Atypical triad of IgA nephropathy: reversible acute kidney injury, gross hematuria, and severe bilateral flank pain

Susan Kim · Warren Chang

Received: 28 March 2011 / Accepted: 6 November 2013 / Published online: 17 December 2013
© Japanese Society of Nephrology 2013

Abstract Reversible acute kidney injury very rarely complicates the course of immunoglobulin A (IgA) nephropathy. We report an atypical case of reversible acute kidney injury, gross hematuria, and severe bilateral flank pain as the presenting triad of IgA nephropathy. Renal biopsy revealed mesangial IgA deposition without glomerular crescents. The patient's renal dysfunction, mediated by red cell tubular obstruction, interstitial nephritis, and tubular necrosis, resolved without intervention. We conclude that IgA nephropathy should be considered in the differential diagnosis for transient acute kidney injury with gross hematuria, and should be appropriately treated based on known prognostic factors.

Keywords IgA nephropathy · Acute renal failure

Introduction

Immunoglobulin A (IgA) nephropathy is characterized by predominant IgA deposition in the glomerular mesangium. While variable in presentation from asymptomatic microscopic hematuria to rapidly progressive glomerulonephritis, cases often follow an acute respiratory or gastrointestinal illness. Although well recognized as a progressive renal disease, reversible acute kidney injury rarely complicates the course. We report an atypical case of

IgA nephropathy presenting with a triad of reversible acute kidney injury, gross hematuria, and severe bilateral flank pain. IgA nephropathy should, therefore, be considered in the differential diagnosis for transient acute kidney injury with gross hematuria, and should be appropriately treated based on known prognostic factors.

Case report

A 35-year-old Caucasian woman with a history of urinary tract infections presented to the emergency room with 1 week of severe bilateral flank pain and gross hematuria after an episode of “flu-like” illness. The patient recalled that she had two prior episodes of bilateral flank pain with gross hematuria previously. Both were preceded by “flu-like” illnesses and resolved after treatment for presumed urinary tract infections. Her blood pressure was 166/101 mmHg and her serum chemistry was as follows: sodium 135 mEq/L, potassium 3.6 mEq/L, chloride 104 mEq/L, bicarbonate 22 mEq/L, glucose 102 mg/dL, blood urea nitrogen 78 mg/dL, and creatinine 5.2 mg/dL. Her baseline serum creatinine was 1.2 mg/dL. Urine evaluation demonstrated non-nephrotic-range proteinuria (0.6 mg protein/g creatinine). Her gross hematuria rapidly cleared, but urine microscopy revealed 10–25 isomorphic red blood cells (RBCs) per high-power field with no RBC or tubular casts. Serum hepatitis, anti-nuclear, anti-neutrophil cytoplasmic, anti-streptolysin O, and anti-glomerular basement membrane antibodies were not detected. Complement levels were normal. An abdominal computed tomography (CT) scan showed no evidence of pyelonephritis, nephrolithiasis, or urinary tract obstruction. Renal biopsy showed mesangial matrix accumulation and hypercellularity, tubulointerstitial patchy inflammatory

S. Kim (✉) · W. Chang
Department of Internal Medicine, St. Mary's Medical Center,
450 Stanyan Street, San Francisco, CA 94117, USA
e-mail: susankim338@gmail.com

W. Chang
Division of Nephrology, St. Mary's Medical Center,
San Francisco, CA 94117, USA

infiltrate of mononuclear leukocytes and eosinophils, and diffuse epithelial cell injury of the tubules on light microscopy (Fig. 1). Glomerular crescents, segmental sclerosis, and endocapillary proliferation were not visualized, but tubular RBC casts with mild acute tubular necrosis were identified. Immunofluorescence microscopy showed mesangial staining for IgA with C3 (complement 3) arteriolar staining of the glomeruli (Fig. 2). Electron microscopy showed mesangial expansion with electron-dense immuno-type deposits, and coarsened, effaced epithelial cell foot processes. A diagnosis of IgA nephropathy was made.

The patient was admitted to the hospital when dehydrated. However, she remained non-oliguric and her renal function improved (creatinine 1.8 mg/dL) with

Fig. 1 Light microscopy. Mesangial matrix accumulation and mesangial hypercellularity, tubulointerstitial patchy inflammatory infiltrate of mononuclear leukocytes and eosinophils, and diffuse epithelial cell injury of the tubules

Fig. 2 Immunofluorescence microscopy. Mesangial staining for IgA (immunoglobulin A)

conservative management that included rest and intravenous hydration. At the 2-week follow-up, her serum creatinine was 1.2 mg/dL, showing that her renal function had recovered completely. The microscopic hematuria and low-grade proteinuria persisted. Treatment was, thus, initiated with an angiotensin-converting enzyme (ACE) inhibitor at her 2-week follow-up visit.

Discussion

While IgA nephropathy is well recognized as a progressive renal disease, reversible acute renal failure rarely complicates its course in adults [1]. Self-limited acute kidney injury has been reported in association with gross hematuria, with renal function usually recovering after the hematuria resolves [1]. Renal biopsies in IgA nephropathy patients with acute renal failure have shown crescentic glomerulonephritis, acute tubular necrosis, acute interstitial nephritis, and extensive tubular red blood cell casts [2].

The cause of acute renal failure due to gross hematuria in IgA nephropathy is not certain. It may be attributed to tubular damage from RBC obstruction [3], but renal failure has also been reported without evidence of intratubular obstruction [4]. Other proposed mechanisms of injury include direct tubular toxicity by RBC contents [5] and glomerular microcirculation dysfunction [6]. Renal injury in this patient was most likely due to acute interstitial nephritis and acute tubular necrosis with RBC obstruction.

Reversible macroscopic hematuria-associated acute kidney injury, although rare, has been increasingly described as a complication of IgA nephropathy and complete recovery of baseline renal function after cessation of macroscopic hematuria is being more commonly observed [7]. Though the majority of these patients recover renal function without intervention, the presence of macroscopic hematuria may also portend severe kidney injury, with approximately 30 % of these patients requiring short-term dialysis [8].

Features known to be associated with poor prognosis in IgA nephropathy include older age at onset, absence of recurrent macroscopic hematuria [7], hypertension, and proteinuria (>500 mg/day); proteinuria is the only parameter that independently predicts the progression of renal dysfunction [9]. Based on these prognostic factors, evidence-based treatment recommendations include prednisone for patients with more than 3 g of proteinuria per day, mild glomerular changes on biopsy, and preserved renal function (eGFR >70 mL/min) [10]. Fish oil has been recommended for those with progressive renal dysfunction (eGFR <70 mL/min) [10]. Cyclosporine, cyclophosphamide, warfarin, and dipyridamole have generally not been recommended unless crescentic and/or rapidly progressive

glomerulonephritis is detected [10]. Hypertensive patients with proteinuria should be treated with an ACE inhibitor or angiotensin receptor blocker (ARB) [10].

The significance of reversible acute kidney injury in the long-term prognosis of IgA nephropathy remains uncertain. Perhaps crescentic glomerulonephritis is more likely to incur permanent renal damage when compared to acute tubular necrosis and interstitial nephritis [2]. Multiple episodes of transient renal failure with gross hematuria may lead to progressive renal decline at a more gradual rate than the results from a single occurrence of kidney injury [7]. When patients with IgA nephropathy suffer from acute renal failure followed by gross hematuria, possible determinants of prognosis may involve features already associated with a poor prognosis in IgA nephropathy, including older age at onset, absence of recurrent macroscopic hematuria [7], hypertension, and proteinuria [9].

Included in the differential diagnosis for acute kidney injury with gross hematuria are nephrolithiasis, infection, anatomic abnormalities, coagulopathies, and other glomerulonephritides, such as post-streptococcal glomerulonephritis, lupus nephritis, membranoproliferative glomerulonephritis, and rapidly progressive glomerulonephritis. While IgA nephropathy is a rare cause of acute kidney injury with gross hematuria, the diagnosis is an important one to make, as appropriate therapies such as prednisone, fish oil, ACE inhibitors, or ARBs, may prove beneficial in the prevention of progressive renal decline.

We report an atypical presentation of IgA nephropathy with the triad of reversible acute kidney injury, gross hematuria, and severe bilateral flank pain. Renal function in this case was recovered with conservative management. Acute renal failure was thought to be attributable to a combination of interstitial inflammation, tubular necrosis, and tubular RBC obstruction, as opposed to crescentic glomerulonephritis. Although it is anticipated that this patient will do well, given her recovery to baseline renal

function, her long-term prognosis remains uncertain. This case demonstrates that IgA nephropathy should be considered in the differential diagnosis for transient acute kidney injury with gross hematuria, and should be appropriately treated based on known prognostic factors.

Conflict of interest All the authors have declared no competing interests.

References

1. Lui SL, Chan KW, Chan TM, Cheng IKP. Reversible acute renal failure in a patient with IgA nephropathy. *HKMJ*. 1995;1:351–3.
2. Wen YK, Chen ML. The spectrum of acute renal failure in IgA nephropathy. *Ren Fail*. 2010;32(4):428–33.
3. Lee HS, Pyo HJ, Koh HI. Acute renal failure associated with hematuria in IgA nephropathy. *Am J Kidney Dis*. 1988;12(3):236–9.
4. Fogazzi GB, Imbasciati E, Moroni G, Scalia A, Mihatsch MJ, Ponticelli C. Reversible acute renal failure from gross haematuria due to glomerulonephritis: not only in IgA nephropathy and not associated with intratubular obstruction. *Nephrol Dial Transplant*. 1995;10(5):624–9.
5. Praga M, Gutierrez-Millet V, Navas JJ, Ruilope LM, Morales JM, Alcazar JM, et al. Acute worsening of renal function during episodes of macroscopic hematuria in IgA nephropathy. *Kidney Int*. 1985;28:69–74.
6. Lupo A, Rugiu C, Cagnoli L, Zucchelli P, Maschio G. Acute changes in renal function in IgA nephropathy. *Semin Nephrol*. 1987;7:356–62.
7. Gutiérrez E, González E, Hernández E, Morales E, Martínez MA, Usera G, et al. Factors that determine an incomplete recovery of renal function in macrohematuria-induced acute renal failure of IgA nephropathy. *Clin J Am Soc Nephrol*. 2007;2(1):51–7.
8. Delclaux C, Jacquot C, Callard P, Kleinknecht D. Acute reversible renal failure with macroscopic haematuria in IgA nephropathy. *Nephrol Dial Transplant*. 1993;8(3):195–9.
9. D'Amico G, Napodano P, Ferrario F, Rastaldi MP, Arrigo G. Idiopathic IgA nephropathy with segmental necrotizing lesions of the capillary wall. *Kidney Int*. 2001;59(2):682–92.
10. Nolin L, Courteau M. Management of IgA nephropathy: evidence-based recommendations. *Kidney Int Suppl*. 1999;70:S56–62.