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Letter to the Editor

Acute tubulointerstitial nephritis after COVID-19 m-RNA BNT162b2 vaccine

Dear Editor,

A new type of coronavirus disease 2019 (COVID-19) has affected many millions of people globally since it was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Despite the different types of vaccines, the pandemic is still not under control. One of the most important vaccine types against COVID-19 so far is the mRNA vaccine. This vaccine has been administered to millions of people for about a year, and its safety and effectiveness have been proven[1,2]. In the clinical trials of the vaccine, side effects of vaccine occurred typically within the first week of the first or second vaccine injection as mild/moderate side effects such as pain in the vaccinated arm, rash, myalgia, fever, and lymphadenopathy, while it also reports serious side effects such as myocarditis and cardiac arrhythmias[1,2]. To our knowledge, no vaccine-related side effects such as kidney dysfunction or urinary abnormality have been reported yet. Herein, we report a case of acute tubulointerstitial nephritis (ATIN) and acute kidney injury after receiving the first dose of the m-RNA-BNT162b2 vaccine.

A forty-four year old female was vaccinated against COVID-19 on June 27, 2021, with the first dose of COVID-19 mRNA vaccine (BioNTech). There were no acute side effects such as arm pain, rash, headache, or fever-related to the vaccine immediately after the vaccination. The patient did not have any known systemic disease and did not have a cough using herbal medicine or medical medicine. After 48 hours of receiving the first COVID-19 mRNA vaccine, the patient started to complain of sudden onset of headache, fever (38.4°C) nausea-vomiting, weakness, and pain in the lower extremities. She was admitted to the hospital after the hemoglobin: 6.6 g/dl, lactate dehydrogenase (LDH): 2100 U/L, and serum creatinine levels: 2.1 mg/dl were detected in the emergency department. Except for direct coombs testing positivity, all other hemolysis tests of the patient were evaluated as normal. Urinalysis showed minimal leukocyturia and micro-haematuria, nephrotic proteinuria (quantitative protein: 10.1 g/day). No microbial finding was detected in the urine culture. Leukocytosis (12.300 WBC/ml) was also detected, with an increase of C-reactive-protein (96.2 mg/dl). Creatine phospho kinase was in the normal range and serology revealed normal complements and negative levels for antinuclear antibodies (ANA) anti-neutrophil cytoplasmic antibodies (ANCA). Serologies for HIV, hepatitis C and hepatitis B were also negative. In addition, no focus of infection was detected, and inflammatory indicators improved in parallel with disease regression. Abdominal ultrasonography revealed no hepatosplenomegaly, and bilateral kidney sizes/parenchymal thicknesses were within normal limits.

The next day, acute hemodialysis (HD) was performed due to anuric course, progression to 6.5 mg/dl in serum creatinine values, and increased metabolic acidosis. Two units of erythrocyte suspension were given due to anemia. After three sessions of HD, we detected extensive inflammation in the tubulointerstitial area and occasional eosinophils, with preserved glomeruli, as a result of kidney biopsy (Figure 1). The patient was evaluated as vaccine induced ATIN. We started the patient on 1 mg/kg/day prednisolone treatment. He

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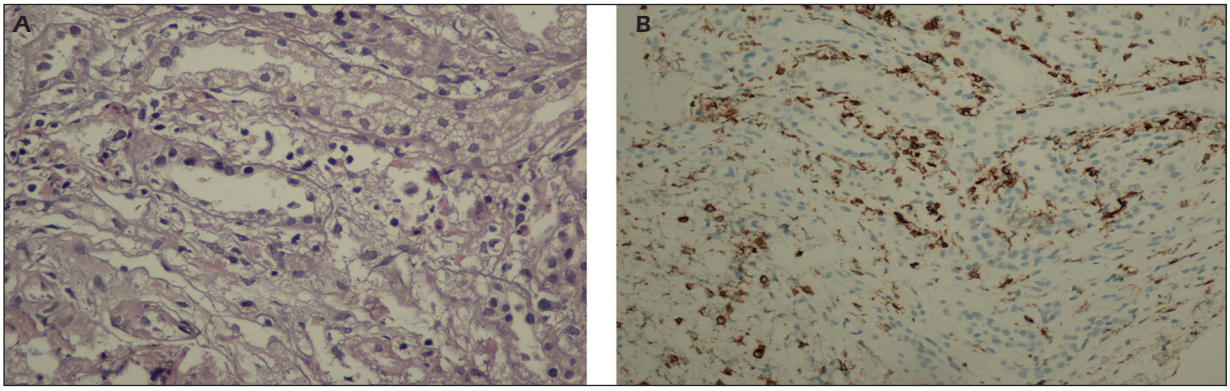

Figure 1. Tubulointerstitial inflammatory infiltration containing eosinophils and lymphocytes and interstitial edema (×400 H&E) (**A**), and the Cd45 staining of interstitial inflammatory cells (×200 IHK) (**B**).

started to become polyuria (4.1 Lt/day) on the seventh day of steroid treatment. In the follow-up, the clinical course gradually improved, with the complete recovery of renal dysfunction and abnormal urine findings.

To our knowledge, we present for the first time a case diagnosed with ATIN after the COVID-19 mRNA vaccine. The patient did not have any known systemic disease or a history of exposure to nephrotoxic drugs. We detected anemia, proteinuria, microscopic hematuria, and acute renal failure in the patient approximately 48 hours after the first m-RNA vaccine. Due to these findings, we detected acute tubulointerstitial nephritis, as a new and rare side effect related to m-RNA vaccine, as a result of a kidney biopsy.

Many causes of ATIN are known. It is a frequent cause of acute renal failure, characterized by the presence of inflammatory cell infiltrate in the interstitium of the kidney. Immuno-allergic reactions to certain medications, mainly non-steroidal anti-inflammatory drugs and antibiotics are by far the most important etiology for ATIN, but other conditions such as infections, toxins, and vasculitis are known to induce ATIN. Spontaneous initial recovery is very frequent after avoidance of the causal substance, but in some cases, rapid corticosteroid treatment may be necessary[3]. In our case, serum and urine abnormalities indicate renal dysfunction, completely resolved with steroid treatment, and indicate that the renal damage is temporary.

In the literature, it has been shown as case reports that acute kidney injury developed after different vaccinations. It was reported that transient acute renal failure developed due to inactivated influenza vaccine, and the patient completely recovered[4]. However, a renal biopsy was not performed in that case. Influenza vaccine-related rhabdomyolysis and acute kidney injury have been reported, especially in patients receiving statin therapy[5,6]. Our patient stated that she had an inactivated flu vaccine two years ago, but no side effects were observed after this vaccine.

In conclusion, we report the case of a 44-year-old female patient who developed reversible acute kidney injury due to ATIN after receiving the first dose of the m-RNA-BNT162b2 COVID-19 vaccine. With a review of the limited literature related to the side effects of the COVID-19 mRNA vaccine, and with no other etiology explaining the sudden onset of kidney findings, we attribute these side effects as the side effects of the mRNA BNT162b2 vaccine. However, we emphasize that the high morbidity and mortality rates associated with COVID-19 should be considered and such rare side effects of the vaccine can be ignored. Vaccination is the main struggle method and life-saving measure against COVID-19 disease.

Conflict of Interest

The authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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