An Unusual Case of Acute Kidney Injury with Edematous Kidneys and Venous Micro Thrombi: A Case Report

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Abstract

This case report describes a young patient with Acute Kidney Injury (AKI) stage 3, low grade micro-hematuria (3-5 dysmorphic red blood cells in each high power field [RBC/HPF]), low grade proteinuria (Urine Protein To Creatinine (UPCR) of around 1 gm/gm), edematous kidneys on ultrasound, and unusual histologic finding on kidney biopsy. The main complaints on presentation were low back and flank pains for a few days. He took 10 tablets of acetaminophen and 2 tablets of ibuprofen over the last few days before the symptoms started. He did not have any alcohol or illicit drugs use. Investigations have not revealed a cause for this AKI including Doppler ultrasound of the renal arteries and veins, and serologic testing. Anti dsDNA was positive, although ANA and anti-histones were negative. The kidney biopsy revealed mild irregular interstitial edema with limited inflammation. There was no significant interstitial fibrosis or tubular atrophy. There were microthrombi filling distended small veins throughout the renal cortex. Small arteries and arterioles are within normal limits. The patient recovered renal function within 3 weeks with supportive care. There was no need for dialysis.

Keywords: Acute kidney injury; Edematous kidneys; Microthrombi

Background

Information about Acute Kidney Injury (AKI) in general is scanty especially in younger patients. The incidence rate of Acute Kidney Injury (AKI) around the world is not well known [1-4]. Studies in the developed countries show a lower incidence of AKI in comparison with developing countries [4-7]. In addition, it is recognized that in developed regions elderly patients predominate [4,5], in developing countries, AKI is a disease of the young [8] and children [9], in whom volume-responsive “prerenal” mechanisms are common [10]. We present a case of a young adult presenting with unexplained AKI.

Case History

A 20-year-old man with non-significant past medical history who presented to the emergency room with a 2 day-history of low back and bilateral flank pain. He also had mild nausea and feverishness. The patient also reported thirst and polyuria. He did not have edema, rashes, or arthralgia. No respiratory symptoms were reported. He took 10 tablets of acetaminophen and 2 tablets of ibuprofen over those 2 days. He did not have any alcohol or illicit drugs use.

Vital signs were normal. Physical examination was positive for mild costovertebral angle tenderness on both sides. Otherwise, the rest of the physical exam was unremarkable. He had no skin rash.

Initial laboratory testing revealed a serum creatinine of 341 umol/L (3.8 mg/dl), and urinalysis showed proteinuria (2+), and 0-3 and 3-5 RBC/HPF. Urine protein to creatinine ratio was 94 mg/mmol. Urine microscopy revealed few white blood cells, few dysmorphic red blood cells, and granular casts. The patient received intravenous fluids. He then had a chest X-ray which showed lower lobes atelectasis, with small bilateral pleural effusions. Renal ultrasound showed mildly enlarged and edematous kidneys of 14-14.5 cm, cortical thickness of 2.3-2.4 cm, and mildly increased echogenicity. Doppler ultrasound of both renal arteries and veins was normal. Serological studies showed negative Anti-neutrophil Cytoplasmic Antibody (ANCA), and Anti-glomerular Basement Antibody (anti-GBM). Anti-double stranded DNA antibody was low positive. The titer was 10 IU/ml (Ref range 0-9). C3 complement was within the normal range and anti-histone antibody were negative. No drug or alcohol testing was done. The patient was mildly anemic with lowest hemoglobin (Hb) of 113 g/L but Hb and Platelets were relatively stable throughout the course. He had a normal Hb electrophoresis. Peripheral smear was never done. Renal function continued to deteriorate despite supportive care, and a kidney biopsy was performed on day 3 of his admission.

Histopathologic finding Sections cut at multiple levels and stained with H&E (Figure 1A), PAS (Figure 1B), Jones and trichrome stains were examined. They showed renal cortex in which approximately 30 glomeruli were present. Medulla was not included. The glomeruli were mostly normocellular, largely bloodless with sparse leukocytes in occasional poorly expanded capillary lumens. The tubulointerstitial compartment showed mild irregular interstitial edema with patchy accentuation. The proximal tubules had subtle fraying of their luminal brush border best seen on PAS (Figure 1B). A small number of distal tubules profiles had a few damaged or apoptotic cells. Limited inflammation including a few lymphocytes, histiocytes and sparse neutrophils was present in patchy foci of mildly accentuated interstitial edema with reactive stromal cells often in the vicinity of distended veins. There was no significant interstitial fibrosis or tubular atrophy.
The most striking feature was the presence of a microthrombus filling a distended vein branch across the width of one core. The vein wall was difficult to identify but was highlighted by immunohistochemical stain for CD31. There were also mononuclear cells aggregated at the periphery of the microthrombus that were, at least focally, in continuity with flat endothelium. Other distended small veins were present throughout the renal cortex. There were 2 microscopic foci of leaked proteinaceous or extruded thrombus material with associated reactive macrophages and monocytes. Small arteries and arterioles were within normal limits. The scouting sections for direct immunofluorescence showed the presence of up to 5-6 glomeruli of which one had early tuft retraction and capsular fibrosis suggestive of some ischemic damage (Figure 1C).

Subsequent progress: Serum creatinine continued to deteriorate and peaked at 635 umol/L. There was no indication to start dialysis. The patient was treated conservatively with intravenous hydration, pain medications and low salt/low potassium diet. Creatinine started improving slowly and was down to 88 umol/L (0.9 mg/dl) on day 21 after the presentation. Proteinuria has also resolved completely. He had no further back or flank pain.

Discussion

We describe a young and previously healthy patient with AKI and interesting finding on kidney biopsy of venous microthrombi and localized inflammation. The patient presented with flank pain, and
low-grade micro-hematuria and proteinuria. He clinically behaved like Acute Tubular Necrosis (ATN), with progressive kidney function recovery over a few weeks but the kidney biopsy was surprising.

The literature review has revealed limited information and reports that describe similar presentations and close histologic findings in the setting of illicit drugs use such as ecstasy or a large amount of alcohol consumption. Our patient denied both. We suspect an immunologically mediated process which caused endothelial injury. This injury may have been compounded by hypercoagulability, or abnormal blood flow possibly due to dehydration, could have potentially triggered those microthrombi. Additionally, NSAIDs may have also affected the intrarenal blood flow and contributed to this presentation. Redfern A et al., describes a case series on similar unexplained pathologic finding of renal arcuate venous microthrombi with associated localized inflammatory response. In case series of 6 patients, all of them reported to have consumed alcohol and notably 4 out of 6 patients were either using NSAID or Acetaminophen for pain. Hematuria and proteinuria along with negative immunology screen was reported on [11]. The other striking features are the presence of flank pain as a presenting complaint and demographically young patients [11-13]. Most often patients have had successful renal recovery with conservative management however there have been reports where temporary dialysis has been necessary [11,14]. The possibility of post-infectious glomerulonephritis was entertained but he had normal C3 and negative cultures. Anti-streptolysin O titer was normal.

The above are speculations, and the exact cause of this AKI remains uncertain. The first mechanism of Acute Kidney Injury (AKI) from NSAIDs is due to reduced renal plasma flow caused by a decrease in prostaglandins, which regulate vasoconstriction at the glomerular level. NSAIDs disrupt the compensatory vasoconstriction in renal prostaglandins to vasoconstrictor hormones released by the body [15]. Inhibition of renal prostaglandins results in acute deterioration of renal function after ingestion of NSAIDs. The second mechanism of AKI is acute interstitial nephritis (AIN), which is characterized by the presence of an inflammatory cell infiltrate in the interstitium of the kidney. AIN is caused by an immunological reaction after NSAID exposure of about a week [16]. AIN is now recognized as a major cause of drug induced AKI and accounts for about 15% of all patients with unexplained AKI [17]. As an entity, AIN due to NSAIDs is under recognized as well. In our patient the biopsy did not show evidence of AIN and there was absence of widespread Acute Tubular Necrosis (ATN) as well. Increased awareness of such presentation and further identification of similar cases may help clarify this entity and explain its etiology and pathophysiology.

Conclusion

AKI with severe bilateral flank pain in this young gentleman remains a mystery despite extensive renal work up including a kidney biopsy. At the best we could hypothesize NSAID induced ATN however in our patient, there was neither interstitial nephritis nor widespread ATN. Further research needs to be done into such similar odd presentation of AKI to explain the pathophysiology. Fortunately in this particular patient the AKI was self-limiting; the renal function improved and did not require dialysis avoiding long term morbidity.

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