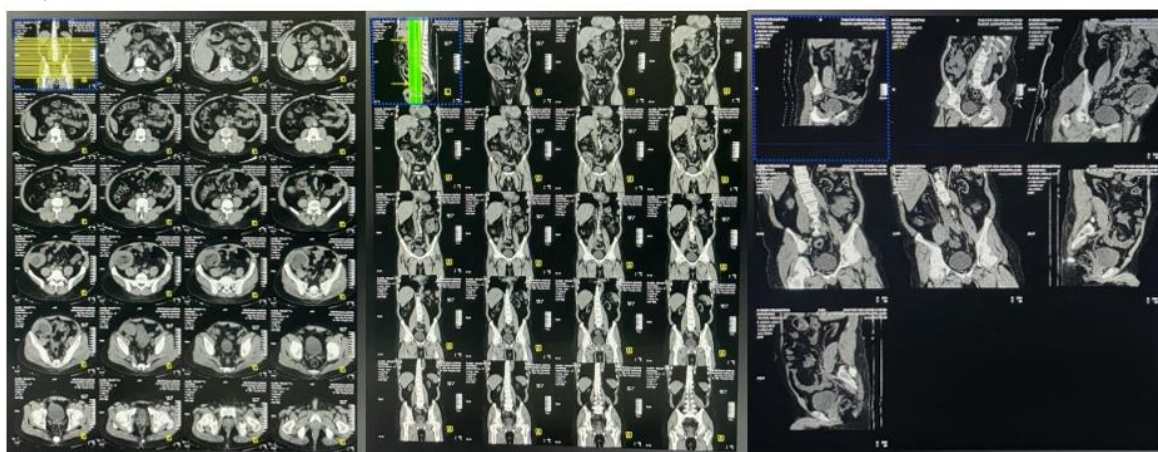


Figure 2. MSCT Scan Urologi Result

Based on the MSCT Urology Scan, it was found that there was atrophy of the right and left kidneys, grade III hydronephrosis with proximal hydroureter in the transplanted kidney, and no stones were seen in the urinary tract.

DISCUSSION

By definition, complications after kidney transplantation are divided into acute complications if they occur 1-2 weeks after transplantation and chronic complications if they occur > 3 months to years after transplantation. Complications in this patient are, by definition, chronic complications because complaints and laboratory abnormalities occurred within the last 1 year. A successful kidney transplantation improves not only renal excretory function but also metabolic-endocrine function, among others, through the restoration of erythropoietin synthesis. However, in some cases of transplant recipients, the grafted kidney does not function optimally, and several complications occur. After a kidney transplant, complications may occur, which can be classified into two groups, namely medical and surgical complications. The most important post-kidney transplant medical complications are rejection reactions ranging from acute, hyperacute and chronic.⁴

In this case, it is possible that rejection or chronic rejection has occurred, which is a

medical complication after a kidney transplant. Chronic rejection is the loss of function of a transplanted organ, occurring slowly over several months to years after the organ functions normally. Chronic rejection is more dangerous, characterized by replacement fibrosis of the graft organ parenchyma. This chronic rejection is mediated by chronic antibodies, which have an unfavorable long-term prognosis because treatment is rarely effective and is also difficult to treat. The use of immunosuppression in chronic rejection is not very useful because the damage has already occurred, and the patient often has to return to dialysis. The incidence varies greatly in the literature, with clinical manifestations ranging from mild, sometimes undiagnosed, to severe. 10 Chronic rejection may have no visible symptoms, and kidney failure occurs slowly and progressively.^{2,4}

Currently, long-term loss of graft function after transplantation is caused by multifactorial causes, both immunological and non-immunological causes. Monitoring of graft kidney function is carried out by measuring serum creatinine levels or glomerular filtration rate (GFR). However, these markers are not specific for rejection. They cannot indicate the final event of the rejection process, so by the time they are detected, tissue damage may be irreversible. Research conducted by Po-Chang Lee et al. in 2002 found that the presence of HLA (Human Leukocyte Antigen)

antibodies was a factor causing chronic immunological rejection. In this study, chronic rejection was successfully treated by administering the first-line calcineurin inhibitor (CNI), namely tacrolimus and mycophenolate mofetil. Where the serum creatinine value becomes stable, and the antibody titer decreases. The biopsy results of all patients in this study who experienced chronic rejection showed the formation of HLA antibodies. Biopsy remains the gold standard for the diagnosis of transplant failure and as an indicator of prognosis, but biopsy is an invasive and expensive technique that can cause surgical complications.^{6,7}

Chronic rejection after kidney transplantation is mediated by antibodies formed from the transplant recipient or active antibody-mediated rejection (ABMR). In this case, the patient also experienced post-transplant anemia. The anemia that occurs cannot be treated by administering erythropoietin therapy. A successful kidney transplant will increase blood erythropoietin levels 2x within 2-3 months of administration. Meanwhile, hemoglobin levels will recover in 2-6 months. Endogenous erythropoietin production after kidney transplantation varies even though function is normal. This condition is influenced by conditions called Epo deficiency and Epo resistance. This condition causes differences in the occurrence of anemia in post-kidney transplant patients.⁸

Other causes of anemia in post-transplant patients can be viral infections (cytomegalovirus, parvovirus B19), bone marrow toxicity from immunosuppressants (azathioprine, mycophenolic acid), or antihypertensive drugs (ACEi and ARB) must also be managed clinically. Treatment with erythropoietin has a positive impact on graft function, but excessive use of erythropoietin (hemoglobin levels >12.5 mg/dL) increases mortality due to thrombotic side effects and hypertension. According to the KDIGO guidelines erythropoietin should be started when hemoglobin levels fall below 10 mg/dL, with an optimal target hemoglobin of between 11–12 mg/dL.⁹

Post-transplant surgical complications, in general, are urological and vascular complications that have a substantial influence on morbidity and mortality. Urological complications occur in 4-8% of patients, including obstruction and urethral/ureteral stenosis. Cases of obstruction characterized by hydronephrosis of the kidney graft occur in almost 2% of patients, usually within the first 6 months after transplantation. The most common location is at the site of implantation of the ureter into the bladder, where more than 90% of ureteral stenosis occurs in the distal 1/3 of the ureter. Abnormalities in the form of narrowing of the ureterovesical junction, which can be caused by scar tissue due to ischemia or rejection, technical errors in ureteroneocystostomy or due to kinking. Post-transplant vascular complications occur in 1-2%, including renal artery stenosis, infarction, arteriovenous fistula, pseudoaneurysm and renal vein thrombosis.¹⁰

Hydronephrosis is a condition where the renal calyx and pelvis experience dilatation as a result of urine accumulation in the renal calyx or pelvis. This can be caused by congenital abnormalities in the form of ectopic ureters, ureteroceles, pelvic-ureter duplications, or acquired due to thrombosis, which causes urethral stenosis, ureterovesical stenosis, ureteropelvic junction or secondary to vesicoureteral reflux. Ureteral obstruction that occurs > 3 months after kidney transplantation occurs due to ureteral ischemia repeated acute rejection causing vasculitis. These lymphoceles cause extrinsic compression, immunosuppressive drugs, BK virus nephropathy and ureteral stones.^{11,12} Rejection or rejection reactions in kidney transplantation are the causes of Non-reflux non-obstructive HUN. Ureteral obstruction with decreased kidney function causes symptoms in the form of pain and colic due to denervation of the kidney allograft, usually appearing in advanced conditions. 10 Kidney allografts experiencing hydroureteronephrosis are correlated with worsening kidney function and an increased incidence of pyelonephritis.

The complication of hydronephrosis after kidney transplantation has an incidence of less than 10% and is significantly associated with morbidity.¹³⁻¹⁵

CONCLUSION

Kidney transplantation in patients with PGTA is the best kidney replacement therapy because it improves the patient's quality of life. Post-kidney transplant complications vary widely in incidence. Broadly speaking, it is divided into surgical and medical

complications. In terms of the time of occurrence, it is divided into hyperacute, acute and chronic. The most common medical complication after a kidney transplant is rejection or rejection reaction. Meanwhile, the most common surgical complications are in the urology department, including hydroureteronephrosis. Often, post-transplant complications cause loss of function of the transplanted kidney so patients with PGTA must return to dialysis.

REFERENCES

1. PERNEPHRI. 11th Report Of Indonesian Renal Registry 2018. Available from: <http://www.indonesianrenalregistry.org.id>
2. Magee CC, Pascual M. Update in renal transplantation. Archives of internal medicine. 2004 Jul 12;164(13):1373-88. 5
3. United States Renal Data System (USRDS). Percentages & counts of reported ESRD patients: by treatment modality. 2017. [Internet]. [cited 2022 Sep 14]. Available from: <https://www.usrds.org>
4. I Made Juliana, Loekman JS. Post-Kidney Transplant Complications. Journal Of Internal Medicine. 2012;8(1):79-90
5. Collins B, Shapiro R, Jhonston T, Kim ED, Talavera F. Kidney Transplantation (online) 2021 (Accessed April 28, 2023). Downloaded from URL: <https://emedicine.medscape.com/article/430128-overview>
6. Etxebarria A, Díez-Martín E, Astigarraga E, Barreda-Gómez G. Role of the Immune System in Renal Transplantation, Types of Response, Technical Approaches and Current Challenges. Immuno 2022;2: 548–570
7. Po-Chang Lee, Terasaki PI, Takemoto SK, Po-Huang Lee, Chung-Jye Hung, Yi-Lin Chen, Alen Tsai, Huan-Yao Lei. Development of HLA Antibodies preceded all Chronic Rejection Failure of Kidney Transplants. Transplantation. 2002;74(8).
8. Nampoory MRN, Johny KV, Al-Hilali N, Kanagasabhapathy AS. Erythropoietin deficiency and relative resistance cause anemia in post-renal transplant recipients with normal renal function. Nephrology Dialysis Transplantation, Volume 11, Issue 1, January 1996, Pages 177–181
9. Carminatti M, Tedesco-Silva H, Silva Fernandes NM, Sanders-Pinheiro H. Chronic kidney disease progression in kidney transplant recipients: A focus on traditional risk factors. Nephrology (Carlton). 2019;24(2):141-147
10. Ojo AO, Held PJ, Port FK, et al. Renal transplantation in ESRD. NEJM 2003;349:931- 40.
11. Cooper JE. Evaluation and Treatment of Acute Rejection in Kidney Allografts. Clin J Am Soc Nephrol. 2020;15(3):430-438
12. Naik RH, Shavar SH. Renal Transplantation Rejection (online) 2023 (Accessed 10 May 2023). Downloaded from URL: <https://www.ncbi.nlm.nih.gov/books/NBK553074/>
13. Justitia I., Nandana PI. Right Severe Hydronephrosis Caused by Complete Type Pelvic-Ureteral Duplication with Ureterovesical Junction Stenosis. Medical Journal, 2017;2(1):26-9
14. Kanakarathne S, Asokan G, Olakkengil S, Bhattacharjya S. Post Renal Transplant Hydronephrosis – Obstructive or Not – A Longitudinal Single Center Study. J Comm Med and Pub Health Rep. 2022;3(01):1-3
15. Indonesian Nephrology Association. Consensus on Kidney Transplantation of the Indonesian Nephrology Association (Pernefri) 2013. Central Jakarta: Pernefri. 2013