Title

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CLINICAL VIGNETTE

The Nephrologist as Rainmaker: The Art of Watchful Waiting for Renal Recovery in Patients with Acute Kidney Injury

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Introduction

Acute Tubular Necrosis (ATN) is a common cause of Acute Kidney Injury (AKI) due to various hemodynamic and pharmacologic nephrotoxic insults. The diagnosis can be clinically made based on urinary electrolytes or observed clinical course. It does not always need to be biopsy-proven when suspected on its own. The diagnosis of ATN, in many cases, can be reversible, and renal recovery may occur if the degree of tubular damage is not extensive.[1]

Several caveats should be considered when monitoring a patient with acute kidney injury biochemically for recovery. The first is that urine output, while an encouraging sign, needs to be accompanied with improvement in serum levels of nitrogenous wastes (blood urea nitrogen, or creatinine as indexes for unmeasured nitrogenous wastes). Secondarily the fluctuations in serum creatinine need to be carefully examined with the timing of the patient's last hemodialysis. Twenty-four-hour urine creatinine clearances and urea clearances can also be obtained as a more accurate measurement of estimated glomerular filtration rate (eGFR), though with caution in interpreting the results given physiological principles discussed later. In some patients, it is important to consider post urinary obstruction as a barrier to recovery of renal function.[2]

Monitoring electrolytes to avoid dangerous abnormalities after stopping dialysis is essential. Pharmacotherapy of blood pressure similarly needs to be more closely monitored after stopping maintenance hemodialysis in patients who have recovered. We discuss three patients who achieved renal recovery after acute kidney injury and examine their clinical course, the delayed nature of recovery from acute kidney injury, and the close monitoring that was needed to ensure successful transition off hemodialysis and to routine Chronic Kidney Disease (CKD) care.

Patient 1

An 82-year-old Caucasian male who presented with acute pancreatitis resulting in sepsis and ATN. He subsequently had a posterior limb cerebrovascular accident (CVA) along with elevated troponin from demand ischemia-induced non-ST-elevation myocardial infarction. He had a nearly preserved GFR initially with sCr of 0.9-1 mg/dl and eGFR of 80-90 ml/min indicative of subclinical CKD stage II. During his hospital stay, he developed worsening acute tubular necrosis due to sepsis resulting in hypotension, oliguria, and respiratory distress. He was started on continuous renal replacement therapy (CRRT) and intubated given progressive volume overload. He was treated for sepsis with antibiotics and vasopressors and successfully transitioned to intermittent hemodialysis as pressor requirements waned. He was successfully extubated but suffered from significant residual weakness from his CVA. Renal function remained impaired with serum creatinine above 6, and he was discharged with instructions to receive three times a week hemodialysis (given ongoing oliguria) with monitoring for renal recovery. He continued to require three times per week dialysis with a relative lack of urine output for six weeks.

His serum creatinine remained at 5-6 mg/dL, but his daughter noted that he had an increased urinary output with about 0.5L / day. His dialysis was changed to twice a week, with ultrafiltration parameters to avoid hypotension. He then noted pain in his suprapubic area for which he went to the emergency department with suspicion of obstruction, and he had a post-void residual of 1 liter. Upon placement of a Foley catheter, the patient not only had a sustained increase in his urine output, but his serum creatinine improved. After about one week, his serum creatinine recovered to 2 mg/dL with 1-1.5 L of urine output per day. With the sustained biochemical clearance without dialysis for nearly five days, we decided to remove the hemodialysis catheter, and a 24-hour urine creatinine clearance confirmed an eGFR of 30ml/min. sCr then continued to improve to 1.72mg/dL and most recently at 1.03mg/dL. Cystatin C improved in parallel to a level of 1.7 mg/L with an estimated GFR by cystatin C of 43ml/min. Figure 1 shows the serum creatinine trend.

Patient 2

A 51-year-old male presented at an outside medical system with shock after a motorcycle accident. He experienced a right malleolus closed fracture and another fracture of his tibia. He was also noted to have AKI with a serum creatinine of 4.4 mg/dL on admission to the local trauma center. He was started on maintenance hemodialysis due to the oliguric ATN and discharged to receive chronic dialysis. The patient presented to

UCLA Health requesting a second opinion regarding his renal recovery.

He was dialyzed initially three times a week, but his urine output steadily improved. We counseled the patient that renal recovery can take an extended period due to a process of organic tubular repair. He agreed to monitor his urine output, and he noted a gradual increase in urine volume with sCr fluctuating between 5-6 mg/dL. We decreased dialysis to twice a week with close monitoring of his electrolytes and kidney function. 24-hour creatinine clearance estimated GFR at 30ml/min-though his serum creatinine was still 5mg/dL. Blood urea nitrogen, improved to 20-30 mg/dL, and potassium, sodium, and phosphorous all were within normal limits. Dialysis was reduced to once a week and later stopped with improved serum creatinine to 3.2 mg/d. Estimated GFR by cystatin C was at 30ml/min with a serum level of cystatin C of 2.5 mg/L. Figure 2 shows serum creatinine trend.

Patient 3

A 76-year-old Caucasian female underwent a tooth extraction with a prior mitral valve replacement. She developed endocarditis and was hospitalized at an outside hospital. The patient remained with stable creatinine around the baseline of 1.5 mg/dL. One month later, she developed cholecystitis and underwent cholecystectomy with the postop complication of the internal bleed. She underwent CT angiography with embolization of the bleeding vessels. She developed kidney injury from IV contrast and had ongoing hypotension resulting in acute renal failure, which required starting CRRT. The patient remained septic and hypotensive for nearly a week and was successfully transitioned to intermittent inpatient hemodialysis for one week before discharge. She was discharged to follow up with the outpatient dialysis unit. She presented to UCLA for evaluation of her need for dialysis.

The patient was receiving hemodialysis three times weekly and was afraid to miss a dialysis session. She noted improved urine output and serum creatinine decreased from peak of 5.9 mg/dl upon starting dialysis, to 2.5 mg/dL. It was not clear if the lower creatinine was due to adequate dialysis clearance or renal recovery. Urine output gradually increased, and the dialysis was changed to twice a week while monitoring her electrolytes and chemistry for impending renal recovery. With continued improvement in serum creatinine of 1.5mg/dL, dialysis stopped after four weeks of outpatient hemodialysis treatment.

The patient's serum creatinine fluctuated between 1.5 and 2 mg/dL off hemodialysis. She remained dialysis free to date, and her kidney recovery was maintained.

Discussion

Renal recovery is always a possibility, but it may not occur in patients with severe renal injury, as completely necrosed nephrons cannot be repaired by mesenchymal stem cells in the tubules.[3] It is, nonetheless, essential to monitor patients for renal recovery given the risks of mortality, cardiovascular disease, and general morbidity in the dialysis populations. Dialysis should be adjusted in AKI patients to avoid hypotension from overly aggressive ultrafiltration.

Macedo reported 19% of patients with acute kidney injury recovered after discharge from initial hospitalization and 64% had experienced renal recovery by 18 months post-renal injury.[4] Given the delayed nature of this process, the importance of urine output monitoring and careful biochemical parameter monitoring become self-evident.[5] In the presented cases, some barriers could have misled the diagnosis of renal recovery. In the first patient, development of urinary obstruction prevented complete recovery of renal function. While the second and third case, reqired extended time for restoration of tubular function. Since the watershed vasa recta feed the tubules, these areas are often the first to infarct with renal ischemia, and can take a long time to recover.[6]

A high index of suspicion is needed to detect incomplete recovery of renal function. The utilization of multiple methods is recommended rather than relying on a single parameter. We measured 24-hour urine clearance, electrolyte, urine volume, and, cystatin C in correlation with the clinical picture.[7] It is vital to assure that a decrease in serum creatinine observed in post-AKI patients is not due to hemodialysis, but due to improved kidney clearance. 24-hour urine creatinine collections, tend to overestimate eGFR given creatinine secretion by the tubules, and urea clearance tends to underestimate GFR due to urea reabsorption from the urinary space. This is mainly in the cortical collecting duct under the influence of anti-diuretic hormone. Thus 24-hour urine creatinine and urea clearance can be problematic, even if their results are averaged.[8] 24-hour cystatin C clearance is emerging as a new tool to supplement the traditional, but less reliable methods.[9,10]

Some patients with severe CKD or dialysis requiring AKI may have falsely low serum creatinine. Creatinine is a muscle enzyme and patients with small body mass are expected to have lower serum creatinine. When demographics, gender, and weight are taken into account, they have low eGFR for that spuriously low serum creatinine.[8,9] The difference between these patients and patients who genuinely recover after AKI is the urine output. As a rule, recovering AKI patients are not oliguric and are often, polyuric. The polyuria occurs due to increased osmolal clearance of creatinine and other nitrogenous wastes by the newly repaired renal tubules, and care must be taken to avoid post-ATN diuresis and volume depletion and ATN especially in the acute setting. Once patients recover attention is needed to maintain serum potassium, uric acid, and phosphorous levels via dietary or other interventions, as well as continuing the support required with iron infusions and erythropoiesis-stimulating agents. Table 1 has a summary of the clinical course of three patients presented.

Table 1.

Table 1			Summary of Cases of ATN recovery				
Patient number	Patient age	Patient gender	Race	AKI due to	Modalities used	Recovery obstacles	Time on Dialysis
1	82	M	Caucasian	ATN	CRRT,iHD	Obstruction	2 months
2	51	M	AA	ATN	iHD	Duration of AKI	5 months
3	77	F	Caucasian	ATN/CIN	CRRT, iHD	None	2 months

AA, African American; AKI, acute kidney injury; ATN, acute tubular necrosis; CIN, contrast induced nephropathy; CRRT, continuous renal replacement therapy; iHD, intermittent hemodialysis; M, male

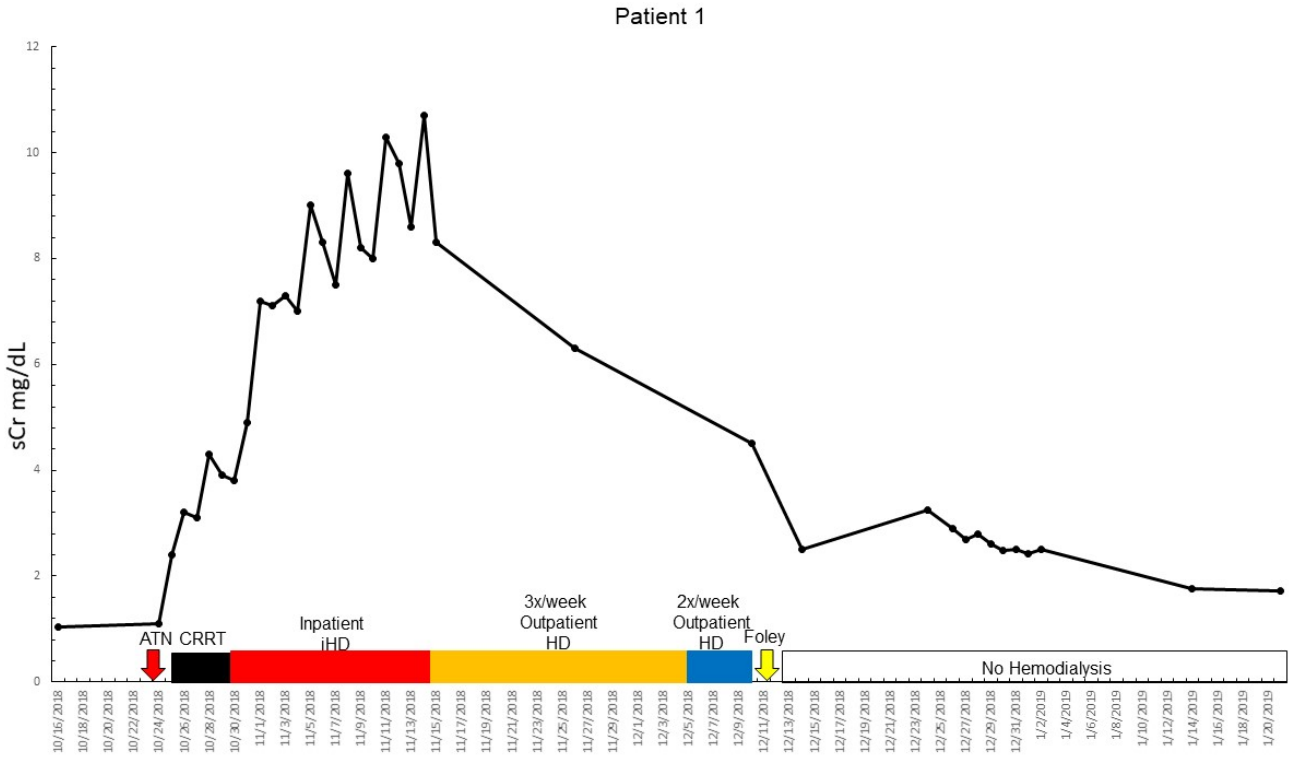

Figure 1 Serum Creatinine (mg/dL) versus date for Patient 1. ATN, acute tubular necrosis; CRRT, continuous renal replacement therapy; iHD, intermittent hemodialysis; sCr, serum creatinine.

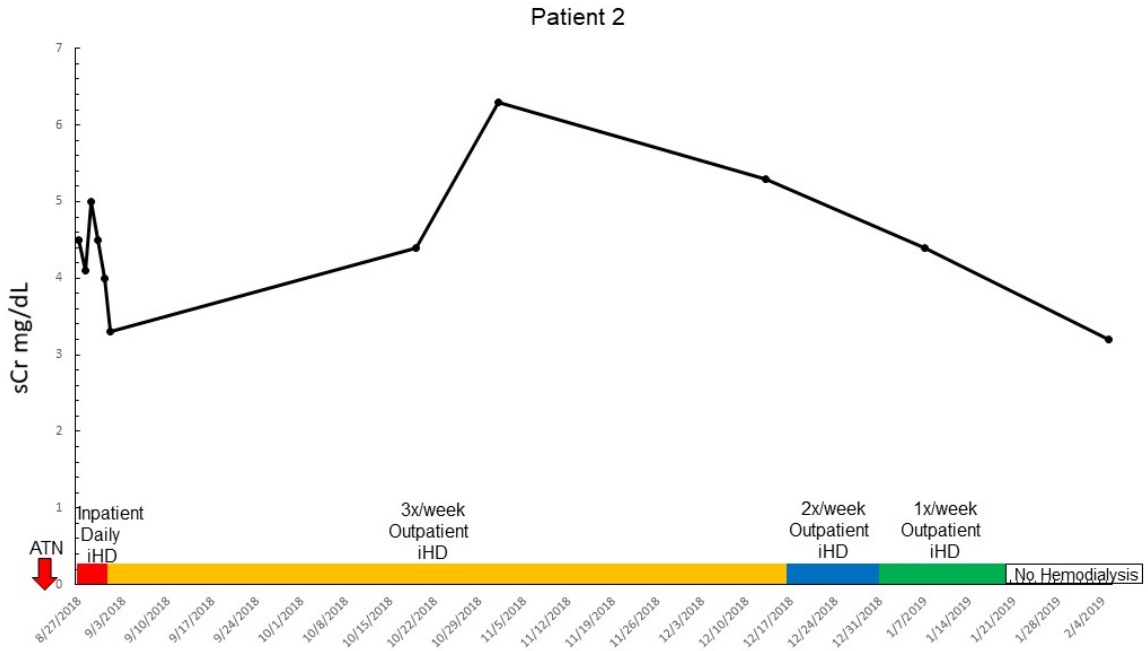

Figure 2 Serum Creatinine (mg/dL) versus date for Patient 2. ATN, acute tubular necrosis; HD, intermittent hemodialysis; sCr, serum creatinine.

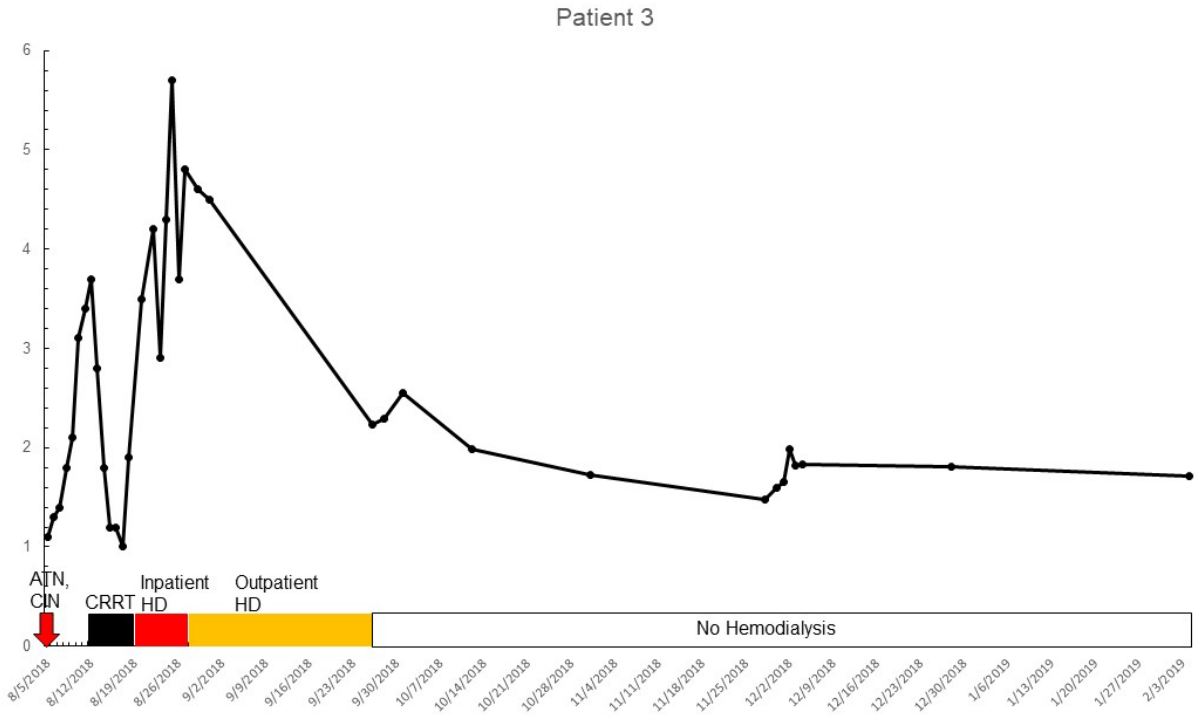

Figure 3 Serum Creatinine (mg/dL) versus date for Patient 3. ATN, acute tubular necrosis; CIN, contrast-induced nephropathy; CRRT, continuous renal replacement therapy; iHD, intermittent hemodialysis; sCr, serum creatinine.

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