

Acute Kidney Injury and Dialysis in Children: Illustrative Cases

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Summary: Pediatric nephrologists and critical care physicians are faced with a heterogeneous patient population with varied epidemiology caring for children with acute kidney injury or other diseases that may require renal replacement therapy provision. We have composed 4 detailed case scenarios to highlight the challenges and interdisciplinary approach required for optimal care provision to children, and that serve to direct the different articles contained in this special issue of *Seminars of Nephrology* devoted to acute kidney injury in children.

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CASE 1: THE PATIENT WITH SEPSIS AND MULTIORGAN DYSFUNCTION SYNDROME

A 14-year-old boy comes home from school complaining to his parents of fatigue, flu-like symptoms, and generalized body aches; he later develops headache, nausea, and emesis and chooses to go to bed early. The parents check on the boy later that evening and find the child's head is very warm to the touch but his hands and feet are "cold like ice cubes." When they turn on the bedside lamp, they notice that his skin appears gray and mottled; they become frightened and try to arouse him but he will not wake up. His parents call 911 and an ambulance comes to the house to transport the child to the hospital. At transport his blood pressure is noted to be 70/20.

On arrival to the emergency department the child has evidence of shock with systolic blood pressure of 65 mm Hg by palpation, heart rate of 120/minute, and cold extremities. He is unresponsive. His initial weight is 52 kg. He received 2 L of normal saline during transport with tran-

sient improvement in perfusion and blood pressure; he receives an additional 3 L of normal saline in the emergency department. He is intubated and a continuous infusion of dopamine is started at a rate of 20 $\mu\text{g}/\text{kg}/\text{min}$. His blood pressure is 80/30; he is noted to have petechiae. Blood cultures, complete blood count, serum chemistries, prothrombin time/activated partial thromboplastin time, and an arterial blood gas are drawn; the blood gas result reveals a pH of 6.95, and partial pressure of oxygen of 57 mm Hg. He is given a dose of intravenous ceftriaxone and is transferred to the intensive care unit for further management.

Initial laboratory values reveal an increased white blood cell count at 35,000/ μL , prolonged coagulation studies with a prothrombin time 21.3 seconds and activated partial thromboplastin time 64 seconds, low total CO_2 on serum chemistries of 11 mmol/L, and a serum creatinine level of 1 mg/dL. He remains hypotensive and the critical care team starts a continuous infusion of epinephrine in addition to the dopamine. Through the night and into the next morning the patient receives intermittent boluses of isotonic crystalloid for episodes of low blood pressure totaling an additional 5 L of normal saline. His coagulation studies worsen and his petechiae progress to the point that he develops ecchymoses on his hands and feet; he receives 500 mL of fresh-frozen plasma. The total fluid volume administered to the patient

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over the initial 12 hours of hospitalization is 8,840 mL; urine output over the same 12-hour period is 850 mL. Repeat serum creatinine in the morning reveals a value of 1.6 mg/dL. The blood culture grows *Neisseria meningitidis*.

Over the next 24 hours, the patient's blood pressure stabilizes in the range of 90 to 100/50 with the use of intravenous fluids and vasoactive infusions. The serum creatinine level is now 2.8 mg/dL. The patient weighs 64 kg; total fluids in for the 24-hour period have been 6,240 mL, total urinary output over the same 24-hour period has been 1,450 mL. Physical examination is significant for edema and worsening purpura of the hands and feet. Oxygenation is becoming more difficult; the chest radiograph shows diffuse hazy markings throughout the lungs. The critical care team requests nephrology consultation.

Educational Points From the Case

After reviewing this case and the subsequent discussion, the reader should be able to do the following:

- Recognize the importance of aggressive, goal-directed volume expansion for the initial acute treatment of hypoperfusion states in septic shock.
- Understand the risks associated with volume overload in the critically ill child.
- Become familiar with management strategies to prevent or limit progression of volume overload in the setting of multiorgan dysfunction.
- Describe the impact of acute kidney injury (AKI) on outcome for the child with multiorgan dysfunction.

CASE 2: THE CHILD WITH AKI ASSOCIATED WITH STEM CELL TRANSPLANTATION

A 9-year-old girl with relapsed high-risk acute lymphoblastic leukemia receives a matched unrelated donor hematopoietic stem cell transplant. Pretransplant conditioning regimen included fractionated total body irradiation and cyclophosphamide. Her posttransplant course has been complicated by fever without an identifiable source; she has been receiving meropenem and gentamicin for the past week and

recently liposomal amphotericin B was added to her regimen. In addition, she has had problems with graft-versus-host disease, manifesting as skin rash and gastrointestinal irritation; she is receiving tacrolimus intravenously with trough levels between 12 and 15 ng/mL. She receives total parenteral nutrition and other intravenous infusions, with a total daily input of 2,000 to 2,500 mL depending on her need for blood products.

On daily screening laboratory studies, her serum creatinine level is noted to be 0.9 mg/dL, higher than her previous value of 0.7 mg/dL. Her urinary output as reported by the nursing staff had been between 2 and 2.5 mL/kg/h; however, urine output is now reported to be approximately 1.5 mL/kg/h. The transplant service elects to increase daily fluids to a goal of 3,000 mL/24 hours to support renal function. The next day, her serum creatinine level is 1.1 mg/dL and her urine output is still reported at 1.5 mL/kg/h; early the next morning the patient develops respiratory distress and is transferred to the intensive care unit. Her serum creatinine level is 1.8 mg/dL, urine output was calculated to be 1 mL/kg/h over the previous 24 hours. The patient's weight, which had been stable near 40 kg, is now measured at 45 kg; her blood pressure, previously normal, is 140/90. The chest radiograph reveals vascular markings consistent with pulmonary edema. She receives a dose of intravenous furosemide, which increases her urinary output to 100 mL/h for 2 hours but has little effect on her respiratory status. She is intubated and placed on mechanical ventilation.

Over the next 24 hours, the patient's urinary output dwindles to 0.5 mL/kg/h and her serum creatinine level increases to 2.6 mg/dL. Oxygen requirement on mechanical ventilation increases. Critical care and transplant teams request a consultation with the nephrology service.

Educational Points From the Case

After reviewing this case and the subsequent discussion, the reader should be able to do the following:

- Identify the multiple risk factors leading to AKI associated with hematopoietic stem cell transplant.

- Discuss the variable relationship between urinary output and renal function (glomerular filtration rate) and the limitations of serum creatinine as a marker of glomerular filtration rate.
- Understand the special risks associated with volume overload in the stem cell transplant patient and strategies to prevent volume overload.
- Provide a rationale for different approaches to evaluation and management of the stem cell transplant patient who has become volume overloaded, including conservative methods and early, aggressive renal replacement therapy options.

CASE 3: THE INFANT WITH AKI ASSOCIATED WITH CARDIOPULMONARY BYPASS USED IN CORRECTIVE CONGENITAL HEART SURGERY

A 2-week-old, 3.1-kg infant with pulmonary atresia and ventricular septal defect is scheduled to undergo a palliative surgical intervention with a Blalock-Taussig shunt to provide pulmonary blood flow through a conduit from the innominate artery (systemic circulation) to the right pulmonary artery (pulmonary circulation). A continuous prostaglandin infusion was started soon after birth to maintain ductus arteriosus patency and discontinues at the time of surgery. Two hours after surgery severe bradycardia, hypotension, and cyanosis occur. The patient is resuscitated promptly by infusion of 0.1 $\mu\text{g}/\text{kg}/\text{min}$ of epinephrine and 10 $\mu\text{g}/\text{kg}/\text{min}$ of dopamine. The infant undergoes cardiac catheterization that shows a subtotal shunt occlusion with pulmonary blood flow reduction. He is emergently transferred to the operating room to perform surgery for a new shunt placement. At the end of surgery, the patient is weaned from cardiopulmonary bypass and the perfusionist performs ultrafiltration in the operating room to the goal hematocrit of 40%. The surgeon removes the cannulae and covers but does not surgically close the chest. The child is transported to the cardiac intensive care unit, where he receives infusions of 0.03 $\mu\text{g}/\text{kg}/\text{min}$ of epinephrine, 10 $\mu\text{g}/\text{kg}/\text{min}$ of dopamine, and 1 $\mu\text{g}/\text{kg}/\text{min}$ of milrinone to maintain a

mean arterial pressure of 50 mm Hg. His arterial partial pressure of oxygen is 35 mm Hg and his O_2 saturation is 75%. The urinary output decreases from earlier values of 2.5 to less than 1 mL/kg/h. His serum creatinine level, which was 0.3 mg/dL immediately after surgery, is now 0.62 mg/dL. The patient receives a dose of furosemide without an increase in urinary output. The intensivist prescribes a continuous infusion of furosemide at 0.2 mg/kg/h intravenously to support urinary output and maintain fluid balance. In the next 12 hours, fluid balance becomes slightly positive (+100 mL). On the following day, the serum creatinine level increases to 0.9 mg/dL and urine output decreases to 0.5 mL/kg/h. Head and limb edema become evident. After fluid restriction and parenteral nutrition halving, an additional 10-mg furosemide dose is given without diuresis. An evaluation of fluid accumulation from admission in the intensive care unit reveals a net positive fluid balance of 280 mL. The intensivist contacts the nephrologist to discuss the case.

Educational Points From the Case

After reviewing this case and the subsequent discussion, the reader should be able to do the following:

- Understand the physiologic principles related to AKI in the newborn and the special concerns for the child with congenital heart disease.
- Determine the indications and approach for the use of diuretics in the critically ill child.
- Identify conservative measures to limit the risks of developing AKI in an infant who undergoes cardiac surgery.
- Evaluate and appropriately prescribe the different options for renal replacement therapy for the infant after surgery for congenital heart disease.

CASE 4: MEDICAL MANAGEMENT AND RENAL REPLACEMENT THERAPY PROVISION TO THE INFANT WITH AN INBORN ERROR OF METABOLISM

A 5-day-old newborn infant starts to refuse feeding, has repeated vomiting, and “seems sleep-

ier” to his parents. The patient is an infant male, born to a 24-year-old primigravida female who had good prenatal care and no complications during her pregnancy. The child was born at 39 weeks’ gestation, had Apgar scores of 8 at 1 minute and 9 at 5 minutes, and weighed 3,520 g at birth. He had initially been feeding well on the breast and also with the bottle. Since birth, intermittent regurgitations were present. The following day, the parents notice that the baby is tachypneic. Afterwards, the infant falls asleep and does not awake. The parents bring him to the local emergency room.

The physical examination is significant for a 7-day-old, dehydrated, pale-appearing infant with low muscle tone. Body weight is 2,910 g. Heart rate is 152 beats per minute, respiration is 65 breaths per minute, blood pressure is 82/38. The emergency room team intubates the patient, performs laboratory tests, and performs a full evaluation for neonatal sepsis, including blood cultures, urine culture, and lumbar puncture. Test results from the laboratory show thrombocytopenia ($35,000/\mu\text{L}$), leukopenia (2,200 white blood cell/ μL), severe metabolic acidosis (pH 7.04, partial pressure of carbon dioxide 18 mm Hg, bicarbonate 7 mmol/L, base deficit 18), and a normal C-reactive protein level. The child receives intravenous fluids, alkali therapy, and ampicillin and gentamicin. In the following 6 hours, the clinical picture further deteriorates with progressive lethargy, appearance of abnormal movements, and persistence of severe metabolic acidosis. Repeated laboratory examinations show a serum ammonia level of $1,200 \mu\text{mol/L}$ and positive urine ketones. The emergency room physician contacts the children’s hospital to arrange emergent transport of the infant for management of hyperammonemia. Children’s Hospital Neonatal Intensive Care Unit, Metabolic, and Dialysis Units are alerted.

At admission in the neonatal intensive care unit, the patient is found to be in stage 3 coma, dehydrated, hypotensive (65/28 mm Hg), and oliguric. After a 200-mL bolus of saline, his blood pressure improves (81/39 mm Hg). Inotropic support is started with dopamine at a dose of $6 \mu\text{g/kg/min}$.

Under suspicion of an inherited metabolic disease causing severe neonatal hyperammonemia,

the medical treatment and the diagnosis protocol for inborn errors of metabolism are rapidly started. A metabolic work-up including blood ammonium and lactate, plasma amino acids, acylcarnitines, urine organic acids, and orotic acids is collected together with routine blood chemistry, blood cell count, blood cultures, and urine cultures. Brain and abdominal ultrasounds show neither hemorrhage nor other pathologic findings.

The patient receives intravenous boluses of 4% arginine hydrochloride at a dose of 750 mg over 2 hours together with 600 mg carnitine and 1 mg intramuscular hydroxocobalamin. A 10% dextrose solution is started at 120 mL/kg/24 hours. Carbamylglutamate at a dose of 450 mg is administered by nasogastric tube. Laboratory results show a sodium level of 126 mmol/L, potassium level of 5.7 mmol/L, chloride level of 91 mmol/L, bicarbonate level of 11 mmol/L, glucose level of 180 mg/dL, blood urea nitrogen level of 28 mg/dL, and creatinine level of 1.2 mg/dL. An increase of plasma ammonium level to $1,570 \mu\text{mol/L}$ is found. After the first 2 hours of treatment, plasma ammonium level is $1,350 \mu\text{mol/L}$.

Biochemistry laboratory results show an abnormal profile of urine organic acid with increased excretion of 3-hydroxypropionate, propionylglycine, tiglylglycine, 3-hydroxybutyrate, acetoacetate, and methylcitric acid. Plasma acylcarnitine analysis shows an abnormal profile, with a prominent increase of propionylcarnitine. Free carnitine is reduced and the ratio of propionylcarnitine to free carnitine is greatly increased. The profile of plasma amino acids displays increased levels of glycine ($1,250 \mu\text{mol/L}$) and alanine ($876 \mu\text{mol/L}$), with normal glutamine levels. A diagnosis of propionic acidemia is then made. Given the poor response to medical treatment, the team decides to initiate dialysis therapy.

Educational Points From the Case

After reviewing this case and the subsequent discussion, the reader should be able to do the following:

- Recognize the need for a high index of suspicion for rare metabolic disorders in the ill newborn.

- Understand the importance of rapid evaluation and coordinated care for the newborn with an inborn error of metabolism.
- Describe the physiologic basis of conservative management strategies to address metabolic disorders and appropriate methods to evaluate success versus the need for alternative methods.
- Evaluate the indications, options, and appropriately prescribe the techniques for extracorporeal support to remove endogenous toxins.