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ARTICLE **SHORT COMMUNICATION**

The Importance of Urine Sediment Analysis in the Diagnosis and Management of Acute Kidney Injury

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ABSTRACT

The Urine sediment analysis is an extremely valuable yet underutilized test. Our case discussion aims to highlight its diagnostic value and emphasize the role of physicians in the performance of the test as diagnosis and management strategies may differ, leading to clinical improvement and more specific therapeutic interventions.

KEYWORDS - Acute Kidney Injury, Cast, Acute Tubular Necrosis, Acute Interstitial Nephritis, Urine Sediment Analysis

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INTRODUCTION

The pursuit of accurate and sensitive testing methods to evaluate acute kidney injuries continues. Still, a growing body of evidence highlights the importance of readily available urine sediment analysis as a tool to approach this disorder [1]. Our case discussion highlights the critical diagnostic value of urine sediment microscopy analysis. In addition, it emphasizes the role of the ordering physician or resident in performing this analysis instead of relying upon the laboratory, which is often inaccurate when performing urine sediment analysis.

CASE HISTORY

A 72-year-old man with a past medical history of diabetes, hypertension, smoking, and cocaine abuse was admitted to the hospital for evaluation of a left leg ulcer that had failed outpatient therapy with clindamycin due to barriers to compliance and follow-up, then complicated by cellulitis. He responded to intravenous vancomycin with a resolution of cellulitis, but he did not have pedal pulses on the left side; his ankle-brachial index was 0.3, and his arterial angiogram revealed superficial femoral artery occlusion with distal reconstitution of the profunda femoris that was sub-optimally perfusing the limb. He underwent femoral-posterior tibial artery bypass using 130 milliliters of intravenous contrast.

Within the ensuing three days, the patient did not develop any acute kidney injury (AKI). Still, his postoperative course was complicated by Clostridium difficile infection and Klebsiella pneumonia bacteremia, presumably due to prior antibiotic use and gut translocation, respectively. He was then started on intravenous cefepime and

oral vancomycin. The next day he underwent a computed tomography scan of his abdomen with oral and intravenous contrast. The patient did not develop AKI after this third exposure of contrast. His creatinine continued to be stable around his baseline of 1.3 mg/dl with an estimated glomerular filtration rate (eGFR) of about 63 ml/min/1.73 m2. On postoperative day (POD) 10, the patient again lost peripheral pedal pulses and had hypotension with a drop in systolic blood pressure to <90 mmHg.

He was evaluated in the operation room the next day. He was found to have graft occlusion - this time, thrombectomy, thrombolysis, balloon angioplasty, and PolyTetraFluoroEthylene (PTFE) bypass graft placement was done. A total of 38 milliliters of intravenous contrast was used. Two days after this procedure, creatinine rose from a baseline of 1.35 to 1.7 mg/dl was noted. This rise continues the following day to 2.1 mg/dl. Thus, a creatinine increases of more than 0.3 mg/dl and more than 1.5 times the baseline fulfills the Kidney Disease Improving Global Outcomes (KDIGO) diagnostic criteria for AKI.

Unfortunately, there was no reliable documentation of urine output on those days. On POD 6 (of the second operation), the patient started to have an altered mental status, leading to the holding of his anticoagulation; unfortunately, this resulted in a loss of peripheral pedal pulses the next day. On POD 7, Nephrology was consulted; Now, creatinine had climbed to 5.2 mg/dl, and the patient had become oliguric. The patient had an indwelling urinary catheter placed that did not show retention, and a bedside bladder scan showed 0 ml. Recent computed tomography imaging of his kidneys showed that they were normal sized without any evidence of obstruction.

The patient had had episodes of hypotension during his hospital stay, resulting in ischemic acute tubular necrosis. A review of his medications did not reveal any nephrotoxins. All medications, including cefepime, had been adjusted by the pharmacy based on the daily changes in his eGFR. Urine microscopy and analysis from the laboratory on that day stated the urine was cloudy in appearance, showed 2+ protein and 3+ blood, and was negative for casts, glucose, ketones, nitrite, leukocyte esterase, and epithelial cells were less than 5 per high power field. The levels of complement 3 and complement 4 were normal. Random urine sodium was high at 76 mEq/L, and the fractional excretion of sodium was calculated to be 2.4%. Based on this information alone, a diagnosis of intrinsic AKI was made. However, the cause could not be ascertained. The prognosis was also uncertain. A fresh urine sample was then collected from the indwelling urinary catheter and analyzed by the resident under the guidance of the fellow and attending physician following our institution's standard guidelines. The urine examination at low power revealed the presence of multiple muddy brown casts suggesting dense ATN (figure 2). Examination under high power confirmed the presence of muddy brown casts (figure 3). The analysis also revealed the presence of WBC casts suggestive of interstitial nephritis (figure 4) and plenty of calcium oxalate monohydrate crystals (figure 1).

Based on this new information, the diagnosis and management strategies were revised. The presence of casts confirmed the presumptive diagnosis of an intrinsic renal pathology. The utilization of simple quantitative sediment scoring systems predicted that the patient had a poor prognosis for renal recovery, and arrangements for temporary hemodialysis access were made [2]. We utilized the AKI Cast Scoring Index (CSI) developed by Chawla et al. (Table 1); our patient, his score was that of grade 4, which is the most severe and least likely to recover. In general, this likelihood of kidney recovery is inversely proportional to the number of casts found per low-power field of urine microscopy [3, 4]. Given WBC casts and altered mentation, the antibiotic regimen was switched to intravenous Meropenem and Vancomycin, and cefepime was discontinued. The presence of calcium oxalate monohydrate crystals was likely due to severe diarrhea from the Clostridium difficile infection.

Malabsorption syndromes increase the risk of forming calcium oxalate crystals by multiple mechanisms. The first of these mechanisms is the volume depletion and the resultant decrease in urine volume, thus, raising the chances of forming calcium oxalate crystals by the immediate increase in their concentration. Second, relevant to our patient, the change in the intestinal flora may decrease the enteric degradation of oxalate and a subsequent increase in the available oxalate to be absorbed. This change can be due to the concomitant use of antibiotics. One such microorganism that can be affected and has been extensively studied is Oxalobacter formigenes, a Gram-negative, anaerobic bacterium that metabolizes oxalate in the intestinal tract [5]. A third mechanism is the malabsorbed fatty acids' competition with intestinal oxalate in binding with intraluminal calcium ions, leading to less chelated oxalate and more available free oxalate to be absorbed [6]. The patient was thus given intravenous fluid to prevent crystalline nephropathy and reverse volume depletion, one of the few indications of intravenous fluid resuscita-

tion in acute oliguric renal failure. The patient also received supportive treatment for ATN in terms of monitoring for electrolytes, continuous adjustment of medications according to changing serum creatinine, blood pressure control, and urine output monitoring. Later that day, the patient's condition worsened, and he developed fever, diffuse edema, and blistering of the left lower limb. He underwent left-below-the-knee amputation the next morning and then stabilized with a recovery of mentation and vitals by the next day. Subsequently, the patient responded to treatment showing clearance of the casts from the urine and improvement of creatinine. He required only 1 round of intermittent hemodialysis to support his kidneys, after which he established a new baseline that was, unfortunately, much lower than his previous one. He was then transitioned to oral antibiotics with linezolid and vancomycin and discharged with close follow-up with a subacute rehabilitation plan.

RESULTS AND DISCUSSION

There are several essential teaching points in this case. First, the patient had three different diagnoses, which significantly helped steer the clinical management. If it were not for the careful examination with the finding of crystals, we would have avoided the fluid, given his acute tubular necrosis. In addition, we would have continued with the same antibiotic without any changes. Second, the KDIGO Guidelines on AKI recommend prompt evaluation of patients with AKI to determine the cause and mention the use of urine microscopy in its workup [7]. Finally, while urine sediment analysis is easy to perform, inexpensive, and uses a technology that is readily available in all hospitals, it is often not performed or performed incorrectly [1]. In our case, urine microscopy gave us a profound insight into the various etiologies, enabling us to improve the quality of care provided to our patient.

In comparison, the laboratory urine analysis was unhelpful, inaccurate, and misleading. A literature review shows that our experience was not unique - a nephrologist-performed interpretation of urinalyses was more likely diagnostically superior to a laboratory performed urinalysis [8]. The test's lack of popularity is often attributed to time constraints, a deficiency of expertise in interpreting findings, the absence of accepted universal guidelines regarding specimen preparation, and interobserver variability. This underutilization is, despite being a urinalysis, a reimbursable procedure (CPT code 81015). Small-scale studies have shown that some of these deficiencies may be less significant than previously believed, with cast scoring systems showing good reproducibility and interobserver agreement [2]. Despite the development of automated analyzers, several studies in various parts of the world have shown that manual microscopy continues to be superior and essential for diagnosis [9, 10]. This is mainly because automated analyzers have difficulty identifying and differentiating between casts or crystals [11-14]. This observation holds when applied to patients with acute kidney injury [15].

Furthermore, although newer biomarkers may identify AKI earlier than rising creatinine levels, the practical clinical application of these markers remains elusive because, unlike urine microscopy, they individually cannot suggest a cause or site of injury nor predict outcomes [16]. However, urine sediment scoring systems have prognostic significance [17, 18] and can predict outcomes when combined with biomarkers and clinical context [19, 20]. All this evidence reinforces that to deliver high-quality care to our patients, we must refocus efforts on the rediscovery of this lost art as the incidence of AKIs is rising [21]. Emphasis should be on urine sediment analysis and training for medical students, residents, and subspecialists - especially in internal medicine, pediatrics, pathology, geriatrics, nephrology, critical care, and transplant medicine. Financial reimbursement for the time spent on the analysis could further promote its use. As mentioned earlier, CPT code 81015 refers to the microscopic urine study without using automation assays or kits. This code has been recognized by the Center for Medicare and Medicaid Services to be a billable code at least since October 2014 [22]. Hence, performing this cheap, quick, and, more importantly, very high-yield test is no financial burden. There remains scope for research into developing national/international guidelines on the methodology of urine sediment analysis and the elucidation of diagnostic and prognostic applications in managing acute kidney injuries. With studies already showing that early nephrologist intervention in AKI improves patient outcomes [23, 24]. Hopefully, widespread implementation of these techniques will further enhance patient care.

Table 1. Acute Kidney Injury Cast Scoring Index (CSA). The approach to viewing the slide was to search for casts (GCs or ECCs), then view the entire slide. Granular cast index. GC = Granular casts; ECC = epithelial cell casts; LPF = low-power field (×10). The table is adapted from Chawla et al. Nephron Clin Pract 2008;110:c145–c150.

Grade	Definition	
1	None	No evidence of GCs or ECCs
2	Rare	Rare GCs or ECCs; at least 1 GC or ECC seen on the entire slide, but <10% of LPFs
3	Moderate	Many GCs or ECCs, but not seen on every LPF; casts seen on >10% but <90% of LPFs
4	Sheets	Sheets of muddy brown casts; GCs or ECCs seen on >90% of LPFs

Figure 1. Calcium Monohydrate Crystals. High Power Field.

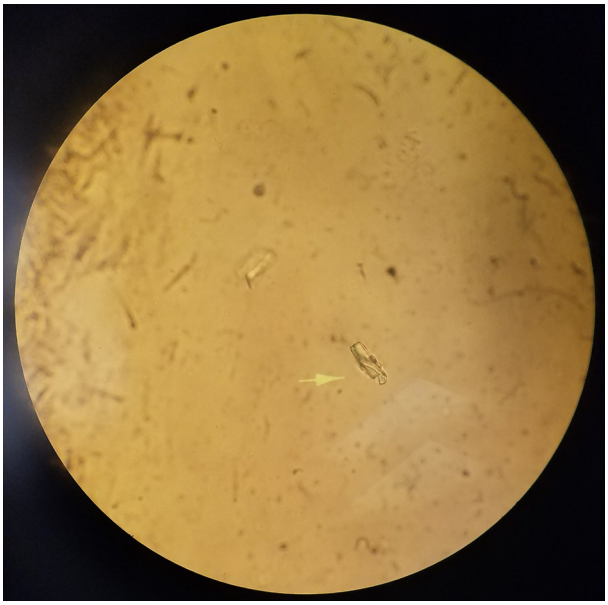


Figure 2. Multiple Granular Casts, low power field.

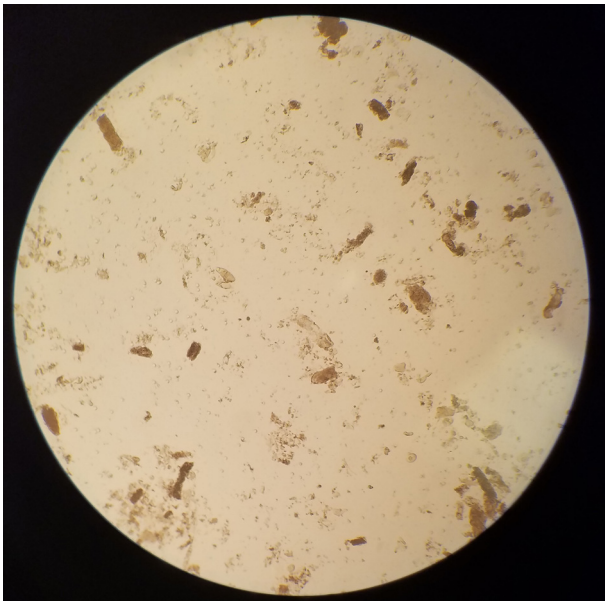


Figure 3. Granular Cast, Multiple White Blood Cells, White Blood Cells Cast. High Power Field

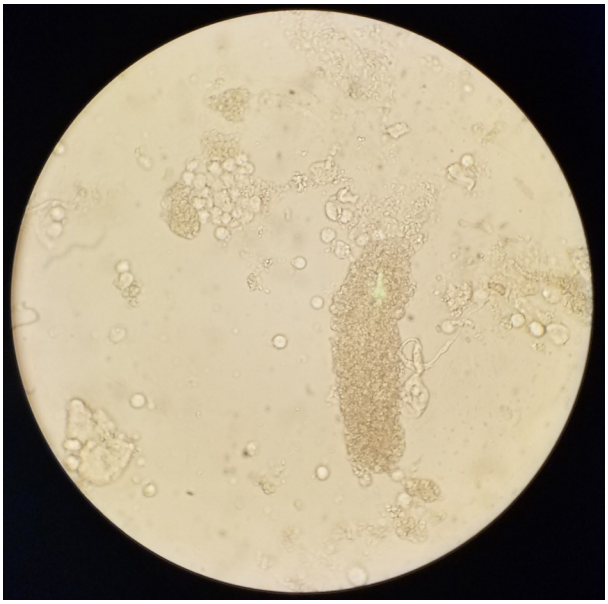
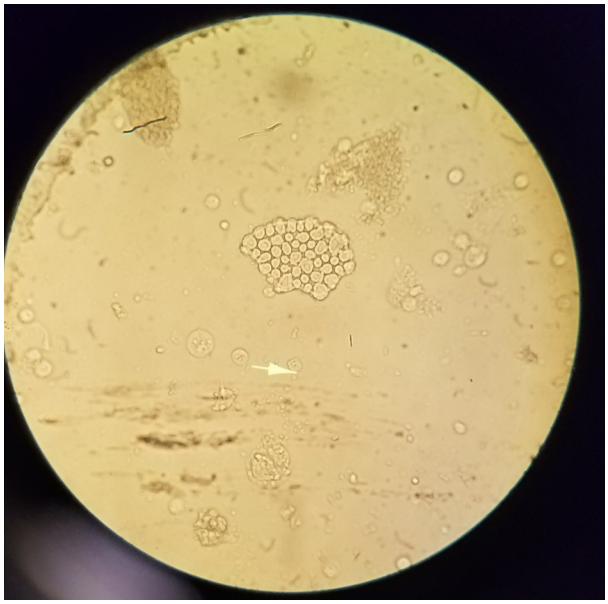


Figure 4. White Blood Cells Cast, White Blood Cells, Red Blood Cells, Part of a Granular Cast. High Power Field.



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