Family-centered shared decision-making in choosing modalities for renal replacement therapy in a pediatric patient with malignant disease

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Abstract
Onconephrology is a new specialized field, and pediatric nephrologists should inititatively and professionally take part in the treatment of children with malignant disease along with the pediatric oncologist and other health care providers. Case: A 3-year-old female patient with advanced neuroblastoma and systemic metastasis, which had a poor prognosis, underwent autologous hematopoietic stem cell transplantation (auto-HSCT) with massive chemotherapy. The complications resulted in acute kidney injury (AKI) requiring continuous hemodiafiltration (CHDF). Although the systemic condition of the patient partially recovered, her renal function did not fully recover and intermittent hemodialysis (IHD) was required. However, she was intolerant to IHD, and sustained low-efficiency dialysis (SLED) was performed for 3 months. Remaining metastases in the bones and end stage kidney disease (ESKD) requiring renal replacement therapy (RRT) made her parents anxious and fearful, which was assisted by much discussion about care and treatment of the patient with healthcare providers including pediatric nephrologist. Her parents eventually chose palliative home care, with peritoneal dialysis (PD) using cycler, due to a small abdominal cavity, after the removal of the neuroblastoma. In pediatric patients with coexisting malignant disease and ESKD, the modalities of RRT should be selected based on the status of the malignant disease and the systemic condition, and should be undertaken with family-centered shared decision-making that respects the rights of pediatric patients.

Introduction
Onconephrology is a recently developed specialized field that focuses on the treatment of pediatric and adult patients with malignant disease. There are adverse renal complications associated with malignant disease and its treatment. Chemotherapy, radiation therapy, and immunosuppressive therapy may result in fluid overload, electrolyte disorders, acid-base imbalance, acute kidney injury (AKI), chronic...

Key words: malignant disease / end stage kidney disease / modalities of renal replacement therapy / family-centered shared decision-making / rights of pediatric patients

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kidney disease (CKD) and subsequent end-stage kidney disease (ESKD)\(^1\). Pediatric nephrologists collaboratively with pediatric oncologists should provide treatment to improve both the prognosis and quality of life of pediatric patients with malignant disease.

**Case Report**

**Case report:** A 3-year-old female patient.

**Present illness:** An abdominal mass was detected by another pediatrician when the patient complained of fever and pain in the left knee. She was referred to our hospital for further investigations and evaluation.

**Past illness and familial history:** Unremarkable.

**Physical examination on admission day:** Height: 94.0 cm, weight: 12.4 kg, and body surface area (BSA): 0.552 m\(^2\). Mental development was normal. An abdominal mass and the liver were palpable at the center of the abdomen.

**Clinical course (Fig. 1):** The patient’s abdominal mass was diagnosed as a neuroblastoma arising from the adrenal gland with metastases to the liver and multiple bone lesions involving the right humerus, the twelfth thoracic vertebrae, and bone marrow (Fig. 2). The tumor was stage M according to the International Neuroblastoma Risk Group classification, and stage 4 according to the International Neuroblastoma Staging System classification. The associated survival rate was 34–47%. Chemotherapy including cyclophosphamide, tetrahydrouryl-adriamycin, etoposide, and cisplatin, and ifosfamide was administered to induce remission. On day 82 of admission, peripheral blood stem cells were collected in preparation for autologous hematopoietic stem cell transplantation (auto-HSCT), and on day 177 of admission, the primary neuroblastoma lesion was excised from the adrenal gland. On admission day 298, irradiation for the remaining metastasis in the bone marrow was administered. Although auto-HSCT with massive chemotherapy including melphalan, etoposide, and carboplatin was administered on day 319, the patient developed mucositis with massive diarrhea causing hypovolemia and pre-renal AKI. Uncontrolled infection associated with neutropenia, effects of chemotherapeutic nephrotoxic drugs and antimicrobial agents exacerbated the pre-renal AKI that further developed into parenchymal AKI. The patient was transferred to the pediatric intensive care unit (PICU) because of decreased urinary output (230 mL/day) that did not respond to a fluid challenge, fluid overload and progressive metabolic acidosis (Table 1). Renal replacement therapy (RRT) in the form of continuous hemodiafiltration (CHDF) was performed via the femoral vein using a temporary double lumen catheter on day 330. In addition, granulocyte and immunoglobulin infusion to control an infection associated with neutropenia resulted in hypoxia caused by pulmonary edema and pleural effusion, and required mechanical ventilation for 6 days. Auto-HSCT engraftment enabled recovery from neutropenia; hypoxia improved and mechanical ventilation was withdrawn, but CHDF was still required owing to oliguria. After moving from the PICU to the pediatric ward on day 345, intermittent hemodialysis (IHD) replaced CHDF, via the subclavicular vein using an implanted permanent double lumen catheter with cuff, because renal function was expected to return to normal following AKI. However, she could not tolerate IHD over 2 days, and experienced disequilibrium syndrome. Therefore, on day 393, sustained low-efficiency dialysis (SLED) was initiated at her bedside, using an implanted double lumen catheter and a continuous RRT (CRRT) machine for 8 hours every alternate day. SLED was continued for 3 months, because renal function did not completely recover and urinary output was 200–400 mL/day, which indicated ESKD and needed RRT. Although the patient recovered slightly, could eat a little and sit unassisted on her bed for short periods, the metastases from the neuroblastoma still persisted in the bone and bone marrow.

The team, comprising the pediatric oncologist, pediatric nephrologist, pediatric surgeon, dialysis specialist, medical social worker, nutritionist, physical therapist, and nurses for pediatric and dialysis patients, collaboratively and continuously discussed the patients’ condition and reached the consensus that the prognosis was poor. They agreed that a more aggressive treatment for the neuroblastoma would be a burden, which might further shorten the patients’ life. Also, a chronic maintenance RRT was needed. The parents were informed regarding this consensus and were asked their intentions about the management of neuroblastoma and ESKD. However, the parents expressed to the nurses their fear about the remaining metastasis, and faced anxiety that they needed to decide the treatment and care for the patient by themselves. This was eased by facilitating repeated discussions with the nurses and providing them with practical information including palliative care that could aid them in their decision-making. The parents eventually opted for
palliative care at home, because the patient wanted to be at home.

Although the patient had abdominal surgery to remove the neuroblastoma, PD was chosen because the patient desired palliative at-home care; and there was no institute that could offer maintenance IHD near her home. In addition, she was intolerant to IHD. Because of the small abdominal cavity after the surgery, continuous cyclic peritoneal dialysis (CCPD) using an automatic dialyzer (cycler) for nightly PD (NPD) was applied. The dwell volume of PD was gradually increased over a month to avoid abdominal distention accompanied by pain and vomiting and to determine the point at which maximum ultrafiltration was obtained. The CCPD prescription was the following: numbers of day dwell were 2 times per day with 200 mL/dwell volume, and cycle frequency was 12 per cycling session for 14 hours in NPD with 400 mL dwell volume. She
Table 1 Data on the day 0, 330, 646 (at discharge), and 1455 (2 years later after discharge)

|         | 0        | 330      | 646*     | 1455*    | days |
|---------|----------|----------|----------|----------|------|
| Height  | 94       | 102      | 102.5    | 103.9    | cm   |
| Weight  | 12.4     | 12.2     | 14.1     | 16.4     | kg   |
| WBC     | 9530     | 30       | 3340     | 8420     | /μL  |
| RBC     | 3.55×10⁶ | 2.37×10⁶ | 2.93×10⁶ | 3.87×10⁶ | /μL  |
| Hb      | 9        | 7.3      | 9.8      | 13.1     | g/dL |
| Ht      | 28.7     | 20.9     | 31.2     | 39.5     | %    |
| Plt     | 287000   | 48000    | 88000    | 212000   | /μL  |
| TP      | 5.6      | 5.9      | 5.1      | 6        | g/dL |
| Alb     | 2.6      | 2.7      | 2.8      | 3.6      | g/dL |
| Cr      | 0.22     | 2.01     | 1.79     | 1.9      | mg/dL|
| eGFR    | 143.1    | 19.5     | 21.9     | 21.3     | mL/min/1.73 m² |
| BUN     | 2.9      | 35.8     | 39.2     | 45.4     | mg/dL|
| LDH     | 585      | 1409     | 134      | 189      | U/L  |
| AST     | 28       | 210      | 28       | 28       | U/L  |
| ALT     | 8        | 57       | 37       | 18       | U/L  |
| Na      | 132      | 131.1    | 142      | 140      | mEq/L|
| K       | 4.5      | 3.42     | 4.3      | 3.2      | mEq/L|
| Cl      | 96       | 108      | 104      | 98       | mEq/L|
| Ca      | 9.1      | 6.9      | 9.1      | 9.2      | mg/dL|
| IP      | 4.5      | 2.5      | 7.8      | 5.9      | mg/dL|
| UA      | 2.7      | 6.9      | 3.6      | 5.4      | mg/dL|
| CRP     | 16.1     | 9.01     | 0.24     | 0.22     | mg/dL|
| u-Na    | 23       |          |          |          | mmol/L|
| FENa    | 0.58     |          |          |          | %    |
| u-NGAL  | >1500    |          |          |          | ng/mL|
| pH      | 7.489    | 7.417    | 7.41     | 7.41     |      |
| pCO₂    | 43       | 28.8     | 46       | 49       | mmHg |
| HCO₃⁻   | 31.8     | 18       | 28       | 30       | mmol/L|
| BE (mmol/L) | 7.9     | -5.6     | 3.1      | 4.8      | mmol/L|

*eGFR: estimated glomerular filtration rate
FENa: fractional excretion of sodium
u-NGAL: urinary neutrophil gelatinase-associated lipocalin
*; The value is data after initiation of peritoneal dialysis.

was eventually discharged on day 646 with PD (Table 1), and vitamin A and specific substance Maruyama expecting inhibition of growth of the metastasis.

Although the metastases remain in the bone, and her height has been almost unchanged in the 2 years after her discharge, residual renal function is still preserved with a urinary output of 200–400 mL/day (Table 1). Peritoneal equilibration test (PET) shows high transporter (dialysate-to-plasma concentration ratio (D/P) for creatinine=0.82, dialysate-to-baseline dialysate concentration ratio (D/D0) for glucose=0.28). Trial increase of dwell volume from 400 mL to 600 mL in NPD unexpectedly decreases ultrafiltration, which could be due to a small abdominal cavity. Therefore, the prescription of CCPD is the same as at discharge. She is able to stand and walk again and continues her education at home through visiting teachers.

**Discussion**

A 3-year-old girl with neuroblastoma suffered AKI after auto-HSCT and was treated with CHDF in PICU. However, the renal function did not fully recover; therefore, SLED was continued in the pediatric ward for 3 months, due to intolerance to IHD. Although her systemic condition improved
partially, metastases persisted in the bone and residual renal function was still poor. The medical team including the pediatric nephrologist encouraged and assisted her parents in decision-making regarding her treatment and care including choice of modality of RRT. Eventually, the parents chose in-home palliative care keeping in mind the patients’ desire, with CCPD using cycler due to her small abdominal cavity after the surgery for removing the neuroblastoma.

In critically ill pediatric patients with AKI in PICU, the modality of RRT is chosen based on efficacy and safety. Although the optimum RRT modality in AKI has not been proven\(^2\), in pediatric patients with hemodynamic instability, CRRT is more appropriate than IHD\(^3\). In the present case also, AKI after auto-HSCT was treated by CRRT in PICU, because of hemodynamic instability due to systemic infection and respiratory failure.

In contrast, in the recovery phase of AKI, in critically ill patients with less hemodynamic instability, modality of RRT is chosen based on efficacy, safety and consideration for rehabilitation\(^4\). IHD is preferred to CRRT, because of the short immobilization time required to maintain stable blood flow during RRT, which is beneficial for rehabilitation. In addition, increasing the frequency of IHD reduces the patients’ burden by decreasing the volume of ultrafiltration per session in the recovery phase\(^5\). In the present case also, IHD was first applied to her in the recovery phase after discharge from PICU. However, the devices and IHD machines for chronic maintenance dialysis are still designed for adult patients in Japan; therefore, extracorporeal volume of the circuit for dialysis including dialyzer is in excess of circulating blood volume in children, which often causes intolerance for IHD. Accordingly, in the present case, SLED was applied using a CRRT machine designed for both adults and children. Although immobilization time in SLED is longer than that in IHD and shorter than that in CRRT, SLED is preferred to IHD, because it facilitates adequate solute and fluid removal with less hemodynamic instability. SLED is also less demanding for medical staff than CRRT because it does not require a night procedure, which is also preferable for patients as it does not impact sleep times, and rehabilitation\(^6\). These beneficial points facilitated the continued use of SLED in the pediatric ward for 3 months in our case. In addition, it was possible to use a permanent HD catheter with cuff implanted at subclavian vein for longer use without any catheter-associated infection.

Either PD or IHD is usually applied in the chronic maintenance phase of ESKD even with malignant disease\(^7\). Although PD is usually preferred to IHD in younger children who weigh less and are suffering from ESKD, abdominal surgery is a relative contraindication for PD, and the small abdominal cavity due to peritoneal scarring and adhesions associated with surgery reduces efficacy in PD. However, it was proposed that abdominal surgery should not always be a contraindication in patients who desire PD\(^8\). In case the abdominal cavity is small for PD, because intraperitoneal pressure is inversely correlated with ultrafiltration\(^9\), CCPD, using cycler by frequent short dwell time and small amount of dwell volume, is preferred for obtaining sufficient ultrafiltration, which is also favorable for the peritoneal membrane showing high transporter in PET\(^10\). In the present case, the remaining renal function generating urinary output also contributed to managing PD favorably during palliative care at home.

Especially in patients with malignant disease, it is difficult to choose the optimal modality of RRT for ESKD, or to decide on withdrawal of RRT which must take into consideration the total prognosis, remaining renal function, tolerance for dialysis, and the patients’ preferences, for which a shared decision-making (SDM) is proposed\(^11\)\(^12\). The Renal Physicians Association described that SDM is constructed as an approach in which healthcare providers and patients discuss the best way forward, and where patients and their families are encouraged to consider options and to avail their preferred management options\(^13\)\(^14\). In case of poor prognosis, the decision making such as withdrawal of RRT is an emotional burden for nephrologists, which SDM could reduce while preserving patient-centered care\(^15\). Conversely, SDM, and especially family-centered SDM, could be extremely burdensome and difficult for family members who must decide the direction of treatment including choice of RRT and withdrawal of RRT in critically ill cases with poor prognosis\(^16\). Similarly, in the present case, the parents suffered extreme anxiety at having to determine the direction of treatment for their daughter by themselves. The anxiety could be lessened only by expressing their concerns and emotions, and communicating more frequently with healthcare providers, and the pediatric nephrologist who provided accurate and detailed information\(^14\). In case of choosing withdrawal of maintenance hemodialysis due to poor prognosis, there may be
lots of conflicts that can not be resolved among the family of patient and healthcare providers even after sufficient discussions regarding care and treatment options for the patient. Such conflicts are recommended to be addressed by an ethics committee comprising of several specialists, separate from the healthcare providers[17]. Additionally, in family-centered SDM, informed assent from pediatric patients should be obtained in older children, and even infants should be treated as individuals having independent rights[14]. In the present case, the family wanted their daughter to be treated at home, as she wished, and so they are at home with palliative treatment in the form of PD.

Conclusion

In pediatric patients with malignant disease, modalities of RRT should be selected based on the state of disease and the patients’ overall condition. The choice should involve family-centered SDM with respect to the rights of the pediatric patients, including infants.

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Informed Consent

Informed consent was obtained from the parents of the patient.

Conflict of Interest

All the authors have declared the absence of any competing interest.

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