A case report of relapse of minimal change disease after the first dose of Pfizer-BioNTech Covid-19 vaccine in King Abdul-Aziz Specialist Hospital, Taif, Saudi Arabia

Faisal K. Alhomayani [1], Shatha K. Alhalbi [2], Elaf M. Althobaiti [2]

(1) Consultant, nephrology department, King Abdul-Aziz Specialist Hospital, Taif, Saudi Arabia
(2) Medical intern, King Abdul-Aziz Specialist Hospital, Taif, Saudi Arabia

Corresponding author:
Dr. Shatha K. Alhalbi
Taif city, Saudi Arabia
Tel.:0593245934
Email: shatha.nae@gmail.com

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Abstract

Background: Documented cases of de novo glomerular disease or relapse of pre-existing glomerular disease was acquired shortly after administration of COVID-19 messenger RNA (mRNA) vaccinations.

Objectives: to present a case of a 64-year-old female who received the Pfizer-BioNTech COVID-19 vaccination as a first dose and then experienced a relapse of minimal change disease (MCD) presenting with nephrotic syndrome.

Case presentation: The presenting symptom was ankle swelling and frothy urine which started 9 days after the first dose of vaccine. Albumin level was 24 g/L, urine albumin/creatinine ratio was 668 mg/mmol, Creatinine had risen to 1.3 mg/dl, urine analysis showed 3+ protein. light microscopy showed 17 patent glomeruli, one of which was globally sclerosed. There was mild focal increase in mesangial matrix with occasional atrophic tubules with minor interstitial scarring affecting less than 5% of cortical area. There was moderate fibrointimal thickening. In electron microscopy, 100% of podocyte foot process were effaced with microvillation and marked cytoplasmic vacuolation. The findings were consistent with minimal change disease (MCD) with mild chronic renal parenchymal damage. The patient started furosemide 80 mg daily for 21 days after the onset of complaints. prednisolone 1 mg/kg was initiated 1 week and patient`s symptoms improved. The patient achieved a complete remission 4 weeks after initiation of prednisolone.

Conclusion: For the best management of MCD as a potential side effect following COVID-19 vaccination, more knowledge is required.

Keywords: case, relapse, MCD, Pfizer-BioNTech, Covid-19, Taif

Introduction

At the end of 2019, a novel coronavirus (SARS-CoV-2) was identified as a cause of significant mortality and morbidity worldwide (1). Several COVID-19 vaccines were developed and widely used to fight this contagious disease (2). These vaccines are very effective at preventing serious illnesses, hospitalization and death from all current virus variants (2).

Multiple side effects of use of these vaccines have been identified including a reported case with de novo glomerular disease or relapse of pre-existing glomerular disease developed shortly after administration of COVID-19 messenger RNA (mRNA) vaccines (58-59-60 up to date) (3).

Here, we are reporting a case of a 64-year-old female who developed relapse of minimal change disease (MCD) presenting with nephrotic syndrome after her first dose of the Pfizer-BioNTech COVID-19 vaccine, an mRNA-based vaccine against severe acute respiratory syndrome coronavirus 2 (SARS CoV-2).

Case presentation

A case of 64-year-old female with past history of nephrotic syndrome presented at King Abdul-Aziz Specialist Hospital, Taif, Saudi Arabia. She was proved by biopsy to have minimal change disease that had been diagnosed 10 years ago when she was 54 years. The case was treated successfully with prednisolone for around 25 weeks. She had been on regular follow-up with the nephrology service since then, and did not show any evidence of relapse during this period. Recently, 9 days after her first dose of Pfizer-BioNTech COVID-19 vaccine, the patient presented with full-blown nephrotic syndrome.

Clinical Findings: The presenting symptom was ankle swelling and frothy urine that started around 9 days after her initial dose of vaccine. She was not taking any medications, including nonsteroidal anti-inflammatory drugs. Physical examination revealed bilateral peripheral pitting edema up to her mid thighs. She was afebrile and hemodynamically stable with a blood pressure of 122/67 mm. Her oxygen saturation was 98% in room air. There was no evidence of autoimmune diseases, infection, allergic exposure, or an underlying malignancy and the rest of the examination was unremarkable.

Diagnostic Focus and Assessment: The patient was admitted in hospital for 21 days after the onset of the complaints and laboratory investigation revealed an albumin level of 24 g/L and urine albumin/creatinine ratio of 668 mg/mmol. Creatinine had risen to 1.3 mg/dl from a baseline of 80 mg/dl. Urinalysis showed 3+ protein. Laboratory investigation for antinuclear antibody (ANA), urine and serum protein electrophoresis, hepatitis B and C, HIV serologies all were negative. C3 and C4 were within normal limits. A diagnostic kidney biopsy was performed approximately 3 days after admission (24 days after onset of the symptoms and 33 days after his first dose of Pfizer-BioNTech COVID-19 vaccine (Figure 1).

Light microscopy showed 17 patent glomeruli, 1 of which was globally sclerosed. There was mild focal increase in mesangial matrix with occasional atrophic tubules seen with minor interstitial scarring affecting less than 5% of cortical area. Six small arteries showed moderate fibrointimal thickening. Immunofluorescence microscopy revealed non-significant mesangial positivity for C1q (1+), C3 (1+) and IgM (traces). Electron microscopy revealed almost 100% of podocyte foot process were effaced with microvillation and marked cytoplasmic vacuolation. There were no electron-dense deposits. Overall, the findings were consistent with MCD with mild chronic renal parenchymal damage (glomerulosclerosis 6% , IFTA less than 5%) and arteriosclerosis (Figures 2 and 3).

Figure 1. Timing of vaccination, symptoms, admission and kidney biopsy

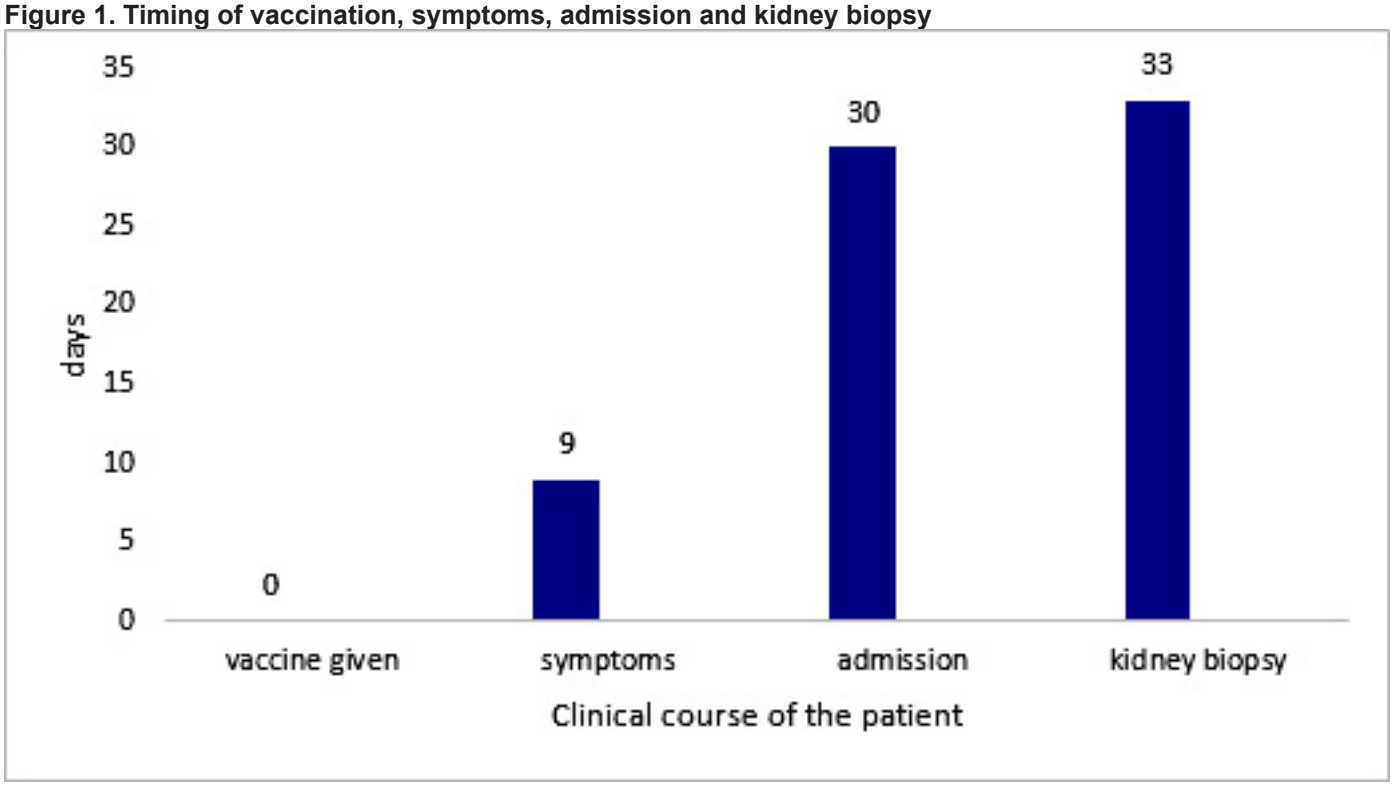


Figure 2. Findings of MCD with mild chronic renal parenchymal damage (glomerulosclerosis 6% , IFTA less than 5%)

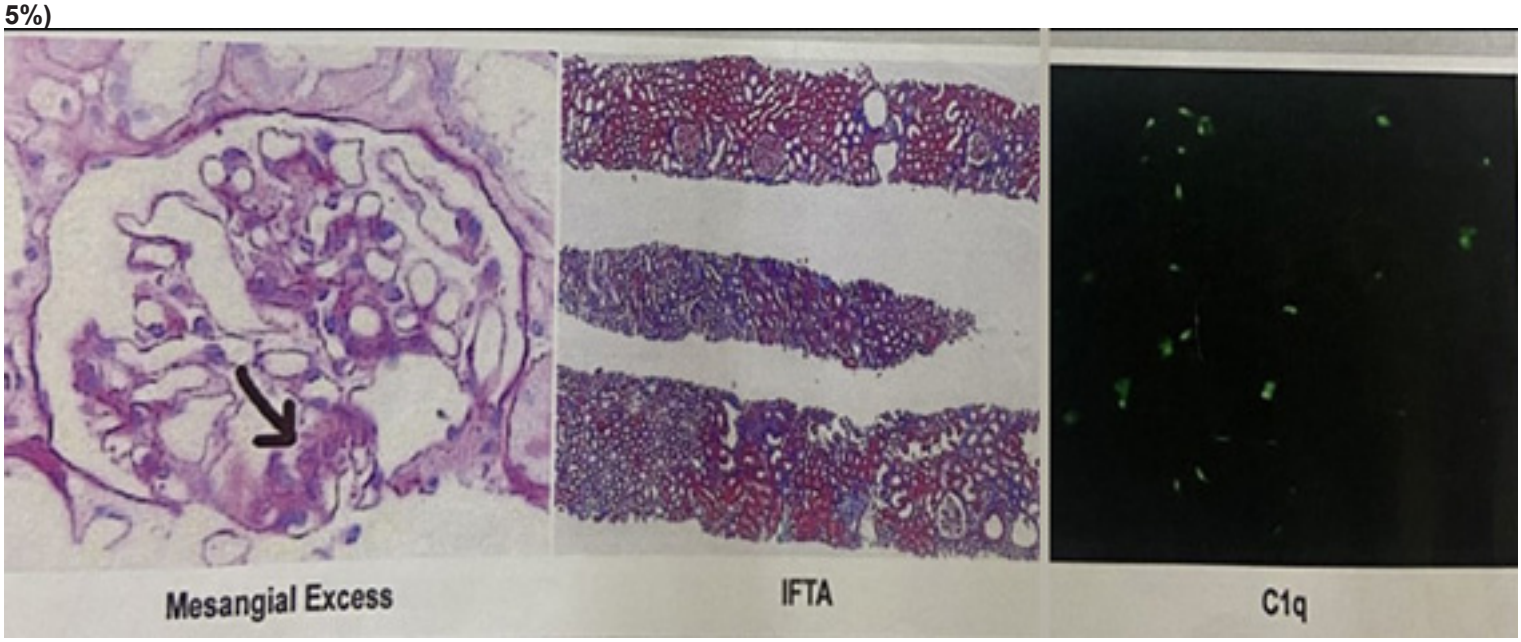
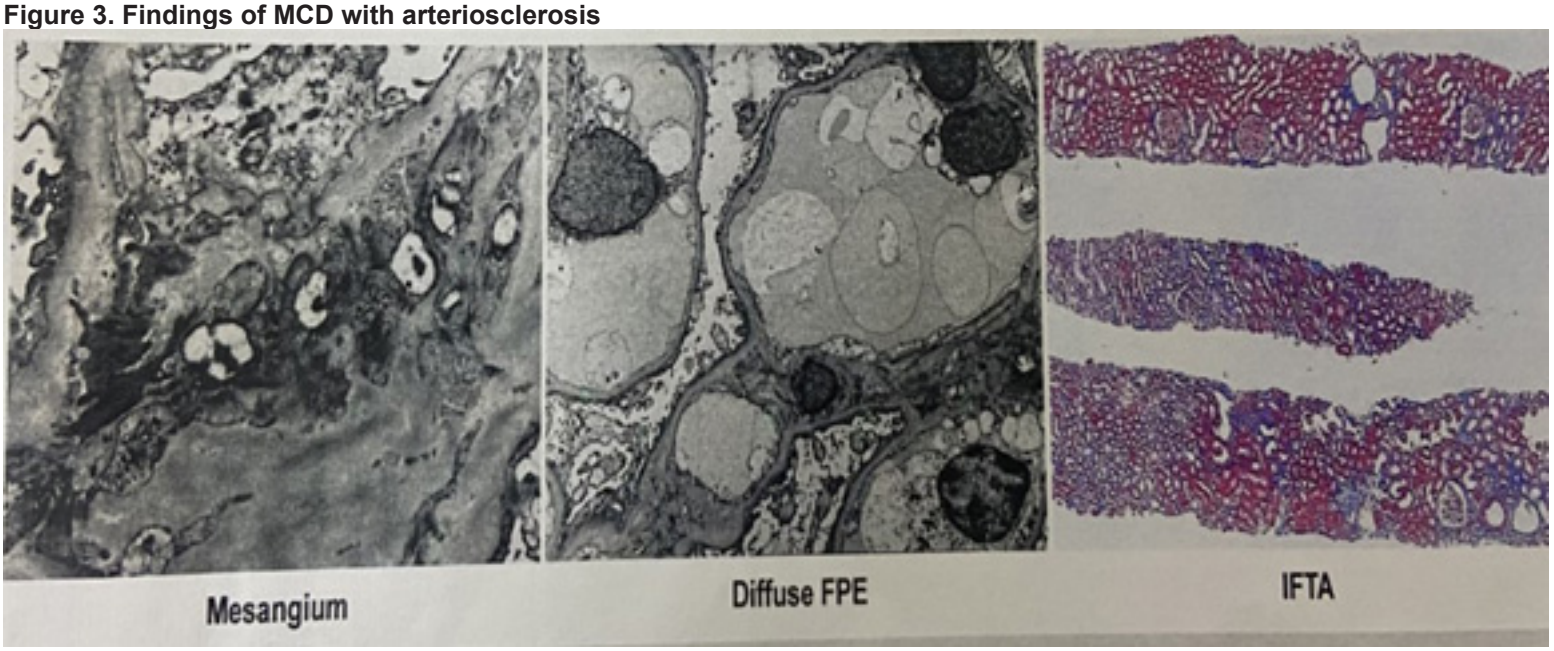


Figure 3. Findings of MCD with arteriosclerosis

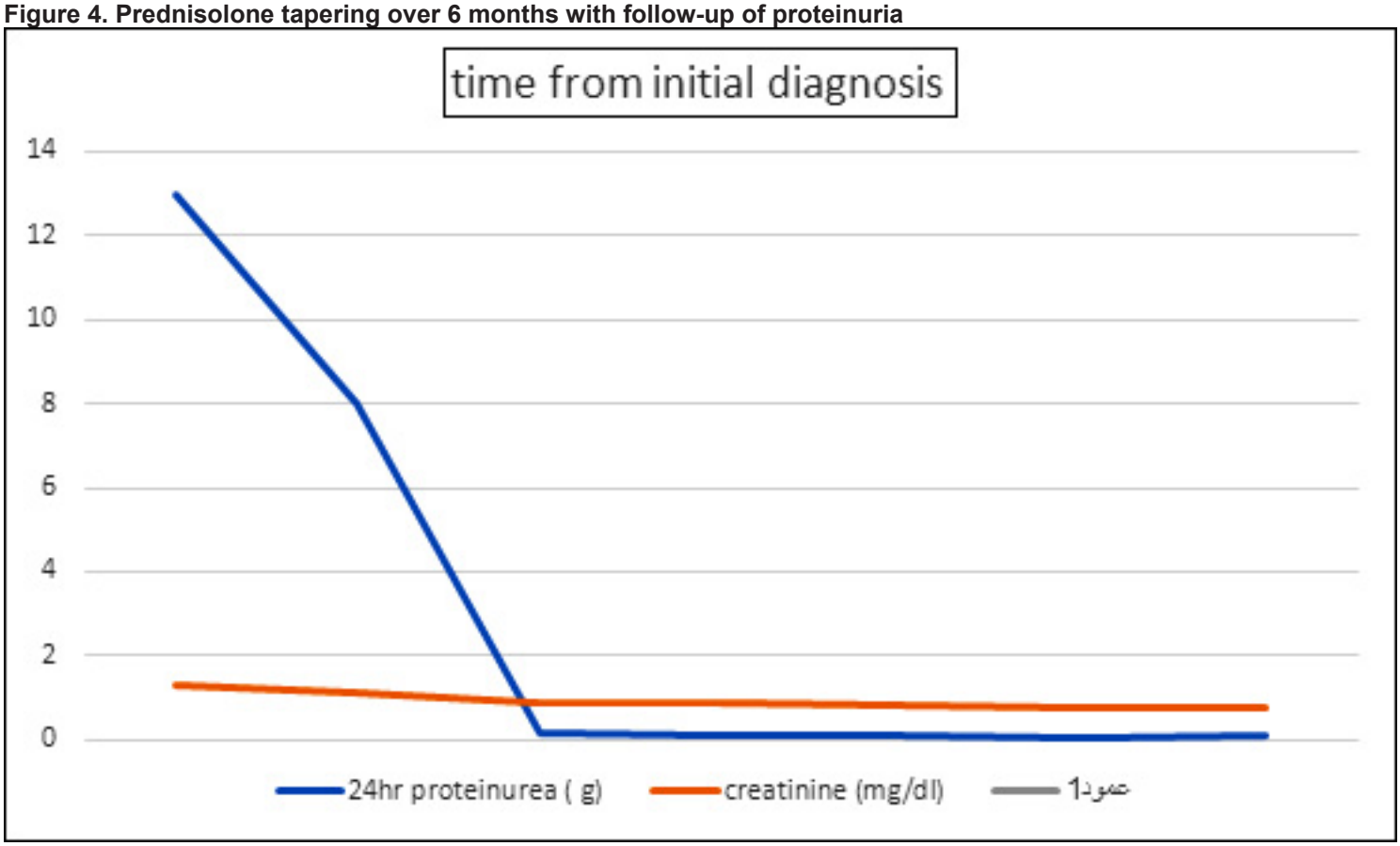


Therapeutic Focus and Assessment: The patient started furosemide 80 mg daily for 21 days after the onset of complaints. Prednisolone 1 mg/kg (total 70 mg daily) was initiated 1 week later when the biopsy result was available. The patient's symptoms were getting better quickly with rapid weight loss starting 7 days post Prednisolone initiation, with 8 kg being lost over the subsequent week. Repeated investigations were done 2 weeks post kidney biopsy. The investigations demonstrated trended down kidney function with a creatinine of 1.1 mg/dl, and an improvement of serum albumin from 20 to 30 g/L and 24-hour urine collection of proteinuria 7.5 g. The patient achieved a complete remission 4 weeks after initiation of Prednisolone, then prednisolone was tapered slowly over a period of 6 months with careful follow-up of proteinuria.

Table 1. Prednisolone tapering over 6 months with follow-up of proteinuria

Time of starting treatment (week)	24 hr proteinuria (g/day)	Creatinine (mg/dl)
0	13	1.3
1	7.5	1.1
4	0.150	0.92
6	0.085	0.87
8	0.70	0.81
12	0.068	0.80
16	0.072	0.75
20	0.070	0.78

Figure 4. Prednisolone tapering over 6 months with follow-up of proteinuria



Discussion

There are several COVID-19 vaccines validated for use by the public. The first mass vaccination program started in early December 2020 and these provided strong protection against serious illness, hospitalization and death from the COVID-19 pandemic (2). However there are growing numbers of cases with glomerular diseases of both de novo glomerular disease and relapse of pre-existing glomerular disease that have been reported shortly after administration of COVID-19 messenger RNA (mRNA) vaccines (Moderna mRNA-1273 and Pfizer-BioNTech BNT162b2) . However, these cases are rare and the causal link with the COVID-19 vaccine is not clearly established. De novo glomerular diseases have been described following COVID-19 vaccination include IgA nephropathy (4,5), Anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (4), Minimal change disease (6,7,8,9), and Anti-glomerular basement membrane (anti-GBM) nephritis (5). In addition, a relapse of the glomerular diseases has been reported following COVID-19 vaccination and includes IgA nephropathy (10), Primary membranous nephropathy (11), and Complement-mediated thrombotic microangiopathy (12). Three case reports of minimal change disease are summarized in (Table 2).

The COVID-19 vaccines use different ways to stimulate host immunity by enhancing T cells response resulting in production of cytokines like interferon γ, tumor necrosis factor α, and interleukin 2 that can lead to podocytopathies and enhance B-cell production of immunoglobulins in predisposed patients (4). These cytokines are likely the key factors for triggering either de novo or relapse of glomerular disease in those patients (4). Our case supports a link between COVID-19 vaccine and relapse of MCD. Although a causal association cannot be firmly confirmed, we believe that clinicians should be aware of MCD presenting with nephrotic syndrome as a possible side effect.

The number of de novo or relapse of MCD cases after Covid-19 vaccine is not significant based on reported literature but it must be taken into account that not all patients with relapsed nephrotic syndrome post-COVID vaccine were biopsied and doubtless not all cases of de novo MCD have been reported (5,6). Therefore, the actual number is likely higher.

The majority of the relapse of MCD cases have been reported post Pfizer-BioNTech administration. But de novo cases complicated with Moderna COVID-19 mRNA vaccination (9) and with the non-mRNA-based AstraZeneca vaccine have also been reported (16).

Complete remission of nephrotic syndrome can be achieved with steroid alone or with addition of calcineurin inhibitors in the majority of MCD cases (17). However, we don't have solid guidelines that help the nephrologist to either proceed or not with second dose or (booster) dose of vaccine in those populations or use a different vaccine type to reduce the risk of relapse.

Table 2. Case reports with presumed relapse of MCD following vaccination for COVID-19

Authors	Country	Age	Sex	Vaccine	Dose	Onset of symptoms (days)	Presentation	Biopsy	Treatment
Komaba et al., 2021	Japan	65	Male	Pfizer	First	8	NS	Not done	Steroid + Cyclosporine Not reported
Kervella et al., 2021	France	34	female	Pfizer	First	10	NS	Not done	Steroid Partial Response and relapse after second dose
Schwotzer et al., 2021	Switzerland	22	Male	Pfizer	First	3	NS	Not done	Steroid + tacrolimus Complete response

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Conclusion

More information is needed to guide optimal management of MCD as a potential consequence after COVID-19 vaccine.

Ethical considerations: Written consent informed consent was provided by the patient for the preparation and publication of this case report and ethical approval for the study was obtained from the research ethics committee of King Abdul-Aziz Specialist Hospital, Taif, Saudi Arabia.

References

1. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents 2020;55(3):105924-105933.
2.World Health Organization (WHO). Coronavirus disease (COVID-19): Variants of SARS-COV-2 . 2021. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-%28covid-19%29-variants-of-sars-cov2
3. Bomback AS, Kudose S, D'Agati VD. De Novo and Relapsing Glomerular Diseases After COVID-19 Vaccination: What Do We Know So Far? Am J Kidney Dis 2021;78(4):477-480.
4. Anderegg MA, Liu M, Saganas C, et al. De novo vasculitis after mRNA-1273 (Moderna) vaccination. Kidney Int 2021; 100:474.
5. Tan HZ, Tan RY, Choo JCJ, Lim CC, Tan CS, Loh AHL, et al. Is COVID-19 vaccination unmasking glomerulonephritis? Kidney Int 2021; 100:469-471.

6. Lebedev L, Sapojnikov M, Wechsler A, Varadi-Levi R, Zamir D, et al. Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine. Am J Kidney Dis 2021; 78:142-145.
7. Maas RJ, Gianotten S, van der Meijden WAG. An Additional Case of Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine. Am J Kidney Dis 2021; 78:312.
8. D'Agati VD, Kudose S, Bomback AS, Adamidis A, Tartini A. Minimal change disease and acute kidney injury following the Pfizer-BioNTech COVID-19 vaccine. Kidney Int 2021; 100:461-463.
9. Holzworth A, Couchot P, Cruz-Knight W, Brucculeri M. Minimal change disease following the Moderna mRNA-1273 SARS-CoV-2 vaccine. Kidney Int 2021; 100:463-464.
10. Perrin P, Bassand X, Benotmane I, Bouvier N. Gross hematuria following SARS-CoV-2 vaccination in patients with IgA nephropathy. Kidney Int 2021; 100:466-468.
11. Aydın MF, Yıldız A, Oruç A, et al. Relapse of primary membranous nephropathy after inactivated SARS-CoV-2 virus vaccination. Kidney Int 2021; 100:464-465.
12. Ville S, Le Bot S, Chapelet-Debout A, et al. Atypical HUS relapse triggered by COVID-19. Kidney Int 2021; 99:267.
13. Komaba H, Wada T, Fukagawa M. Relapse of Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine. Am J Kidney Dis.2021;78(3):469-470.
14. Kervella D, Jacquemont L, Chapelet-Debout A, Deltombe C, Ville S. Minimal change disease relapse following SARS-CoV-2 mRNA vaccine. Kidney Int. 2021;100(2):457-458.
15. Schwotzer N, Kissling S, Fakhouri F. Letter regarding "Minimal change disease relapse following SARS-CoV-2 mRNA vaccine". Kidney Int 2021;100(2):458-459.
16. Leclerc S, Royal V, Lamarche C, Laurin LP. Minimal change disease with severe acute kidney injury following the Oxford- AstraZeneca COVID-19 vaccine: a CASE report. Am J Kidney Dis 2021;78(4):607–610.
17. Janardan J, Ooi K, Menahem S. Sustained complete remission of steroid- and cyclophosphamide-resistant minimal-change disease with a single course of rituximab therapy. Clin Kidney J 2014 Jun;7(3):293-295.