



Acute Kidney Injury Following COVID-19 mRNA-1273 Vaccination - A Case Report

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Keywords

Acute kidney injury; COVID-19; Vaccination.

Introduction

COVID-19 vaccination has been proved to be variably effective in reducing mortality and morbidity during the pandemic [1,2]. However, a variety of side-effects including death were also reported not infrequently [3,4]. These side-effects, probably immune-related, involved several organs, including the kidney [5]. The spectrum of vaccination-related kidney injuries was widely distributed, including glomerulonephritis, interstitial nephritis, and vasculitis and may present as acute kidney injury [6,7]. Herein, we report a case of acute kidney injury after 3 doses of mRNA-1273 vaccine (Moderna).

Case Presentation

A 58-year-old male visited our emergency room in March 2022, because of an abrupt onset of dizziness and general malaise. Physical examination revealed that he was afebrile with no cardiopulmonary distress, a blood pressure of 128/84 mmHg, heart rate; 74/min, normal heart sound and breathing sound, and normal abdominal examination. Neurological examinations were also unremarkable. Unexpectedly, a serum creatinine of 3.1 mg/dl (eGFR: 22.1 ml/min) was found. The other laboratory studies were unremarkable, including a normal urinalysis. The kidney sonography revealed normal size of both kidneys with normal echogenicity. His past history included hypertension and dyslipidemia; both were under satisfactory control at our cardiovascular clinic for more than 5 years. Notably, he received 3 doses of Covid-19m RNA-1273 vaccine (Moderna) in August 2021, November 2021 and February 2022, respectively. On December 7th, 2021, he received a routine check-up for a Pre-Scheduled Panendoscopy (PES), which showed a normal serum creatinine of 1.1 mg/dl (eGFR: 73.08 ml/min), but there was microscopic hematuria (urinalysis: RBC: 50-99/HPF, WBC: 0-2/HPF). He recalled that there was an episode of painless gross hematuria a few days ago, nearly one month after the second shot of vaccination. It subsided spontaneously. The PES disclosed gastric ulcers and a proton pump inhibitor (lansoprazole) were prescribed. Because there was no grosser hematuria, he did not pay attention to his kidney condition and was not followed up at our Nephrology Clinic until this visit to the emergency room. Under the impression of acute kidney injury [8] with unknown etiology, he was admitted for a kidney biopsy. After admission, a series of immune studies were performed (Table 1), which showed an ANA titer of 1:160, normal Complement 3 (C3) and C4, negative for anti-ds-DNA, anti-glomerular basement antibody and anti-neutrophil cytoplasmic antibody. The complete blood count was essentially normal except for a mild anemia (hemoglobin: 10.5), and the liver function were also normal. A urinalysis again showed negative finding with no hematuria. The Urine Protein Creatinine Ratio (UPCR) was 93.6 mg/g Creatinine (Cr).

Pathologic finding

A kidney biopsy was done on the next day of admission. The sample was sent for Light Microscopy (LM), Immunofluorescence study (IF) and Electron Microscopy (EM) examinations. There were 9 glomeruli in the specimen. Under LM (Figure 1), the glomeruli appeared to be grossly normal with normal cellularity and capillary walls, except for mild focal thickening of Bowman capsule and enlarged Bowman's space. The proximal tubules showed hyaline to foamy change with some tubules showing flattening of the lining epithelium and luminal dilatation. There were some calcifications in the tubular lumina and foci of tubular atrophy and interstitial fibrosis. The IF study was negative for all staining, including IgG, IgA, IgM, C3, kappa and lambda. The EM showed

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Table 1: Laboratory examinations.

Item	12/7/2021	12/21/2021	3/3/2022
Serum creatinine (mg/dl)	1.1		3.1
Urinalysis (RBC)		50-99/HPF ^{**}	0-5/HPF
Urinalysis (WBC)		0-5/HPF	0-5/HPF
UPCR ^{**} (mg/g Cr)			93.6
UACR ^{***} (mg/g Cr)		30	
LDH ^{****} (U/L)			146
ANA			0.152777778
Anti-ds-DNA			1:10
C3 (mg/dl)			79.7
C4 (mg/dl)			23.7
IgG (mg/dl)			1210
IgA (mg/dl)			96.5
IgM (mg/dl)			113
ANCA [#]			Negative
Anti-GBM ^{&} antibody			Negative

^{*}High power field; ^{**}Urine protein/creatinine ratio (mg/g); ^{***}Urine albumin/creatinine ratio; ^{****}Lactic dehydrogenase; [#]Anti-neutrophil cytoplasmic antibody; [&]glomerular basement membrane

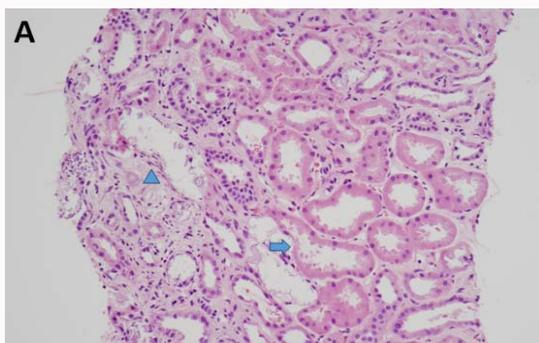


Figure 1A: Light microscopic examination. Hematoxylin Eosin stain, 200x and, revealed mild focal thickening of Bowman's capsule and enlarged Bowman's space. The proximal tubules showed hyaline to foamy change with some tubules showing flattening of the lining epithelium and luminal dilatation (arrow). There were some calcifications in the tubular lumina and foci of tubular atrophy and interstitial fibrosis (arrowhead).

partial foot process effacement and detachment of the podocytes affecting no more than 50% of the capillary loops examined.

Discussion

We reported a case of acute kidney injury after 3 doses of COVID-19 mRNA-1273 vaccine. The patient's serum creatinine rose from 1.1 mg/dl to 3.1 mg/dl in 3 months but the kidney sonogram looked normal, implying a disproportionately higher rate of renal function deterioration. Although a normal renal sonography might be found in some patients with chronic kidney diseases, like diabetic nephropathy, it is our usual experience that the renal sonogram should revealed either a decrease in kidney size or an increase in echogenesity bilaterally if the patient's kidney disease was attributed to be "chronic" because an eGFR of 22.1 mg/min meant a significant loss of renal function and it will take a substantial time to develop. Rapidly Progressive Glomerulonephritis (RPGN) could manifest with a rapid deterioration of renal function and a normal appearance of renal sonogram. However, RPGN usually

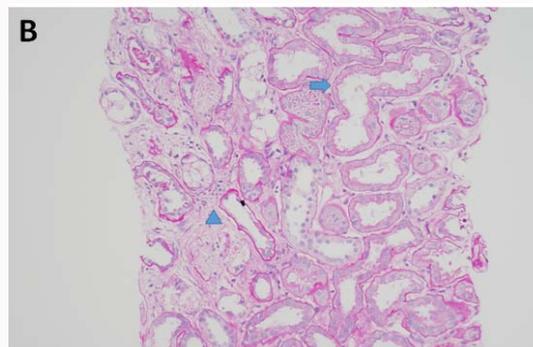


Figure 1B: Light microscopic examination. Periodic acid-Schiff stain, 200x revealed mild focal thickening of Bowman's capsule and enlarged Bowman's space. The proximal tubules showed hyaline to foamy change with some tubules showing flattening of the lining epithelium and luminal dilatation (arrow). There were some calcifications in the tubular lumina and foci of tubular atrophy and interstitial fibrosis (arrowhead).

presented with microhematuria and proteinuria, which was unlikely, subsided without aggressive treatment. Our patient had a completely normal urinalysis at the time of biopsy, making the diagnosis of RPGN unlikely. Likewise, thrombotic microangiopathy, which has also been reported in the literature [7], can be ruled out based on the same reason. The kidney biopsy disclosed focal flattening of the lining epithelium and luminal dilatation, implying acute tubular injury. There was no glomerulosclerosis and no significant interstitial fibrosis and tubular atrophy, making the diagnosis of a "chronic" kidney injury very unlikely. Because there was a gap of 3 months between the onset of gross hematuria and the kidney biopsy, we speculated that an intensive glomerular or tubular injury could have occurred during the 3 months although the patient was asymptomatic. The current biopsy findings thus may only represent residual changes of the injury. Alternatively, a sampling error of the biopsy encompassing the relatively "normal" portion of the tissue might explain the dissociation of clinical and pathologic findings. Previous reports about COVID-19 vaccination associated kidney injuries included various kinds of glomerulonephritis, including IgA nephropathy, minimal change disease [9,10], RPGN [11] and others [6,12,13]. Our case had normal appearance of glomeruli, thus the diagnosis of proliferative glomerulonephritis is unlikely at the time of biopsy. However, our patient experienced an episode of painless gross hematuria one month after his second dose of vaccination. Surgical hematuria such as urothelial tumor and urolithiasis were carefully ruled out. Electron microscopy examination also revealed partial loss of podocytes foot process. Thus, we cannot exclude a transient glomerulonephritis [14] had occurred during the disease process. Minimal change disease could manifest with acute kidney injury [15]. However, the hallmark of minimal change disease is nephrotic-ranged proteinuria and general anasarca, which were not present in our patient. Acute Interstitial Nephritis (AIN) also had been reported in association with COVID-19 vaccination [16]. We cannot exclude the possibility that AIN had occurred in our patient during the 3 months, because of the presence of foci of tubular atrophy and interstitial fibrosis seen in LM. Our patient also took a Proton Pump Inhibitor (PPI) (lansoprazole) following the finding of gastric ulcer in PES examination. Acute interstitial nephritis and chronic kidney disease have been reported in patients taking PPI [17,18]. However, the cases reported were extremely rare. Given the huge population taking this drug, the evidence linking PPI use and kidney injury is

still controversial. Moreover, the pathologic finding in our patient was not in support of this diagnosis.

In summary, we reported a case of acute kidney injury after 3 doses of mRNA-1273 (Moderna) vaccinations. Although the causal relationship is difficult to establish, like most of the reported cases in the literature, we failed to find other disease entities to explain the clinical features [19], neither it is *De novo* or relapsing diseases [12,14]. The discovery of a specific biomarker of vaccination-related disease [20] may help to elucidate the question.

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