Case Report

Minimal change disease (MCD) following vaccination with ChAdOx1 nCoV-19 vaccine in a young Indian male: A case report

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Abstract

Various vaccines against coronavirus disease 2019 (COVID-19) have been developed amidst the ongoing pandemic. Few cases of glomerulonephritis after COVID-19 vaccination have been reported globally. We present a case of nephrotic syndrome due to minimal change disease (MCD) most likely associated with the ChAdOx1 nCoV-19 vaccine. A 24-year-old male presented with anasarca and frothy urine after receiving the first dose of the COVID-19 vaccine. On admission, the patient had normal serum creatinine with 24-h urinary protein excretion of 4.1 g/day and severe hypoalbuminemia. Kidney biopsy revealed nonproliferative glomerular morphology with relatively unremarkable-appearing glomeruli on light microscopy and diffuse effacement of the odocyte foot processes on electron microscopy, consistent with diagnosis of MCD. This case highlights the risk of new-onset nephrotic syndrome due to MCD after COVID-19 vaccination.

Keywords: ChAdOx1 nCoV-19 vaccine, COVID-19, minimal change disease, nephrotic syndrome

Introduction

Many vaccines have been developed using different methods for coronavirus disease 2019 (COVID-19). These vaccines have been an effective tool for fighting COVID-19 pandemic despite having variable effectiveness and a few concerns regarding adverse effects. Cases of glomerulonephritis associated with COVID vaccines have been reported from different corners of the world recently. Most cases of new-onset minimal change disease (MCD) after the COVID-19 vaccine have been associated with mRNA vaccines. Association with ChAdOx1 nCoV-19 is not known, except for one report from southern India.[1] Here, we report a case of new-onset nephrotic syndrome due to MCD associated with the ChAdOx1 nCoV-19 vaccine in a 24-year-old male.

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Case Report

A 24-year old male without any comorbidities was admitted with generalized edema and frothy urine for last 10 days. He had received the first dose of ChAdOx1 nCoV-19 vaccine 12 days back. The next day after vaccination, he had pain at the injection site and myalgia that subsided spontaneously without any medication. Two days after vaccination, he developed abrupt-onset puffiness of the face followed by edema in both lower extremities, which gradually progressed to anasarca over the next 7 days. It was associated with the passage of frothy urine. On evaluation, he was detected to have 4+ proteinuria

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and severe hypoalbuminemia (serum albumin 1.7 mg/dl) and was referred to our center.

On admission, the patient had stable vitals with a heart rate of 80 beats per minute and blood pressure of 136/78 mmHg. Physical examination revealed pitting edema in the lower extremities, and per abdomen examination was suggestive of ascites. The patient was hospitalized for further evaluation. On investigation, there was protein 4+ on urinalysis and bland urinary sediment. Other findings were as follows: 24-h urinary protein 4100 mg/day, serum total cholesterol 706 mg/dL, albumin level 1.7 g/dL, hemoglobin 13.6 g/dL, and creatinine level 0.86 mg/dL. Antistreptolysin O antibodies and complements C3 and C4 levels were within the normal range, and hepatitis B surface antigen, hepatitis C antibody, and human immunodeficiency virus antibody were negative. Ultrasound revealed ascites with normal size, shape, echotexture, and corticomedullary differentiation of both kidneys. Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 was negative. Titer of immunoglobulin G antibodies against the spike protein of SARS-CoV-2 was 554 Au/mL.

Kidney biopsy showed 18 glomeruli on light microscopy; one glomerulus had global sclerosis, and the others had nonproliferative glomerular morphology with relatively unremarkable-appearing glomeruli. In the interstitium, there was no significant inflammation or injury, with interstitial fibrosis and tubular atrophy observed in less than 10% of the sampled cortex. Immunofluorescence was negative for IgG, IgA, IgM, C3, C1q, kappa, and lambda chains. Electron microscopy revealed normal glomerular basement membrane (GBM) thickness with diffuse effacement of the podocyte foot processes and no electron-dense deposit or GBM reduplication/structural abnormalities. These histopathologic findings were consistent with a diagnosis of MCD [Figure 1].

The patient was started on oral prednisolone (1 mg/kg) as per the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[2] Seven days after initiation of corticosteroid therapy, peripheral edema gradually decreased and frothy urine resolved on follow-up in OPD. Two weeks after discharge, there was a decrease in spot urine protein-to-creatinine ratio to 0.2 g/g, along with increased serum albumin to 3.7 g/dL. We plan to continue steroids as per the KDIGO guidelines.

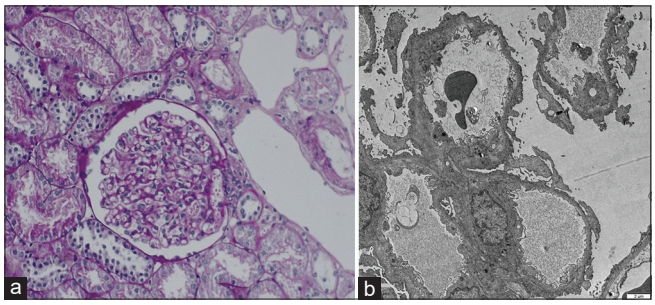

Figure 1: Kidney biopsy showing (a) normal-appearing glomeruli (light microscopy- periodic acid-Schiff stain, ×40). (b) Diffuse effacement of the podocyte foot processes without evidence of immune-type dense deposits as seen under electron microscopy (×3000)

Discussion

Here, we report the case of a previously healthy person presenting with MCD after being administered Oxford–AstraZeneca COVID-19 vaccine. It is a viral vector vaccine developed using the modified chimpanzee adenovirus ChAdOx1 as a vector developed by Oxford University and AstraZeneca (Covishield; Serum Institute of India, Pune, India).[3]

The hallmark of MCD is the foot process effacement of podocytes, visible on electron microscopy, with normal light microscopy and no evidence of immune deposits on immunofluorescence microscopy. The main mechanism in MCD is podocyte injury by circulating factors released by T cells.[4] There are many cases of COVID-19–associated podocytopathies which have been reported.[5] The presence of angiotensin-converting enzyme-2 on podocytes is most likely responsible, as it helps in SARS-CoV-2 invasion.[5]

Nephrotic syndrome due to MCD has been associated with several vaccines, such as influenza, hepatitis B, pneumococcus, and measles.[6] Of late, cases of MCD associated with COVID-19 vaccination have been reported [Table 1]. Both vectored and mRNA COVID-19 vaccines can affect immune regulation, especially T-cell related, leading to the risk of new-onset and relapsing MCD. However, most cases of MCD have been reported with mRNA vaccines, and to date, to the best of our knowledge, new-onset MCD after the ChAdOx1 nCoV-19 vaccine has been reported only once before from southern India.[1]

Vaccination by stimulating antigen-presenting cells and B cells leads to cytokine production, thereby activating T cells, causing podocyte injury and ultimately podocyte foot process effacement.[14] The therapeutic efficacy of steroid-based immunosuppression further strongly reinforces these findings.

From the immunological viewpoint, evidence suggests that during viral infection, a cellular immune response can be observed within approximately 1 week, but T-cell activation can occur 2–3 days earlier,[15] thus accounting for early T-cell–mediated injury within initial few days and subsequent development of MCD, as seen in our patient and few other cases [Table 1].

The inevitable question that arises is whether the appearance of MCD with nephrotic syndrome is coincidental or related to the vaccination. The temporal profile of nephrotic syndrome after the COVID-19 vaccination and the absence of any other precipitating factors point toward the vaccine as a possible trigger. It is uncertain if the patient should be advised to take the second dose and when it can be safely taken.

Table 1: Characteristics of vaccine-associated MCD

References	Age, sex	Type of vaccine	Time after vaccination	Treatment	Outcome
New-onset MCD					
Lim *et al.*[7]	50 years, male	Ad26.COV.2 (Janssen)	7 days	Steroid	CR
Lebedev *et al.*[8]	50 years, male	mRNA/Pfizer	4 days	Steroid	CR
Holzworth *et al.*[9]	63 years, female	mRNA/Moderna	<7 days	Steroid	CR
Maas *et al.*[10]	80 years, male	mRNA/Pfizer	7 days	Steroid	CR
D'Agati *et al.*[11]	77 years, male	mRNA/Pfizer	8 days	Steroid	NR
Anupama *et al.*[1]	19 years, female	ChAdO×1 nCoV-19	8 days	Steroid	CR
Relapse of MCD					
Morlidge *et al.*[12]	30 years, male	Vector/AstraZeneca	2 days	Steroid	CR
Morlidge *et al.*[12]	40 years, female	Vector/AstraZeneca	1 day	Steroid	CR
Salem *et al.*[13]	33 years, female	mRNA/Moderna	3 weeks	Steroid	CR
Salem *et al.*[13]	34 years, female	mRNA/Pfizer	4 weeks	Steroid	CR

CR=complete remission, MCD=minimal change disease, NR=no remission

Conclusion

Nephrotic syndrome like MCD may rarely occur *de novo* as a side effect of COVID-19 vaccination. High index of suspicion, appropriate evaluation, and prompt treatment can lead to remission.

Declaration of patient consent

We certify that consent from the patient was taken for use of his clinical, laboratory data and biopsy images. All efforts will be taken to conceal his identity.

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Conflicts of interest

There are no conflicts of interest.

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