Acute Kidney Injury with Cast Nephropathy Following Creatine Loading in a 17-Year-Old: A Pediatric Case Report

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Research Article

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Abstract

Background: This case highlights a 17-year-old male who developed acute kidney injury (AKI) with cast nephropathy following a six-day high-dose creatine loading regimen. The patient presented with bilateral flank pain, a parallel rise in cystatin C and creatinine, and kidney enlargement on ultrasound despite adequate hydration and the absence of rhabdomyolysis markers. Renal biopsy confirmed cast nephropathy without evidence of light chain disease.

Clinical Impact:This case underscores the potential risks of high-dose creatine use in adolescents and highlights the importance of kidney function monitoring in athletes using sports supplements.

Summary - What is New

This case presents the first reported instance of creatine-induced cast nephropathy in a well-hydrated adolescent, highlighting a novel mechanism of AKI unrelated to dehydration or rhabdomyolysis.

Key Learning Points

- Creatine loading at 20 g/day can cause AKI, even in well-hydrated adolescents.
- Cast nephropathy, typically associated with multiple myeloma, may also occur due to precipitation of non-protein solutes, as in this case.
- Cystatin C is a valuable marker for prolonged tubular dysfunction and should be monitored in cases of suspected nephrotoxicity.
- Further research is needed to explore creatine's impact on renal tubular integrity and its role in cast formation.

Introduction

Creatine, widely used by athletes to enhance performance, is generally considered safe, with rare reports of severe renal side effects.[1, 2] However, though uncommon, cases of creatine-induced AKI are of growing concern, especially in adolescents.[3, 4] Previous reports often attribute AKI to preexisting kidney damage, dehydration, or rhabdomyolysis, but isolated cases of creatine-induced AKI in well-hydrated individuals are rare.[4, 5] This case report describes a novel presentation of AKI associated with creatine use, characterized by cast nephropathy, prolonged cystatin C elevation, and extended renal function recovery.

Case Presentation

Patient Information and Clinical Course

A 17-year-old male athlete presented with severe bilateral flank pain after completing a six-day regimen of high-dose creatine loading (20 g/day). He reported no dehydration, infections, or prior kidney disease.

His past medical history was unremarkable, and he had not taken other supplements or medications, aside from a single dose each of ibuprofen, naproxen, and extra-strength acetaminophen within the previous 24 hours.

Diagnostic Workup

Initial lab tests revealed:

Serum creatinine: 390 µmol/L (normal: 52-120 µmol/L)

Modified Schwartz 2009 eGFR: 18 mL/min/1. 73m² (normal: 90-135 mL/min/1.73m²)

Cystatin C: 1.52 mg/L (normal: 0.61-0.95 mg/L)

Cystatin C-based eGFR[6]: 57 mL/min/1.73m² (normal: 90-135 mL/min/1.73m²)

Urinalysis: Trace hemoglobin, no myoglobin, no significant proteinuria (protein/creatinine ratio: 40 mg/mmol; normal: <23 mg/mmol)

Creatine kinase: Normal (67 U/L; normal <190 U/L)

Light chain studies in urine and serum: Negative

Kidney ultrasound: Significant bilateral enlargement (left: 263.1 mL, z-score +3.47; right: 266.9 mL, z-score +3.58) with cortical thickening and increased echogenicity (Figure 1).

A renal biopsy revealed amorphous hyaline casts in dilated distal tubules, consistent with cast nephropathy (figures 2-5). No evidence of light chain deposition, acute interstitial nephritis, glomerulonephritis or autoimmune disease was found. No definite "zebra bodies" were identified to suggest Fabry’s disease. Few fibrils are present, ranging from approximately 5 - 11nm in diameter. These fibrils are of indeterminate significance. Congo red stain for amyloid is negative; kappa and lambda are negative by immunofluorescence.

Management and Outcome

The patient received intravenous fluids (100 mL/hour) to support renal perfusion, and pain was managed with opioids due to inadequate response to acetaminophen. Creatine supplementation was discontinued. Serum creatinine normalized within six weeks, but cystatin C remained elevated for four months, indicating a protracted recovery.

Patient Perspective

Despite his hydration efforts, the patient expressed surprise at the severity of the kidney injury. He acknowledged the risks of creatine supplementation and agreed to avoid performance-enhancing supplements in the future.

Discussion

This case describes a novel presentation of creatine-induced AKI with cast nephropathy, distinct from previously reported cases associated with dehydration or rhabdomyolysis [7] and unrelated to light chain disease [8]. While the extensive workup ruled out light chain disease, the appearance of cast nephropathy is rare in non-myeloma-related AKI, making it a novel finding in a pediatric case linked to creatine supplementation. The pathophysiology appears to involve increased intratubular creatine accumulation, altered tubular environment favoring hyaline cast formation, and tubular obstruction leading to inflammation and edema. The parallel rise of cystatin C and creatinine and prolonged recovery suggest a significant tubular component to the injury, as can be seen in marathon runners [7]. The development of bilateral flank pain after a maximum loading dose of creatine for six days highlights the potential acute toxicity associated with high-dose supplementation, reinforcing the need for awareness of creatine's risks, even in well-hydrated, physically active adolescents.

While cast nephropathy is most associated with multiple myeloma, we have diligently ruled out light chain disease. The casts were most likely from creatine and not hyaline casts precipitated by dehydration and concomitant acute tubular necrosis. Emerging evidence suggests non-protein solute accumulation can contribute to tubular obstruction and AKI. Cast formation has been reported in cases of drug-induced tubular injury, such as tenofovir-associated nephrotoxicity, and conditions involving endogenous solute overload, including tumor lysis syndrome and severe rhabdomyolysis [9]. The underlying pathophysiology in these cases involves an altered tubular environment that promotes precipitation of filtered solutes, leading to intratubular obstruction, local inflammation, and subsequent nephron damage. Although creatine is traditionally considered safe in recommended doses, high-dose supplementation may induce a similar process by exceeding renal tubular reabsorption capacity, leading to increased intratubular creatine accumulation and hyaline cast formation. This novel finding warrants further investigation, particularly in pediatric populations with increased creatine use.

We want to raise awareness among nephrologists, pediatricians, and sports medicine professionals regarding the potential renal risks of creatine supplementation in adolescents. Physicians should routinely inquire about **creatine use** in adolescent athletes, as this may often be underreported due to misconceptions about its safety or lack of awareness of its risks. Early recognition of creatine-related nephropathy is crucial; thus, **kidney function screening** should be considered in patients presenting with unexplained AKI and flank pain, mainly when there is a history of creatine use. **Urinalysis** and **kidney ultrasound** may serve as early, non-invasive tools for detecting nephropathy, with findings such as **trace hemoglobin in the urine or renal enlargement** potentially raising suspicion. If AKI is suspected, a timely **renal biopsy** should be performed to confirm the diagnosis. Furthermore, nephrologists should consider advising against **high-dose creatine loading** in individuals with **pre-existing kidney disease, single kidneys**, or a **genetic predisposition to tubular dysfunction**, as these patients may be at greater risk for renal complications. These practical steps help mitigate the risks associated with creatine use and promote safer supplementation practices among adolescent athletes.

Conclusion

This case highlights a novel presentation of creatine-induced AKI with cast nephropathy and prolonged cystatin C elevation in a pediatric patient. It underscores the need for cautious use of high-dose creatine, comprehensive diagnostic evaluation in cases of AKI, and close kidney function monitoring in adolescents using performance-enhancing supplements.

Abbreviations

AKI = Acute kidney injury

Declarations

Acknowledgments: We acknowledge the patients, their families, nurses, colleagues, and laboratory staff at the London Health Sciences Centre for their excellent and precise work.

Informed Consent

Written informed consent was obtained from the patient and his guardians for the publication of this case report, including clinical details and diagnostic images.

Author Contributions: GF conceived the study, collated all patient information, obtained the consent to publish, reviewed the literature, and wrote the first draft. EM reviewed all available literature, formatted the manuscript per the CARE Equator guidelines, and prepared the checklist. He also edited the references as per the journal style. NGC performed the histopathological assessment. MEDGDF supervised EM and provided critical revisions of the draft manuscript. APS provided critical revisions of the draft manuscript. All authors participated in critically revising the manuscript for important intellectual content and approved the final version to be submitted to the journal.

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Conflicts of Interest: All authors had no relationships or circumstances that present a potential conflict of interest.

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Figures

Figure 1

A representative kidney ultrasound image of the patient shows swollen, large, and echogenic kidneys with an increased width of the renal parenchyma.

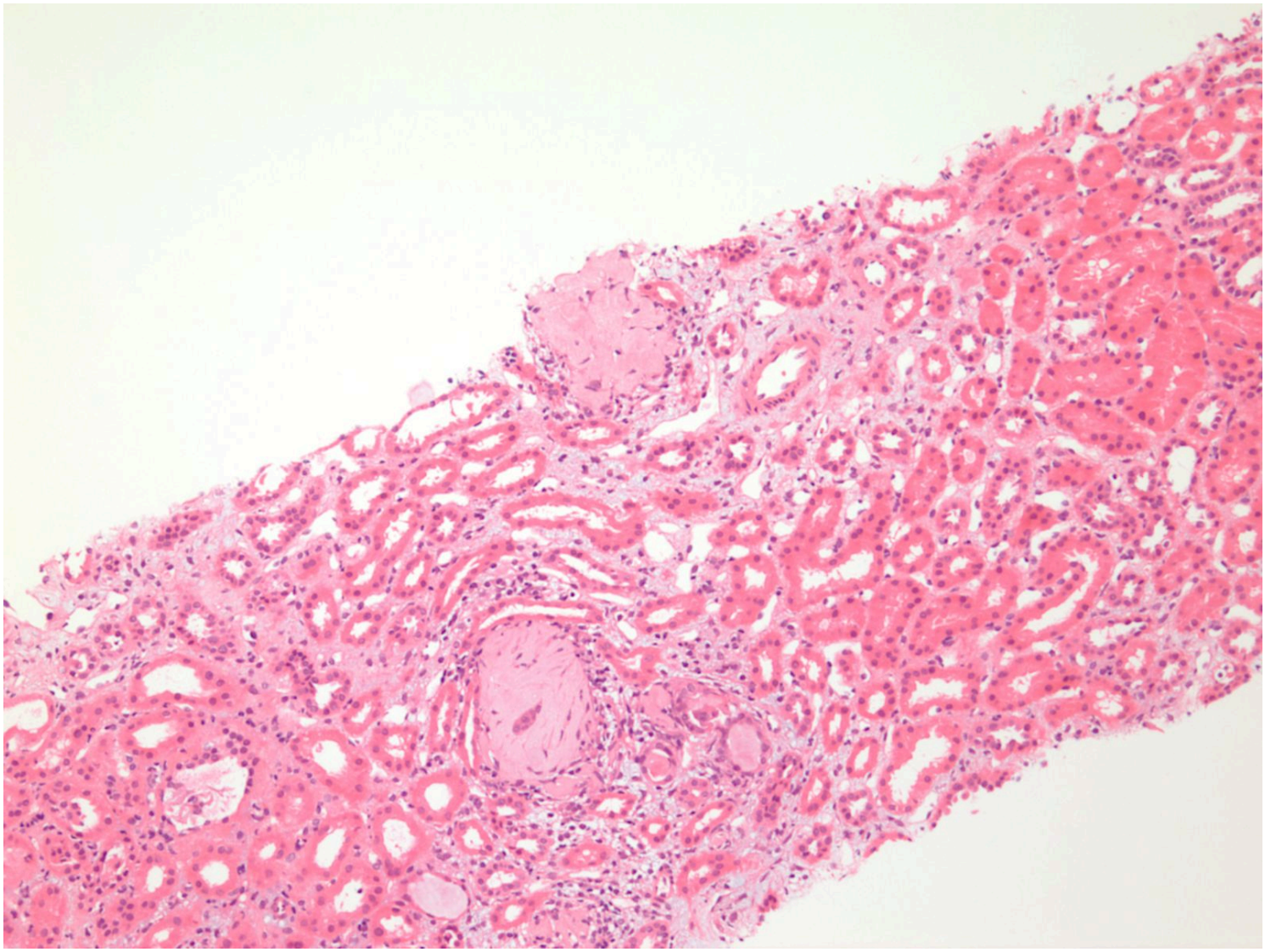

Figure 2

Representative Hematoxylin and Eosin stain (H & E) of the kidney biopsy, showing amorphous materials in several tubules. Magnification: 100x

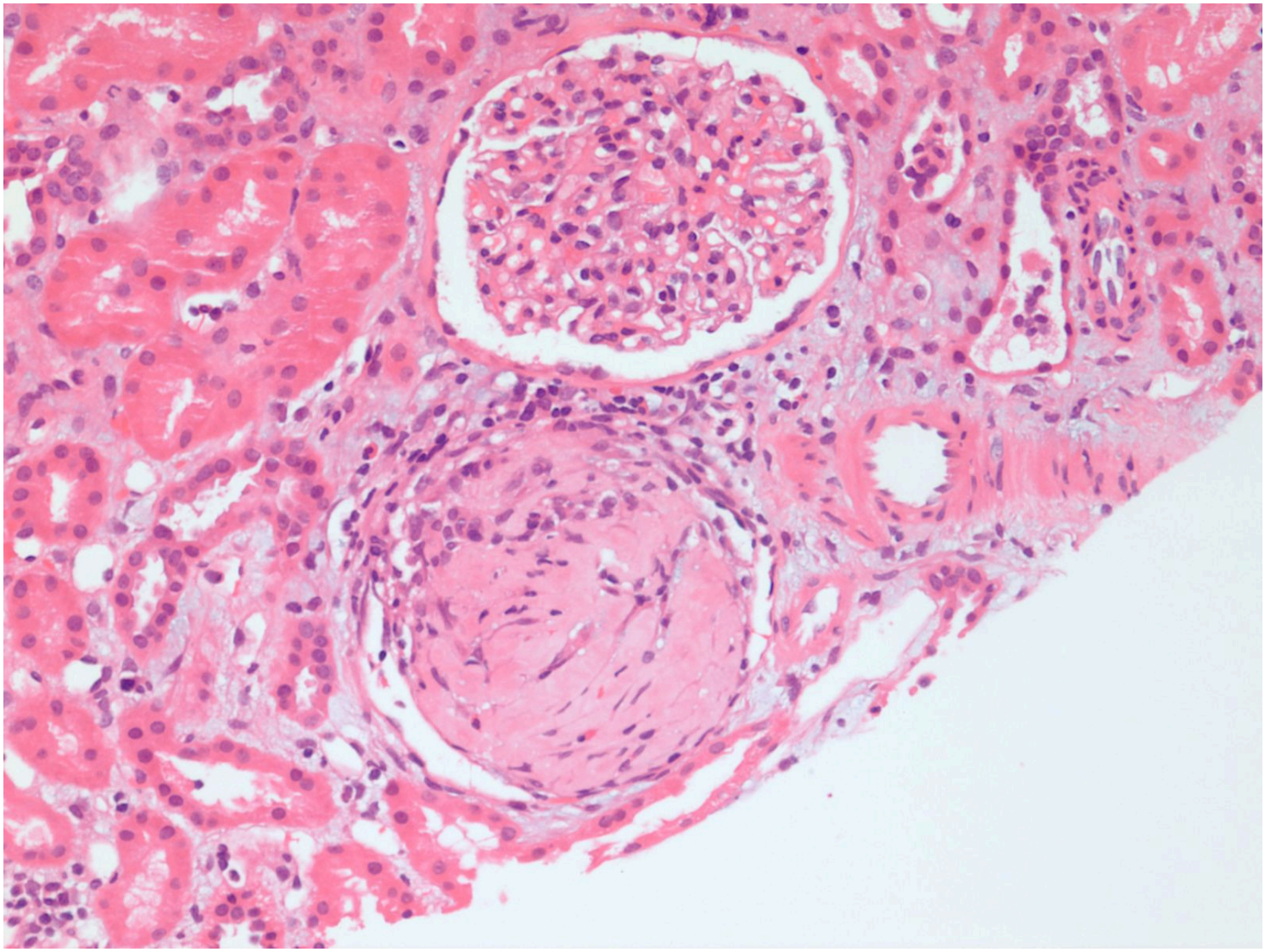

Figure 3

Representative Hematoxylin and Eosin stain (H & E) of the kidney biopsy, showing amorphous materials in a tubule (tubular cast-like material) and a normal glomerulus. Magnification: 200x

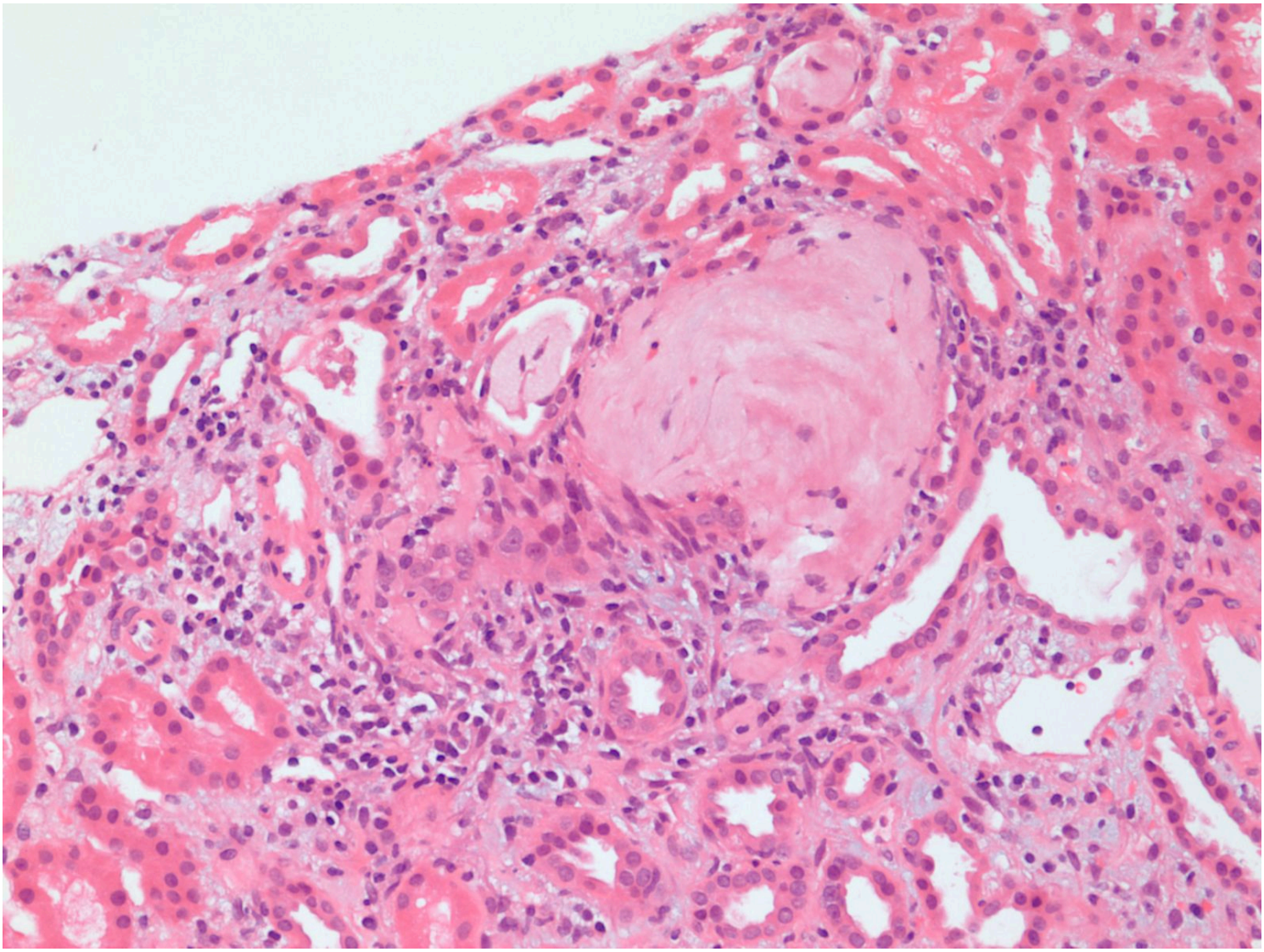

Figure 4

Representative Hematoxylin and Eosin stain (H & E) of kidney cortex, showing amorphous materials in a tubule (tubular cast-like material). Magnification: 200x

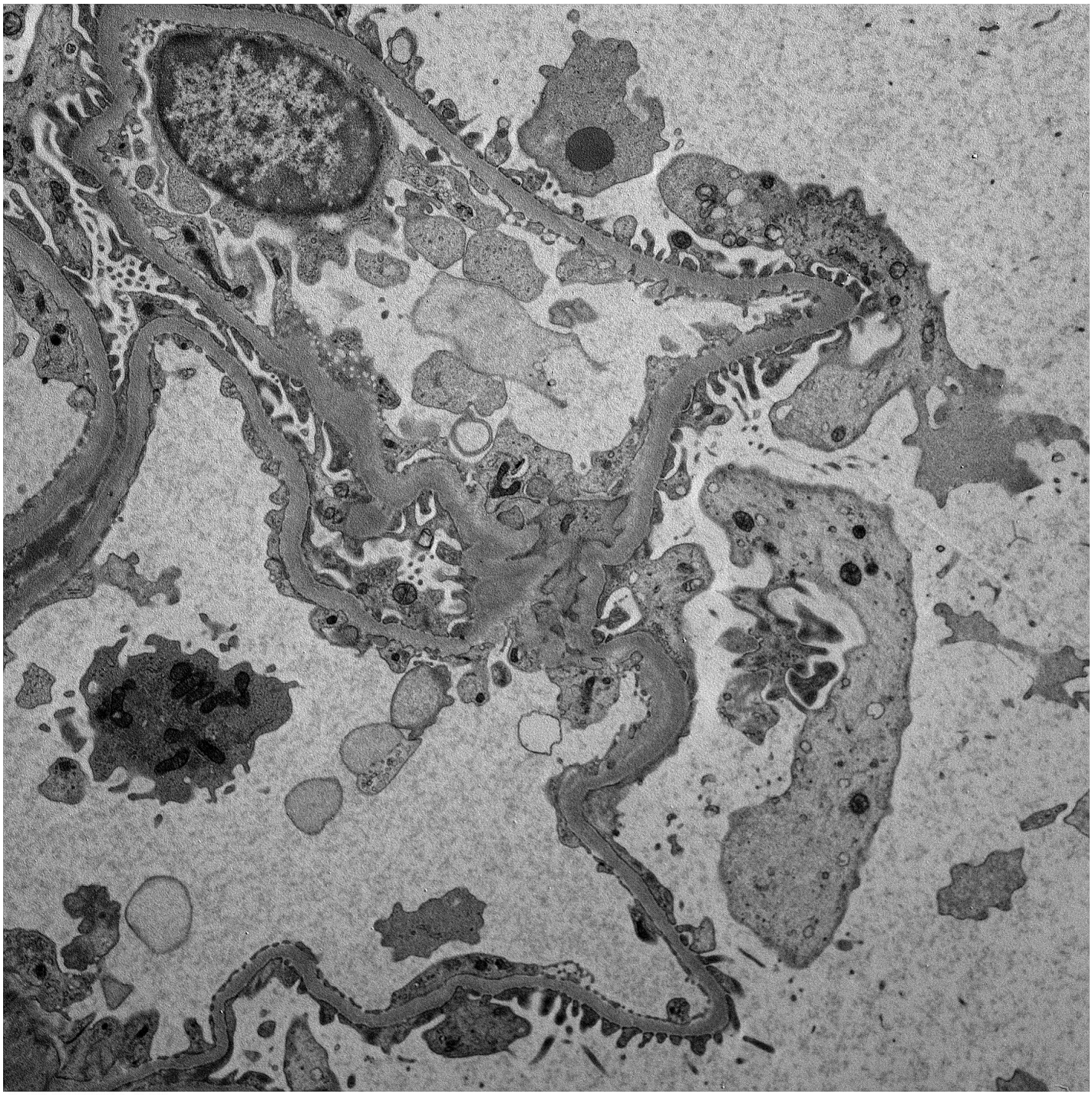

Figure 5

Electron micrograph, normal, no electron-dense deposits.