Acute Interstitial Nephritis after Single Dose of Ketorolac

ISHAN JANI, MD; ARJUN SEKAR, MD; SERGEY BRODSKY, MD

ABSTRACT

Acute interstitial nephritis (AIN) is an immunologically mediated cause of acute kidney injury (AKI), most often drug-induced, with NSAIDs being a leading culprit. We present a 39-year-old woman who developed biopsy-proven AIN following a single intramuscular dose of ketorolac, an exceptionally short latency likely due to prior sensitization. Despite lacking classic systemic features, she exhibited non-oliguric AKI that improved rapidly with corticosteroids. This case underscores that NSAID-induced AIN can occur even after minimal exposure, highlighting the importance of early recognition, drug withdrawal, and timely steroid therapy to optimize renal recovery.

KEYWORDS: Acute Interstitial Nephritis; AIN; NSAID; AKI; Nephrology

INTRODUCTION

Acute Interstitial Nephritis (AIN) is an immunologically mediated response, characterized by inflammation and edema of the interstitium, leading to kidney injury. AIN is a common cause, with some studies suggesting that it is found in 15–35% of all kidney biopsies in patients with AKI. The most common cause of AIN is drugs, with B-lactams being on the top of the list, succeeded by NSAIDs. Studies have shown that patients develop AIN after being exposed to NSAIDs for a median of three months.[1,3] We report a case of a patient who developed AIN after a single dose of ketorolac 30 mg IM.

CASE PRESENTATION

Our patient is a 39-year-old woman who presented to an urgent care clinic for evaluation of fatigue and back pain. She was given a dose of ketorolac 30 mg IM, and ondansetron for nausea and was discharged on the same day. Her symptoms did not resolve and she visited the emergency department (ED) five days later with the same complaints. Lab-work revealed a creatinine of 4.8 mg/dL up from her baseline of 0.8 mg/dL. Urinalysis revealed trace hematuria and proteinuria with no casts or dysmorphic RBCs on urine sediment exam; CT abdomen and pelvis (without contrast) was negative for renal calculi. In the ED, she received 1 liter of normal saline and was admitted to the hospital. Of note, she had a past medical history notable only for GERD and occasional migraines. She did not endorse any home medication use except occasional tylenol and rimegepant. She had a poor appetite for the last three days, but water intake was unchanged. She noted no change in urination. She did admit that she used to take NSAIDs occasionally in the past. However, it has been more than a year since she stopped them.

Further serological evaluation with ANCA, C3, C4 and hepatitis was negative. She remained non-oliguric but her

Figure 1. Creatinine Trend over time during hospitalization and follow-up

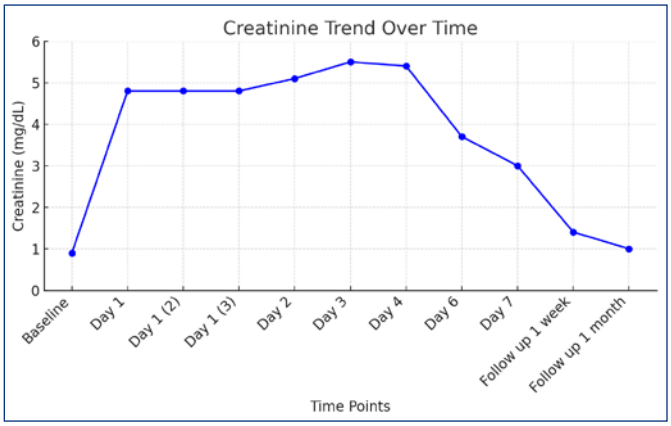
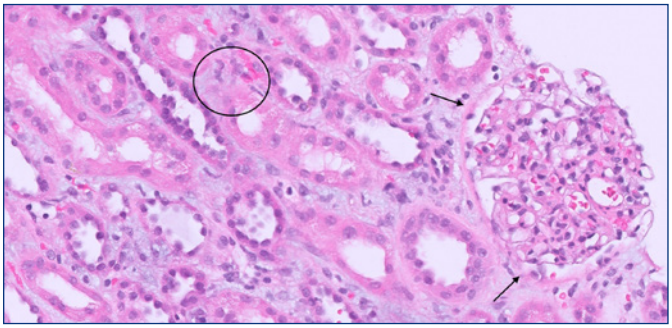


Figure 2. Biopsy showing unremarkable glomerulus, diffuse interstitial edema with active-appearing inflammatory cell infiltrates, acute tubular epithelial cell injury [H&E, x200]. Black circle represents interstitial inflammatory infiltrate. Arrows point towards a relatively preserved glomerulus.



kidney function continued to worsen with her creatinine reaching a ceiling at 5.4 on hospital day 4 after which it started to improve. A kidney biopsy was obtained. Morphologically, glomeruli were unremarkable, but there was acute tubular necrosis and diffuse interstitial edema with active-appearing interstitial inflammatory infiltrates, suggestive of acute interstitial nephritis. There was no evidence of immune complex deposition or monoclonal immunoglobulin deposition by immunofluorescence and electron microscopy.

She was started on a short course of oral steroids. This was for a total of five days as there was rapid improvement in renal function (likely due to withdrawal of NSAIDs). Three weeks later, creatinine was down to 1 mg/dL and she had no new complaints.

DISCUSSION

We present a young woman who developed AIN-mediated AKI with a single dose of intramuscular ketorolac who had sporadic and remote NSAID use in the past. Even with prior sensitization, it is exceptionally rare to develop AIN after just one dose of precipitating medication.

While NSAID-induced AIN often follows weeks to months of therapy, there is evidence that latency can range from as short as one day to several months.[1] The minimum latency for new NSAID exposure in NSAID-induced AIN is typically 10–14 days,[1] but cases with shorter latency (as little as one day) can be possible, especially in previously sensitized individuals.[2] Given her remote history of NSAID use, it is plausible that prior sensitization primed the immune system, rendering her susceptible to an accelerated hypersensitivity response after re-exposure. Importantly, no alternative medications or systemic conditions known to cause AIN were identified, strengthening the causal link to ketorolac.

Clinical presentation of NSAID-induced AIN may be subtle, frequently lacking the classic triad of fever, rash, and eosinophilia, which is present in only about 10% of cases.[3,4] Our patient similarly presented without systemic allergic features and remained non-oliguric, underscoring the diagnostic challenge. Most patients present with nonspecific symptoms (malaise, nausea, vomiting) and non-oliguric AKI, as in our case. Kidney biopsy is needed for confirmatory diagnosis and was confirmed in our case with interstitial inflammation and preserved glomerular structure. Urinalysis findings can be nonspecific in AIN and very often the sediment is bland. The improvement of renal function after drug withdrawal and early corticosteroid initiation is consistent with prior studies demonstrating that timely steroids, particularly when administered within seven days of diagnosis, can improve recovery and reduce the risk of progression to chronic kidney disease. Use of steroids is controversial in AIN. However, there may be stronger evidence when NSAIDs are thought to be the culprit for AIN.[5] The mainstay of treatment is withdrawal of the culprit agent.

An important learning objective which can be identified here is that AIN should be considered in the differential diagnosis of AKI even after a single dose of an NSAID, particularly in patients with prior sensitization, and that early withdrawal of the offending agent and timely initiation of corticosteroids may improve and hasten renal recovery.

References

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Authors

Ishan Jani, MD, Dept. of Internal Medicine, Rochester General Hospital, Rochester, NY.

Arjun Sekar, MD, Dept. of Nephrology, Rochester General Hospital, Rochester, NY.

Sergey Brodsky, MD, Dept. of Pathology, Ohio State University Medical Center, Columbus, Ohio.

Correspondence

Ishan Jani, MD

Ishan.jani@rochesterregional.org