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A Case of Acute Kidney Injury after Contrast Imaging and Empiric Nephrotoxic Antibiotherapy

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Authors' contributions

This work was carried out in collaboration between all authors. Authors HEB, NYO and FIG wrote the draft of the manuscript. Author HEB managed the literature searches. Author s HEB and NYO designed the figures, managed literature searches and contributed to the correction of the draft. Author NYO provided the case, the figures and supervised the work. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Contrast imaging assists with a diagnosis and antibiotics are essential for treatment of complicated infections. Since empiric antibiotherapy and multiple contrast imaging in critically ill children can cause acute kidney injury (AKI), clinicians must pay special attention in this critical decision process.
Presentation of Case: Six-year-old boy had a penetrating trauma via a scythe to his right eye with resultant orbital cellulitis and endopthalmitis. He received multiple empiric nephrotoxic antimicrobial therapy and his orbit was imaged three times with radio-contrast studies in a week. He admitted to pediatric intensive care unit (PICU) with resultant renal failure. The patient survived with normal renal functions by the help of intensive care support including mechanical ventilation, inotropic therapy, renal replacement therapy, surgical intervention, and proper antibiotic dosage with daily

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adjustments per calculated glomerular filtration rate.
Conclusion: Special consideration must be given when using empiric antibiotics and imaging with contrast media in sick children. Both may deteriorate renal functions as in our patient. These predictors, however, need further work to validate reliability.

Keywords: Nephrotoxicity; continuous renal replacement therapy (CRRT); renal failure; sepsis; child.

1. INTRODUCTION

Contrast imaging assists with a diagnosis, and antibiotics are essential for treatment of complicated infections. Albeit both can cause acute kidney injury (AKI) in critically ill children.

Here, we report a six-year-old boy undergoing renal replacement therapy due to AKI most likely occurred due to overexposure of nephrotoxic agents after multiple imaging sessions with contrast imaging and administration of multiple empiric antimicrobial therapies. Our aim is to mention that special attention must be paid when deciding contrast imaging and the use of empirical antimicrobial drugs in critically ill children to prevent renal injury.

2. PRESENTATION OF CASE

Six-year-old boy presented with multisystem organ failure due to septic shock. He had a history of penetrating trauma via a scythe to his right eye with resultant orbital cellulitis and endopthalmitis. His perforated cornea was sutured, and he received empiric broad-spectrum antimicrobial therapy (meropenem for 8 days, voriconazole for 5 days, vancomycin for 1 day, teicoplanin for 7 days, metronidazole for 3 days, clindamycin for 2 day and amikacin for 5 days) before his admission to the pediatric intensive care unit (PICU). During 7 days long hospitalization before his PICU admission he had 2 magnetic resonance imagings (MRI) and one computerized tomography (CT) scan with contrast of his orbit to rule out an abscess (Table 1). Since the studies were interpreted as indeterminate, no immediate surgical intervention was performed. The infection persisted under broad-spectrum antimicrobial therapy and his renal functions had slowly deteriorated. Planned surgical approach was enucleation of the eye and drainage of the abscess, if any when clinically stable. He developed generalized edema with oliguria with deterioration of his renal functions. On admission to the PICU his temperature was 36.5°C, heart rate was 81 beats per minute, respiratory rate was 20 breaths per minute, and his blood pressure was 119/80 mmHg. He had generalized edema, especially on his face and neck. Both eyelids were edematous and necrotic tissues were prominent in right eyelid, and light reflex was absent in the right eye. He was oliguric (0,23 ml/kg/hour) for the first 4 hours after admitting into the PICU and then he developed anuria which was unresponsive to diuretics and bolus fluid infusion.

Table 1. Laboratory values and timing of potential toxic exposures before admission to PICU. bold cells represent days with corresponding antibiotic and imaging exposure

	1st day	**2nd day**	**3rd day**	**4th day**	**5th day**	**6th day**	**7th day**	**8th day**
White blood cell count (10^3/µL)	18.7							17.1
Creatinine (mg/dL)	0.5					0.43		0.99
C-reactive protein (mg/L)	63.0							73.5
Proteinuria (spot urine sample)							+++	+++
CT imaging								
MR imaging								
Meropenem								
Vorikonazole								
Teicoplanin								
Vankomycin								
Metronidazole								
Clindamycin								
Amikacin								

Laboratory results revealed the following: WBC count; 17.1 × 10^3/μL; with 86% neutrophils, 7.4% lymphocytes, 6.4% monocytes, 0.1% eosinophils; hemoglobin; 8.1 g/dL; platelets; 107 × 10^3/μL; C-reactive protein; 30.2 mg/L; blood urea nitrogen (BUN); 82 mg/dL; creatinine 2.0 mg/dL, which increased up to 3.02 mg/dL at the end of first day. His creatinine level was 0.43 mg/dL, and BUN level was 18 mg/dL 3 days before admission to PICU. The first urine sample drawn with a urinary catheter revealed proteinuria (4 positive), urine specific gravity of 1013, trace glycosuria despite normal blood glucose level, white blood cells (14/high power field) and red blood cells (11 /hpf). Further urine examination for the kind of proteinuria or for calculation of fractional excretion of sodium concentration (FENa) to determine underlining pathology of AKI was impossible, because the patient developed anuria rapidly.

His estimated glomerular filtration rate (GFR) based on Schwartz equation was 33 mL/min/1.73 m^2 on admission. A renal ultrasound examination revealed increased parenchymal echogenicity of both kidneys, with normal size according to his age and length.

Blood, urine and discharge from his eyes were cultured. Antimicrobial therapy was continued with moxifloxacin, tobramycin, oxytetracycline and amphothericin B as topical agents and vancomycin, meropenem, liposomal amphotericin B and metronidazole as systemic agents with daily dose adjustments per GFR (Table 2).

At the end of the first day of PICU admission he was intubated due to respiratory failure and inotropic support with dopamine started Table 2. Continuous venovenous hemodiafiltration (CVVHDF) was initiated at the same day secondary to acute anuric kidney injury via a double lumen venous femoral catheter. His glomerular filtration rate was decreased to 22 mL/min/1.73 m^2, when CVVHDF was started. Duration of total treatment was 7 days; the last 3 days only hemofiltration was applied. Adrenalin was added on the second day of CVVHD, and ionotropic support with dopamine and adrenaline was continued for 5 days. At the 5th day adrenalin was tapered to off and dopamine was continued at renal dosage for additional 5 days to preserve renal perfusion. The complications associated with continuous renal replacement therapy (CRRT) were bleeding, occlusion of the set and hypotension. He was extubated one day after the termination of CRRT. He had enucleation of his right eye with application of prosthesis at the 25th day of his PICU admission and was discharged two weeks after his eye surgery. His renal function remained within normal range on follow up at 9th month.

3. DISCUSSION

Acute kidney injury (AKI) is characterized by a sudden decline in glomerular filtration rate with resultant azotemia and increase in serum creatinine concentration [1]. Incidence of AKI varies in different studies but it is a common problem in children admitted to pediatric intensive care units (PICU) [2].

Common causes of AKI are hypoxic/ischemic insults, haemolytic uremic syndrome, obstructive uropathy, glomerulonephritis and drug induced or toxin mediated injury to kidneys [1]. Studies revealed that nephrotoxic pharmacologic agents are an important cause of AKI in children with a rate of 16% [3]. Many different nephrotoxic

Table 2. Laboratory values, blood pressure measurements and GFR at PICU during CRRT. maximum values are shown for repeated laboratory measurements at the same day. for the blood pressure measurements the range is shown

	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
White blood cell count (10^3/μL)	18.6	20.3	9.9	11.8	10.9	14.1	12.8
Creatinine (mg/dL)	3.02	2.52	2.16	1.44	1.00	1.08	1.03
C-reactive protein (mg/L)	30.2	38.7	86.0	103.1	76.9	25.1	13.0
Estimated glomerular filtration rate (mL/min/1.73m^2)	22.0	26.1	30.5	45.8	66.0	61.1	64.0
Systolic blood pressure (mmHg)	65-138	71-120	82-144	85-124	84-148	94-138	93-118
Diastolic blood pressure (mmHg)	40-89	35-83	39-83	37-62	36-80	55-99	61-85
Inotropic medication (DA: dopamine, A: adrenalin)	DA	DA+A	DA+A	DA+A	DA+A	DA	DA

agents can cause AKI in children. These include nonsteroidal anti-inflammatory drugs, antibiotics, antiviral agents, cytotoxic drugs and radiocontrast media [4]. Although these agents can solely damage kidneys, concomitant administration of multiple nephrotoxic drugs increases the risk of developing AKI [4]. Our patient was also exposed multiple nephrotoxic drugs.

Sepsis also accounts for an important proportion of pediatric cases with AKI like 11-18.9% in different studies [3,5]. Both multiple exposure to nephrotoxic agents and underlying eye infection leading to sepsis may have deteriorated renal functions of our patient. It is of special importance to choose the least toxic antimicrobial agents in septic pediatric patients to preserve renal functions.

The incidence of contrast-induced nephropathy (CIN) in children is unknown, but it is one of the most frequent causes of AKI in hospitalized adult patients. Pre-existing renal impairment, diabetes mellitus, dehydration, concurrent use of other nephrotoxic drugs are risk factors for CIN in adults [6]. The risk factors for developing CIN are not well defined in children, multiple factors as in our patient like sepsis and concomitant use of nephrotoxic antibiotics may facilitate CIN.

Mortality rate of AKI differs between 27-51% depending on factors such as younger age, associated systemic diseases and sepsis [5,7]. In PICU; critically ill pediatric patient with AKI have higher mortality than other critically ill children without AKI [7,8]. Sepsis and number of organ failures are independent risk factors for mortality in children with AKI [5]. Mortality in critically ill children requiring continuous renal replacement therapy is 32% [9]. For patients with acute kidney injury who require CRRT, the presence of sepsis and multiorgan dysfunction syndrome (MODS) are associated with higher mortality [10].

The exact cause of AKI in our patient remained unclear because only a renal biopsy could definitely determine the underlining pathology, which was not appropriate in our critically ill patient. Due to the multiple exposure to potentially toxic agents and the speed of events as, rapid rise in serum creatinine concentration, hypotension and circulating volume depletion due to sepsis, we suggest that acute tubular necrosis (ATN) was responsible for AKI. However, we do not have supporting data for ATN, like granular epithelial cell casts or renal tubular epithelial cells in the urine or an increased fractional excretion of sodium (FENa). Proteinuria and hematuria may support the diagnosis of acute tubule interstitial nephritis (AIN). Nevertheless there were no eosinophilia, and any white blood cell casts in the urine, nor any history of common offender like nonsteroidal anti-inflammatory agents favoring AIN.

As a result, even though the exact reason of AKI in our patient is not clarified, with the help of supportive therapy, timely initiation of CRRT, careful antibiotic usage with daily adjustments per calculated glomerular filtration rate, and proper surgical intervention the patient survived with normal renal functions.

4. CONCLUSION

The decision for imaging with contrast media and the choice of empiric antibiotics deserves special consideration in sick children. Physicians need to be very careful, since both may deteriorate renal functions as in our patient.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Ethical approval for this case report was not applicable.

DECLARATION

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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