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Chronic kidney dissease and complex urinary tract infection in children with left renal agenesis : A case report

Maria Ulfa*[1], Tunjung Wibowo[1], Desy Rusmawatiningtyas[1], Kristia Hermawan[1]

[1]Department of Pediatric Health, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/ Dr.Sardjito Hospital, Yogyakarta, Indonesia

Case Report

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***Corresponding author:**
redturbo96@gmail.com

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ABSTRACT

Child with left renal agenesis fulfill the diagnostic criteria for chronic kidney disease due to its structural abnormalities that lasted for more than three months. It is important to monitored the disease progression and also growth, development and quality of life in children with chronic disease. Management of other risk factors that can accelerate disease progression must be carried out comprehensively. The patient's was 9 months old girl with stage I chronic kidney disease and also having recurrent complex urinary tract infections with left renal agenesis. The interventions was to identify other abnormalities of the urinary tract and syndromic disorders, prevention of urinary tract infection (UTI) recurrence, prevention of renal injury, renal scaring and dietary education. After 18 months of observation there was no urinary tract abnormality in imaging results, there was one episode of mild recurrent UTI, no renal injury and there was no sign of renal scaring. The final outcome was no significant decrease in glomerular filtration rate (GFR), growth and development was good and good quality of life. The immunizations was given as scheduled. Monitoring and multidisciplinary intervention of prognostic variables such as urinary tract and syndromic disorders, recurrence UTI, renal injury, renal scaring and diet in children with chronic kidney disease are important for optimal outcome. No decrease of GFR, good growth, development and optimal quality of life and also knowing the progression of chronic kidney disease was the final outcomes of the intervention.

Anak dengan agenesis renal sinistra memenuhi kriteria diagnosis penyakit ginjal kronis disebabkan adanya kelainan struktur ginjal yang berlangsung lebih dari 3 bulan. Monitoring fungsi ginjal penting untuk mendeteksi progresivitas penyakit, disamping pemantauan tumbuh kembang dan kualitas hidup anak dengan penyakit kronis. Manajemen faktor resiko lain yang dapat mempercepat progresivitas penyakit harus dilakukan secara komprehensif. Kondisi pasien saat awal pemantauan yaitu penyakit ginjal kronis stadium I dan infeksi saluran kemih kompleks berulang pada anak dengan agenesis renal sinistra. Intervensi yang dilakukan antara lain adalah identifikasi kelainan lain dari traktus urinarius maupun kelainan sindromik, pencegahan rekurensi infeksi saluran kencing (ISK) dan ultrasonografi (USG) saluran kemih berkala, beberapa tindakan pencegahan renal injury, *pencegahan* renal scaring *dan edukasi diet. Hasil intervensi dan pemantauan selama 18 bulan menunjukkan bahwa tidak ada kelainan saluran kemih dan sindromik dari pencitraan, terjadi satu kali episode rekurensi dari ISK namun tidak membutuhkan perawatan inap, tidak didapatkan kejadian* renal injury *dan tidak didapatkan tanda adanya* renal scaring. *Luaran akhir dari pasien didapatkan penurunan laju filtrasi glomerulus (LFG) yang signifikan, tumbuh kembang dan kualitas hidup baik serta anak mendapatkan imunisasi sesuai jadwal. Pengamatan dan*

intervensi multidisiplin serta modifikasi variabel prognostik seperti kelainan saluran kemih dan kelainan sindromik, rekurensi ISK, renal injury, renal scaring dan diet pada anak dengan penyakit ginjal kronis adalah penting untuk mendapatkan luaran akhir anak yang optimal. Tidak didapatkan nya penurunan LFG, tumbuh kembang dan kualitas hidup yang optimal serta mendeteksi progresifitas penyakit ginjal kronis merupakan sasaran akhir dari intervensi tersebut.

INTRODUCTION

Chronic kidney disease (CKD) is a growing global health problem. Based on the results of the 2013 Basic Health Research by the Ministry of Health of the Republic of Indonesia, 0.2% of the total population of Indonesia suffers from CKD. From this amount, 1% of the population of patients with chronic kidney disease who need dialysis and kidney transplants, spending approximately 5% of the total health financing funds. Identification of CKD at the earliest possible level is important because of its economic and clinical benefits. Early management of CKD patients can delay complications and progression to renal failure through appropriate interventions.[1]

Unilateral renal agenesis (URA) is congenital absence of one kidney due to failure of kidney tissue formation at the embryonic stage. The prevalence of unilateral renal agenesis was approximately 1 in 1000 populations, while bilateral renal agenesis was 1 in 2500. The incidence of renal agenesis is mostly associated with the presence of other malformations in the urinary tract known as congenital anomalies of the kidney and the urinary tract (CAKUT).[2] Previous studies have suggested that unilateral renal agenesis is a harmless congenital disorder, however, the data show that 40-50% of adults with unilateral renal agenesis need dialysis by the age of 30 years.[1]

Patients with unilateral renal agenesis met the criteria for chronic kidney disease due to structural abnormalities with implications on health and lasted for more than 3 months. Meanwhile, the stage of chronic kidney disease is determined by the glomerulus filtration rate (GFR) value of the remaining kidney.[3] The early stage of chronic kidney disease is often asymptomatic, usually found when performed other comorbid screening. In diseases that are rapidly progressing, kidney failure can occur within months of diagnosis but in most diseases it can last several decades.[4]

Urinary tract infection (UTI) is a disease that often occurs in children and its incidence depends on age and gender. The prevalence of UTI in neonates ranged from 0.1% to 1%, increasing to 14% in neonates with fever and 5.3% in infants. In asymptomatic infants, bacteriuria was found in 0.3-0.4%. The risk of UTI in children before puberty is 3-5% in girls and 1-2% in boys. In children with fever less than 2 years of age, the prevalence of UTI is 3-5%. In the collaborative study of some hospitals in Jakarta for about 5 years (1984-1989) there was found an UTI incidence was 0.1% -1.9% from all pediatric admissions cases.[4]

Growth aspect in children with CKD caused by URA is an important thing to be monitored. In children with chronic dissease, developmental disorders could be happened. Disorders can involved the motoric, sensory, social and cognitive aspects. The condition of malnutrition in advanced kidney disease can cause general weakness and influence motor and sensory development. The condition of frequent recurrent infections and re-hospitalization may increase chance of skip school in children that will impaired the cognitive function. Recurrent uremia conditions may lead organic mental disorders, emotional disorders and decreased of learning capacity.[5]

Multidisciplinary approach should consist of promotive, preventive, curative, and rehabilitative aspects. It also had to pay attention to the patient's social, economic and environmental aspects. Holistic management of chronic childhood diseases involves the roles of primary, secondary and tertiary service officers. However, the harmonic coordination between observers, parents and medical officers was needed to support the management of the disease to achieve the expected outcome.[5]

CASE DESCRIPTION

The patient was a neonates diagnosed as left renal agenesis at the age of 14 days, the observation started at the age of 9 months with initial diagnosis of stage I CKD and complex UTI in left renal agenesis. Variables that observed and intervented during observation was including the investigation of other urinary tract abnormalities and other extrarenal abnormalities. Computerized tomography scan (CT scan) results showed left renal agenesis, renal simple cyst in the right kidney without any other abnormalities in the abdominal organs.

Variable of UTI recurrence showed that there was no prophylactic antibiotics given because there was no urinary tract abnormality that had a high risk of recurrent pyelonephritis such as vesicoureteral reflux (VUR) or pelviureteric junction obstruction (PUJO) in the child. Antibiotics was only given as indicated if there was symptoms or the urinalysis results showed a suspicion of UTI. Environmental hygiene and sanitation education to the parents was given for prevention of UTIs, it was include of the education about how to do vaginal hygiene and how to wash properly to the parents. Urinalysis was performed during the observation, there was one episode of recurrent UTI in July 2018 (12th month of observation), there was positif leukocyte esterase (+3) and leucosituria, the chief complaints of children was decrease of appetite, but no fever or pain when urinating. The intervention was administration of antibiotics with cotrimoxazole 2 mg/kgBW/day orally for 4 weeks and planned evaluation of urinalysis and performed urine culture. The results of urine culture showed there was no bacterial growth, then the antibiotics stopped. The compliance of taking antibiotic medication was documented in the daily diary book.

The observer had performed the interventions on the environmental condition including the assesment of the healthy house. One of the intervention was giving the closed trash can, education to open the bedroom window every day, examine the water composition to identify whether there was mineral deposits or hazardous substances in the water that may impaired kidney filtration function.[6] From the result of water examination, the water was safe and fit to be consumed. The results of the healthy house assessment at the beginning and at the end of the observation can be seen in Table 1 as follows.

Table 1. Assessment of the healthy house at the beginning and at the end of the observation

Assessment Time	Score	Criteria
Early observations	1054	Unhealthy
End of observation	1147	Healthy

Education of *Pola Hidup Bersih dan Sehat* (PHBS) was given to the family as an effort to reach the healthy optimal condition through the prevention. The mother also given education for not using diapers for long time periode and frequently. After the child reach the age of 3 years, parents had to start doing toilet training to the child. Abdominal ultrasound evaluation was performed annually to evaluate kidney abnormalities.

Renal injury variable was established by risk, injury, failure, loss, and end stage renal disease criteria (RIFLE criteria). It was defined as an increased of serum creatinine more than 1.5 times or a decrease in GFR of more than 25% compared to the previous examination. From the urine output parameters it was see the patient's diuresis that decreased by less than 0.5 ml/kg BW per hour. The trend of GFR changes during observation was shown in Figure1.

In nine times of GFR examinations, there was a decrease in GFR to a value below 90 ml/minute/1.73m2, it occurs in moth of March and July 2019 (with a value of 87 and 86, respectively). This decrease was not accompanied by other markers of renal function deterioration such as hypertension, proteinuria and other markers of deterioration. The interventions that to prevent the renal injury condition was to educate to fullfill the adequate fluid requirements, monitored the child's urine of its colour and quantity, avoiding use of nephrotoxic drugs and avoidance the use of contrast-induced renal injury for imaging needs.

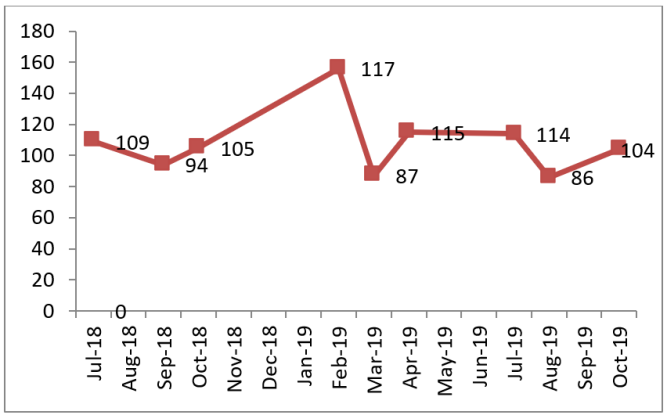

Figure 1. Trend of GFR changes in patient.

Renal scaring variable in recurrent UTI conditions can be seen ideally with dimercapto succinic acid (DMSA) examination. However, due to inavailablity of the moadalities, we only monitored the clinical and laboratory markers in patients that had been use widely as surrogate markers of renal scaring. The markers were the presence of hypertension, proteinuria and hematuria.[7] During the observation, there was no hypertension and proteinuria, but there was persistent hematuria on the urinalysis examination. Nutritional diet was also given in children with renal agenesis for not giving excessive amounts of protein, sugar, salt and dietary purines.The final outcome assessed was the decrease of GFR in the patient. There were two episodes of decreased GFR, but it was not significant and does not meet the RIFLE criteria as renal injury. The trend of GFR changes during the observation can be seen in the previous Figure 1.

Growth outcomes of children assessed by child nutitional status. At the beginning of the observation child was in good nutritional status. During observations there was some period of inadequate weight gain and growth flattering. It was happened in the transitional periode from breastmilk to the complimentary period and also in a periode of UTI reccurence. Development outcome was assessed by developmental screening as scheduled using age-appropriate instruments screening such as Denver II and cognitive adaptive test (CAT)/ (clinical linguistic & auditory milestone scale (CLAMS) every 3 months until the age of 24 months and every 6 months from age of 24 months to 72 months. The results of the development screening showed that there was no developmental delays in children, either from gross motoric, fine motor, personal, social and language aspects.The quality of life in children with chronic dissease was assesed using age appropriate tools. When the child was 9 months old we use pediatric quality of life inventory TM (PedsQLTM) infant scales and the results was showed good results, while the second examination at the end of the observation was carried out using the PedsQL parent report for toddlers (aged 2-4 years) with good results as well.[8] Basic childhood immunizations could be carried out without delay or contraindications. The results of the quality of life assessment can be seen in Table 2.

Table 2. PedsQL Result

Assessment Time	Score
Early observations	92.9 (good)
End of observation	89.6 (good)

DISCUSSION

CT scan was performed to investigate urinary tract abnormalities and other extrarenal conditions associated with syndromic disorders that corelated to unilateral renal agenesis. The result was within normal limit. Due to normal condition of the uterus and other abdominal organs, the syndromic condition such as Mullerian

anomaly and Herlyn-Werner Wunderlich syndrome can be excluded.[9] The abnormality can be further evaluated on subsequent imaging if later symptoms was manifested.

CT scan result revealed that there was a simple cyst. It was a hypodense lesion in the middle of the right pole of kidney with the right kidney size was still within normal limits. Simple cysts are a common disorder in patients with renal agenesis. Simple cysts are often associated with hypertension, renal dysfunction and microscopic hematuria, but it still controversial in several studies. The risk factors for having these cysts were the presence of high serum creatinine, hypertension and atherosclerosis. Some studies also mention the existence of pathologies of arterial and renovascular pathologies as a cause. In children, it was said that in 49% child will have the size of the cyst enlarged, 10% would getting smaller, 31% would persist and 10% would disappear after 3 years of follow-up. This renal simple cyst of the patient was no need for corrective intervention for now.[10]

The urinalysis performed routinely and showed persistent hematuria. Asymptomatic microscopic hematuria in children is often harmless, especially when it occurs along with hypercalciuria conditions.[7] Hematuria, which is said to be an important sign of glomerular injury, is often seen in kidney disease for about 1-2%. Hematuria can potentially become chronic kidney disease if it is accompanied by hypertension and or proteinuria.[11]

There was no abnormality in urine sediment examination. There was no red blood cell casts and insignificant number of erythrocytes in urine. It is suggested that the incidence of hematuria in patients may be due to isolated microscopic hematuria or the condition of persistent asymptomatic microscopic hematuria that occured without hypertension, proteinuria or renal insufficiency however it still need to be closely monitored.[11]

There were two episodes decrease of GFR. It was slightly decreased below the normal range (90 ml/min/m2) that can be due to the immaturity of renal function generally in children under 2 years of age.[12] This can be seen from the GFR trend changes, that showed after an episode decreased of GFR, the GFR on the next examination will set to the normal range of values and the child not showing any symptoms of worsening condition or other acute conditions.

The GFR measurement in child less than 2 years of age, there was still no definite agreement on the used criteria. According to Hogg et al, the classification of GFR in children aged less than 2 years is grouped into normal, moderate or severe decreases in GFR based on the normative range and standard deviation. In some studies, GFR values below 1 standard deviation may be a consideration for clinicians to do intensive monitoring. Drug dosage adjustment in such patient, it is recommended that children with a 1-2 standard deviation decrease in GFR was categorized as moderate GFR decreases. Whereas a decrease in GFR of more than 2 standard deviations is classified as a severe decrease in GFR.[13]

There was one episode of UTI recurrence during the observation, it was suspected caused by poor vaginal hygiene from the caregiver and use of frequent and prolonged diapers. These recurrent episodes only caused minimal symptoms, there was no fever or other serious illness conditions and no need of hospitalization.[14]

It was found several episodes of inadequate weight gain and growth flattering. The conditions was due to some illness conditions when the child having UTI reccurence, upper respiratory tract infection and also the transitional periode from breastmilk to the complimentary food. Another problem that was encountered during the observation was related to environmental health. Observers had screened patients for risk of infectious diseases due to the patient's grandmother, who lived together at the same house, was having chronic cough. The aim of the screening was to rule out a tuberculosis (TB) diagnosis that may decrease the health state of the child. Problem of health insurance and family psychological factors were considered important for continued monitoring patients with chronic diseases such as patients with renal

agenesis, to screen the complications of kidney disease in early stage.

Complete blood count shows the results of anemia suspected due to nutritional problems esspecially in transitional periode of breast milk to complementary foods. Anemia in CKD was defined according to the World Health Organization (WHO) definition as a hemoglobin level below 11 g/dl (ages 6 months to 5 years).[4] After nutritional education to the mother, the child's haemoglobin level showed in a normal range according to age until the end of monitoring.

Periodic electrolytes evaluation showed consistent results of hyperphosphatemia with normal calcium levels. Hyperphosphatemia is defined as a phosphate serum that exceeded value of 4.5 mg/dl. The baseline value of the phosphate before observation were not obtained. This hyperphosphatemia condition can be caused by increased phosphate intake in children who drink excess formula milk, decreased phosphate excretion or abnormalities in intracellular to extracellular phosphate exchange. However, the condition of severe hyperphosphatemia (very high phosphate value) often asymptomatic.[15]

Hyperphosphatemia condition was ussually associated with the underlying disease than in increase of the laboratory value of phosphate only. In this patient, there was no clear underlying disease related to kidney function, because there was no renal injury, such as significant decrease in GFR, hypertension or proteinuria. There was no medication given for this hyperphosphatemia, but it still considered to be closely monitored esspecially for other symptoms related to kidney disease.[16] The intervention for hyperphosphatemia were giving education to the mothers to restrict formula milk quantity as required and giving solid foods with balanced nutrition to achieve the need of calories. In the end of the observation, there was a gradual decrease of the phosphat level and no other worsening clinical condition.

CONCLUSION

Close monitoring and multidisciplinary intervention in patients with chronic kidney disease, complex UTI with left renal agenesis had been carried out for 18 months . The montioring should be continued, especially for outcomes that did not met the optimal condition such as preventing UTI recurrences and optimizing the growth of the child to prevent malnutrition condition. Another consideration was to monitored the recurrent hematuria condition and asymptomatic recurrent hyperphosphatemia and screen the other marker of renal function deterioration along with this condition. As well as preventing the use of nephrotoxic contrast materials when imaging is needed.

CONFLICT OF INTEREST

None declared.

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