



Exacerbation of an undiagnosed pre-existing lupus nephritis following an inactivated COVID-19 vaccination

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ABSTRACT

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There are reports of various renal complications following the administration of different types of COVID-19 vaccines. Further studies are required to investigate the associations and underlying pathogenesis.

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Introduction

Following the widespread use of vaccination with different types of COVID-19 vaccines globally, some side effects are being reported. There have been reports of new-onset or relapse of glomerular diseases following different types of mRNA and inactivated COVID-19 vaccines (1). Herein, we describe an Iranian patient who experienced an exacerbation of an undiagnosed pre-existing lupus nephritis (LN) after the administration of the first dose of an inactivated SARS-CoV-2 vaccine.

A 29-year-old Iranian male was admitted to our hospital one week after receiving the first dose of an inactivated COVID-19 vaccine. He had nausea, vomiting, and progressive dyspnea. His past medical history included controlled hypertension. He denied any history of systemic lupus erythematosus (SLE) or any symptoms such as photosensitivity or arthritis. On admission, his serum creatinine level was 8 mg/dL. His other laboratory workup included high levels of anti-double-stranded DNA (anti-ds DNA) and antinuclear antibody (ANA) titers. Renal ultrasonography revealed small kidneys. Consequently, hemodialysis was initiated and his condition gradually became stable; therefore, he was discharged.

A week after his discharge, a kidney biopsy was conducted. The kidney biopsy reported global sclerosis in most of the glomeruli. Eight glomeruli showed crescents

(cellular) and only 2 glomeruli appeared normal. Significant inflammation and fibrosis were detected in the tubulointerstitial area. In addition, there were chronic thrombotic microangiopathy, arterial edema, arteriolar occlusion, and thrombosis in the vessels. Representative images of renal biopsy are shown in [Figures 1A to 1E](#). The immunofluorescence study of five glomeruli revealed granular deposits in the glomerular basement membrane (GBM) and the mesangium as the following; IgG (2+), C3 (3+), C1q (trace), IgM (negative) and IgA (negative).

A summary of the patients' history and workup is shown in [Table 1](#).

Discussion

There have been reports of new-onset or relapse of glomerular diseases following different types of mRNA and inactivated COVID-19 vaccines such as minimal change disease (MCD), IgA nephropathy (IgAN), anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, and membranous nephropathy (MN) (1). However, to our knowledge, there have been only two previous reports of kidney complications following an inactivated SARS-CoV-2 vaccination. Aydin et al reported a relapse of primary MN in a patient with a previous history of MN following the first dose of Sinovac vaccine (an inactivated SARS-CoV-2 virus vaccine) (2). In

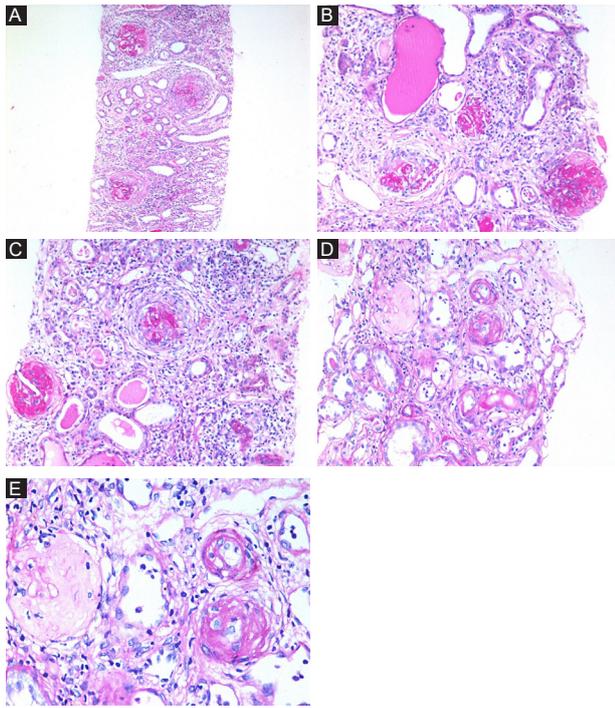


Figure 1. (A) Low-power photomicrograph showing a representative area of renal cortex with three glomeruli, which are almost completely sclerosed. There is moderate degree of tubular atrophy and interstitial inflammation in the background. (PAS, $\times 100$). (B) Medium-power photomicrograph showing renal cortex with three globally sclerosed glomeruli. There is moderate degree of tubular atrophy and interstitial inflammation in the background. One dilated tubule contains hyaline cast (PAS, $\times 200$). (C) Medium-power photomicrograph showing globally sclerosed glomerulus and one with cellular crescent with early organization. There is moderate degree of tubular atrophy and interstitial inflammation in the background. (D) Medium-power photomicrograph showing a representative area of renal cortex with one glomerulus showing ischemic solidification. Two arterioles show prominence of endothelial cells, narrowing of lumina and thickening of walls (PAS, $\times 200$). (E) High-power photomicrograph showing a representative area of renal cortex with one glomerulus showing ischemic solidification. Two arterioles show prominence of endothelial cells, luminal narrowing, and wall thickening (PAS, $\times 400$).

addition, Ozkan et al reported a relapse of MCD following the second dose of an inactivated SARS-CoV-2 vaccine (3). To our knowledge, Tuschen et al have reported the first case of LN relapse of class V and II following the first dose of an mRNA-based COVID-19 vaccine (BNT162b2). This relapse of an immune-mediated disease seemed to be induced by the mRNA-based COVID-19 vaccine (4). Our case is the second report of an exacerbation of LN following a COVID-19 vaccination. However, interestingly, our case occurred after an inactivated SARS-CoV-2 virus vaccination.

Further studies are required to investigate whether there is an association between inactivated SARS-CoV-2 vaccinations and exacerbation of LN as well as the underlying pathogenesis.

Authors' contribution

Primary draft by SH. Pathology slides interpretation by

Table 1. A summary of the patients' history and workup

Vaccine	Inactivated SARS-CoV-2 Vaccine
Past-medical history	<ul style="list-style-type: none"> • 29-year-old Iranian male • History of hypertension
Signs and symptoms	One week after the first dose of vaccination on admission: <ul style="list-style-type: none"> • Nausea • Vomiting • Progressive dyspnea
Laboratory tests	<ul style="list-style-type: none"> • Serum creatinine: 8 mg/dL • Anti-ds DNA titer: Increased • ANA titer: Increased
Imaging	Ultrasound: <ul style="list-style-type: none"> • Small kidneys
Biopsy report	Kidney biopsy (after one week of discharge): <ul style="list-style-type: none"> • Glomeruli: <ul style="list-style-type: none"> ◆ Most of the glomeruli showed global sclerosis ◆ 8 crescentic glomeruli (cellular); only three glomeruli appeared normal • Tubules and Interstitial area: <ul style="list-style-type: none"> ◆ Significant inflammatory infiltration and fibrosis • Vessels: <ul style="list-style-type: none"> ◆ Chronic thrombotic microangiopathy ◆ Arterial edema ◆ Arteriolar occlusion ◆ Thrombosis Immunofluorescence (five glomeruli): <ul style="list-style-type: none"> • Granular deposits along the GBM and in the mesangium: <ul style="list-style-type: none"> ◆ IgA: 0 ◆ IgG: 2+ ◆ IgM: 0 ◆ C3: 3+ ◆ C1q: Trace
Diagnosis	Exacerbation of an undiagnosed pre-existing diffuse LN (class IV) <ul style="list-style-type: none"> • Global Activity: 60% • Chronicity: 40% • IFTA Grade II
Treatment	<ul style="list-style-type: none"> • Hemodialysis

Abbreviations: LN, Lupus nephritis; GBM, Glomerular Basement Membrane; Anti-ds DNA, anti-double stranded DNA; ANA, Antinuclear antibody; IFTA, International Federation of Technical Analysts.

HN, MM; pathology reports interpretation and editing of the manuscript. MAS finalized the paper. All authors read and signed the final paper.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical issues

Ethical issues (including plagiarism, data fabrication and double publication) were observed by the authors.

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