Cite as: Gąsowska K, Zachwieja K, Krasowska-Kwiecień A, Goździk J, Drożdż D: Successful haematopoietic stem cell transplantation in a boy with advanced chronic kidney disease – a case report. Pediatr Med Rodz 2025; 21 (3)

Katarzyna Gąsowska[1,2], Katarzyna Zachwieja[1], Aleksandra Krasowska-Kwiecień[3], Jolanta Goździk[3], Dorota Drożdż[1]

Received: 17.12.2024
Accepted: 12.09.2025
Published online: 29.09.2025

Successful haematopoietic stem cell transplantation in a boy with advanced chronic kidney disease – a case report

Udane przeszczepienie komórek krwiotwórczych u pacjenta z zaawansowaną przewlekłą chorobą nerek – opis przypadku

[1] Department of Paediatric Nephrology and Hypertension, Jagiellonian University Medical College, University Children's Hospital of Cracow, Cracow, Poland
[2] Jagiellonian University Medical College, University Children's Hospital of Cracow, Doctoral School of Medical and Health Sciences, Cracow, Poland
[3] Department of Clinical Immunology and Transplantation, Jagiellonian University Medical College, University Children's Hospital of Cracow, Cracow, Poland
Correspondence: Katarzyna Gąsowska, Department of Paediatric Nephrology and Hypertension, Jagiellonian University Medical College, University Children's Hospital of Cracow, Wielicka 265, 30-663 Cracow, Poland, e-mail: k.mikrut@doctoral.uj.edu.pl

https://doi.org/10.15557/PiMR.2025.0023

ORCID iDs
1. Katarzyna Gąsowska https://orcid.org/0000-0002-5747-4763
2. Dorota Drożdż https://orcid.org/0000-0002-1281-1164

Abstract

A case of a 16-year-old male with stage III chronic kidney caused by reflux-obstructive nephropathy, later diagnosed with severe aplastic anaemia and referred for allogenic haematopoietic stem cell transplantation, is presented. The conditioning regimen prior to the procedure required cyclophosphamide, for which dosing had to be carefully adjusted in view of impaired kidney function to avoid potential complications. Therefore, an unusual approach of pre-emptive use of renal replacement therapy was chosen with no dose reduction of the conditioning regimen. The patient underwent continuous veno-venous haemodiafiltration for to 70 hours after receiving the first dose of cyclophosphamide, with no complications observed. The patient underwent successful conditioning followed by haematopoietic stem cell transplantation, and maintained stable kidney function. In conclusion, such a procedure in a patient with advanced chronic kidney disease requires an individual, patient-oriented approach, with close involvement of a nephrologist in the transplant medical team.

Keywords: bone marrow transplantation, chronic kidney disease, dialysis, haematopoietic stem cell transplantation, severe aplastic anaemia

Streszczenie

Przedstawiony przypadek dotyczy 16-letniego pacjenta z przewlekłą chorobą nerek w stadium III na tle nefropatii refluksowo-zaporowej, u którego zdiagnozowano ciężką anemię aplastyczną i którego skierowano do allogenicznej transplantacji komórek krwiotwórczych. Protokół kondycjonujący wymagał podaży cyklofosfamidu – jego dawkowanie musiało być odpowiednio dostosowane z uwagi na upośledzoną funkcję nerek, celem uniknięcia powikłań. Z tego powodu wybrano nietypowe podejście prewencyjnego wdrożenia terapii nerkozastępczej bez redukcji dawki leku. Pacjenta poddano ciągłej żylno-żylnej hemodiafiltracji przez 70 godzin po otrzymaniu pierwszej dawki cyklofosfamidu, nie obserwując komplikacji. Chłopiec przeszedł udaną procedurę kondycjonowania, a następnie przeszczepienia. Utrzymał stabilną funkcję nerek. Podsumowując, transplantacja komórek krwiotwórczych u dziecka z zaawansowaną przewlekłą chorobą nerek wymaga zindywidualizowanego podejścia oraz bliskiej współpracy nefrologa z zespołem oddziału transplantologicznego.

Słowa kluczowe: przeszczepienie komórek krwiotwórczych, przewlekła choroba nerek, leczenie nerkozastępcze, przeszczepienie szpiku, anemia aplastyczna

INTRODUCTION

Nowadays, as haematopoietic stem cell transplantation (HSCT) has become a curative therapy for various clinical conditions[1,2], different challenges must be faced. The HSCT procedure carries the risk of several potential complications. Chronic kidney disease (CKD) has been frequently listed among those; according to the literature, it occurs in around 30% children who have undergone HSCT[3,4]. In the paediatric population, data on CKD occurring prior to HSCT are scarce. Few case reports on such children are found in the literature, particularly those with an estimated glomerular filtration rate (eGFR) <40 mL/min/1.73 m^2. Among the children treated in our hospital, the presented case is unique, with an eGFR <60 mL/min/1.73 m^2. In adult patients, there are data on similar cases, but still there is no clear consensus on optimal dosing for the preparative regimen before HSCT[5,6]. Cyclophosphamide (Cy) is a commonly used agent in conditioning regimens for HSCT. However, the impact of renal dysfunction on Cy metabolism is not fully elucidated, and it is presumed that pharmacokinetics may be altered in the setting of renal impairment. Data regarding the potential toxicity of Cy metabolites in patients with renal failure remain inconclusive. While some reports address Cy dosing in HSCT patients with impaired renal function, the available evidence is limited, and various treatment strategies have been applied across different clinical settings. At present, no clear recommendations exist.

MATERIALS AND METHODS

We present a case report of a 16-year-old male diagnosed with stage III CKD (eGFR: 37.8 mL/min/1.73 m^2) caused by reflux-obstructive nephropathy due to posterior urethral valve. His past medical history included cystoscopic surgical treatment, and he was currently on conservative treatment of CKD (antihypertensive medications – ACE inhibitor – ramipril, active vitamin D supplementation – alfacalcidol, calcium carbonate, alkylating agents, alpha-blocker, and urinary tract infection prophylaxis with co-trimoxazole).

The patient (body mass: 75 kg, height: 182 cm, body surface area: 1.9 m^2) was admitted to emergency department due to petechiae on physical examination and abnormalities in laboratory tests: white blood cells: 3,390/μL, haemoglobin: 10.6 g/dL, platelet count: 19,000/μL, eGFR on admission: 36.7 mL/min/1.73 m^2. Coagulation parameters remained within normal limits. Initially, the patient was diagnosed with idiopathic thrombocytopaenic purpura and treated unsuccessfully with methylprednisolone and temporary transfusions of red blood cells and platelets. Subsequently, both aspiration and trephine bone marrow biopsy revealed severe aplastic anaemia (SAA). The patient was referred for allogenic HSCT from a matched sibling donor. After nephrological consultation, an unusual approach of pre-emptive renal replacement therapy (RRT) was chosen without reducing doses of the conditioning regimen – intravenous anti-thymocyte globulin (ATG, dosage 7.5 mg/kg; total dose 570 mg – from day [–3] until [–2], with day "0" defined as the day of haematopoietic cells transfusion) together Cy (dosage 200 mg/kg; total dose 15,200 mg – from day [–6] until [–3], with day "0" referred as the day of haematopoietic cells transfusion). Supportive treatment, according to our local protocol, included ciprofloxacin, penicillin, fluconazole, co-trimoxazole, furosemide, ondansetron, steroids, defibrotide, ranitidine, allopurinol, clonazepam, mesna, clemastine, acyclovir, cefepime, and total parenteral nutrition with multidrug analgesia.

After implantation of a double-lumen catheter into the femoral vein, the patient was admitted to the intensive care unit (ICU) and started on continuous veno-venous haemodiafiltration (CVVHDF) 20 hours after receiving the first dose of Cy, which was continued until 20 hours after the last dose of Cy. The procedure was performed in the ICU, and afterwards the patient – remaining in stable condition – was transferred back to the transplantation department. CVVHDF parameters: filter ST100, blood flow (Qb) 80 mL/min, supplement flow 1,000 mL/h (pre-filter: 800 mL/h + post-filter: 200 mL/h), dialysate flow 900 mL/h, total CVVHDF dose: 25 mL/kg/h (1,730 mL/h/1.73 m^2); ultrafiltration rate 50 mL/h. Citrate anticoagulation was used according to protocol: 3.0 mmol/L, with a 10% calcium infusion to the patient, to maintain adequate ionised calcium concentration post-filter and from the patient. The lowest creatinine concentration during CVVHDF was 93 μmol/L, and no severe electrolyte abnormalities were noted. The total duration of CVVHDF was 70 hours. No clinical complications occurred during CVVHDF.

The patient underwent successful conditioning followed by HSCT. From day 2 after HSCT, transient haemorrhagic cystitis and signs of acute kidney injury with features of significant catabolism – well controlled by conservative treatment – were observed. The highest serum creatinine concentration was 412 μmol/L (eGFR: 16.1 mL/min/1.73 m^2) with no hypervolaemia, while the patient remained clinically stable with effective response to fluid, furosemide, and nutritional treatment. By day 7 after HSCT, the serum creatinine concentration had dropped to baseline values (Fig. 1). Prolonged urinary catheterisation was also performed. Graft versus host disease (GVHD) prophylaxis included ATG combined with tacrolimus (TAC) 0.02 mg/kg and mofetil mycophenolate (MMF) 1,200 mg/m^2. Serious complications occurred in the post-transplantation period, including lymphoproliferative disease and central catheter infection requiring additional treatment. However, no severe complications attributable to Cy toxicity were observed. The patient was discharged on day 30 after transplantation with an eGFR of 36 mL/min/1.73 m^2, identical to the pre-transplant baseline. No further deterioration of renal function has since been observed. The patient's eGFR remained stable at 1, 2, 3, 4, and 5 years post-HSCT

DOI: 10.15557/PiMR.2025.0023

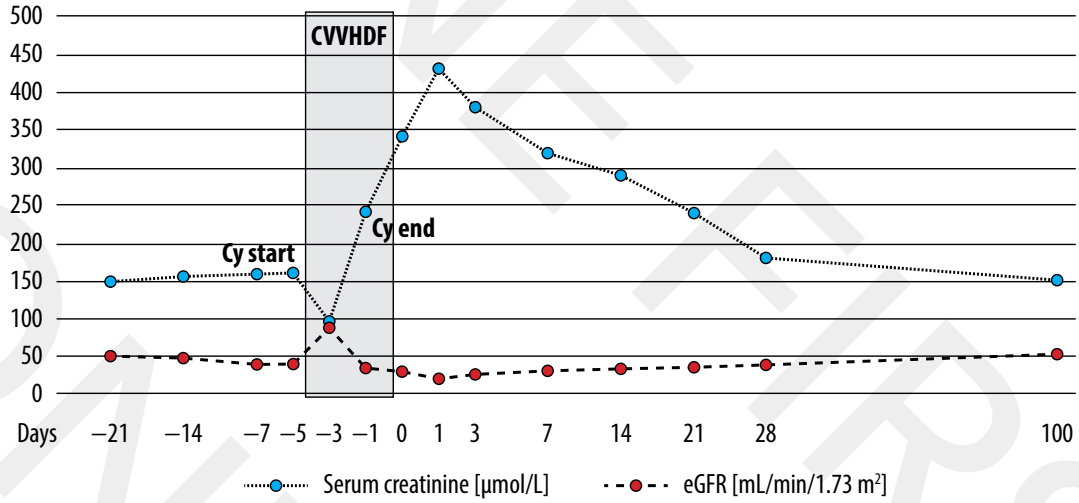

Fig. 1. Changes in the patient's serum creatinine and eGFR during the HSCT procedure

(42.4 mL/min/1.73 m^2 at 5-year follow-up). He continues to receive regular nephrology and haematology follow-up and has maintained a good quality of life, including social and work aspects.

DISCUSSION

Successful HSCT in a child with advanced CKD is exceptional. We present our experience with conditioning using full-dose Cy at a low eGFR <40 mL/min/1.73 m^2. Cy is a commonly used drug in preparative regimens for HSCT. It is a small molecule with a half-life of 5–9 hours. As a pro-drug, it is metabolised mainly by the liver (70–80% via CYP P450), with low binding to plasma proteins and metabolites (e.g. acrolein formed during drug activation in hepatocytes) excreted by the kidneys[7]. Cy presents with the autoinduction phenomenon – intensification of its own metabolism with subsequent doses. Hydration increases the elimination of the drug and its metabolites. Biotransformation is believed not be altered in patients with renal failure. Cy shows dose-dependent toxicity. Nephrotoxicity remains minor, while exposure of urinary bladder cells to acrolein often results in haemorrhagic cystitis. Mesna (an acrolein binder) is used as prophylaxis. Higher serum concentrations are associated with cardiotoxic and myelotoxic reactions as well as damage to reproductive cells[8,9]. Other reports on Cy-related complications mention veno-occlusive liver disease (VOD) and non-specific reactions such as alopecia, nausea, and vomiting.

The clinical problem lies in titrating the serum concentration of Cy in the context of decreased eGFR – a low effective dose would result in incomplete conditioning and potential donor cell rejection, while a high dose carries a significant risk of drug-related toxicity. At the time, there was no method for monitoring the concentration of Cy in peripheral blood. Moreover, Cy pharmacokinetics remains difficult to predict[10]. Guidelines and literature on its dosing in advanced CKD are lacking[11]. There are only isolated reports on the topic and individualised methods of treatment such as Cy total dose reduction, Cy avoidance in myeloablative therapy, non-myeloablative HSCT, intensification of dialysis therapy (in dialysed patients), or modification of GVHD prophylaxis – e.g. avoiding calcineurin inhibitors[11,12].

The literature also emphasises significant inter-individual variability in Cy pharmacokinetics. Therapeutic drug monitoring is rarely available outside research centres and primarily reflects only the prodrug concentration, with limited insights into the pharmacologically active metabolites. This gap causes an incomplete understanding of how Cy metabolites contribute to both therapeutic efficacy and toxicity. Ultimately, dose adjustment of Cy in patients with renal failure should be tailored to individual clinical circumstances.

The literature review showed that, in most published cases of HSCT in patients with advanced renal failure, standard doses of Cy were administered in combination with intermittent haemodialysis (HD) performed 6–14 hours after each infusion. Perry et al. described a successful case of a patient with end-stage renal disease (on chronic HD) undergoing bone marrow transplantation for aplastic anaemia with full-dose Cy, followed by HD initiated 14 hours after each infusion, demonstrating effective clearance of Cy and its metabolites[11].

In a larger study by Bodge et al., nine reports were analysed describing HSCT in patients with varying degrees of renal impairment treated with Cy. Dialysed patients received intensified HD schedules, while those with moderate renal dysfunction (eGFR >20 mL/min/1.73 m^2) were given reduced doses of Cy[5]. Another patient with Fanconi anaemia experienced renal function decline following HSCT and required kidney transplantation[13].

Our patient presented with an eGFR of 37 mL/min/1.73 m^2, corresponding to stage IIIb of CKD. A full dose of Cy was administered due to concerns about potential inadequate myeloablation, which could compromise HSCT success, given the unpredictable pharmacokinetics in renal impairment. By initiating continuous renal replacement therapy,

DOI: 10.15557/PiMR.2025.0023

we aimed to mitigate risks such as cardiotoxicity, VOD, and other Cy-related toxicities, which are reported to be more frequent and severe in patients with renal dysfunction. The patient did not develop any of these complications. CVVHDF was selected as the safest modality in our clinical setting – particularly for a patient requiring strict isolation with continuous monitoring. At the University Children's Hospital of Cracow, CVVHDF is performed exclusively in the ICU, while intermittent HD is not routinely available outside the dialysis station, making it technically challenging for an immunocompromised individual. CVVHDF was initiated approximately 20 hours after Cy administration, not to eliminate the drug entirely, but to enhance renal clearance to near-normal levels. For this reason, low-intensity CVVHDF was used deliberately.

This case represents a rare and noteworthy clinical achievement, as paediatric patients undergoing HSCT with a baseline eGFR below 60 mL/min/1.73 m^2 are exceptionally uncommon, with only a few such cases documented in the literature.

CONCLUSIONS

Successful HSCT in a patient with stage III CKD is a clinical challenge but remains possible thanks to close haematological-nephrological cooperation and careful monitoring of the patient. Aggressive interventions, such as conditioning and HSCT, can be safely performed in children with advanced chronic kidney disease.

Conflict of interests

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Author contribution

Original concept of study; collection, recording and/or compilation of data; analysis and interpretation of data: KG, KZ. Writing of manuscript: KG. Critical review of manuscript: AKK, JG, DD. Final approval of manuscript: DD.

References

1. Sureda A, Corbacioglu S, Greco R et al. (eds.): The EBMT Handbook: Hematopoietic Cell Transplantation and Cellular Therapies. Springer International Publishing, Cham 2024.
2. Niederwieser D, Baldomero H, Bazuaye N et al.: One and a half million hematopoietic stem cell transplants: continuous and differential improvement in worldwide access with the use of non-identical family donors. Haematologica 2021; 107: 1045–1053.
3. Ellis MJ, Parikh CR, Inrig JK et al.: Chronic kidney disease after hematopoietic cell transplantation: a systematic review. Am J Transplant 2008; 8: 2378–2390.
4. Lugthart G, Jordans CCE, De Pagter APJ et al.: Chronic kidney disease ten years after pediatric allogeneic hematopoietic stem cell transplantation. Kidney Int 2021; 100: 906–914.
5. Bodge MN, Reddy S, Thompson MS et al.: Preparative regimen dosing for hematopoietic stem cell transplantation in patients with chronic kidney disease: analysis of the literature and recommendations. Biol Blood Marrow Transplant 2014; 20: 908–919.
6. Haubitz M, Bohnenstengel F, Brunkhorst R et al.: Cyclophosphamide pharmacokinetics and dose requirements in patients with renal insufficiency. Kidney Int 2002; 61: 1495–1501.
7. National Center for Biotechnology Information: PubChem Compound Summary for CID 2907, Cyclophosphamide. 2025. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Cyclophosphamide.
8. von Bernuth G, Adam D, Hofstetter R et al.: Cyclophosphamide cardiotoxicity. Eur J Pediatr 1980; 134: 87–90.
9. Kurauchi K, Nishikawa T, Miyahara E et al.: Role of metabolites of cyclophosphamide in cardiotoxicity. BMC Res Notes 2017; 10: 406.
10. Yule SM, Boddy AV, Cole M et al.: Cyclophosphamide pharmacokinetics in children. Br J Clin Pharmacol 1996; 41: 13–19.
11. Perry JJ, Fleming RA, Rocco MV et al.: Administration and pharmacokinetics of high-dose cyclophosphamide with hemodialysis support for allogeneic bone marrow transplantation in acute leukemia and endstage renal disease. Bone Marrow Transplant 1999; 23: 839–842.
12. Heitink-Pollé KMJ, Lilien MR, Bierings MB: Successful bone marrow transplantation in a girl with Fanconi anemia and preterminal renal failure. Bone Marrow Transplant 2008; 42: 57–58.
13. Miano M, Ginevri F, Nocera A et al.: Successful double bone marrow and renal transplantation in a patient with Fanconi anemia. Blood 2002; 99: 3482–3483.

DOI: 10.15557/PiMR.2025.0023