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A Case of Covaxin-Induced Focal Sclerosing Glomerulonephritis (Collapsing Variety)

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Abstract. We report on the development of focal glomerular segmental sclerosis FSGS (collapsing variety) with nephritic symptoms immediately after receiving the first injection of the Covaxin COVID-19 vaccination and acute kidney damage (AKI) (Bharat-Biotech). A 45-year-old lady who had previously been healthy was taken to a hospital outside of the city after developing a headache and pedal edoema. She had gotten the first shot of the immunisation 10 days ago. She experienced bilateral lower limb edoema 4 days following the injection, which turned into anasarca over time. At her admission, UPCR was 7.2 and serum creatinine was 0.9 mg/dl. Over the following days, kidney function continued to deteriorate, and serum creatinine rose to 3.2 mg/dl. The patient was sent to our institution for a kidney biopsy after an abdominal ultrasound revealed normal-sized bilateral kidneys. After doing a kidney biopsy, the results were consistent with FSGS. MCD, IgA nephropathy, and anti-GBM are only a few examples of the diverse glomerulonephritis. Several m-RNA vaccinations have been associated with nephritis in the past, but not the Covaxin COVID-19 vaccine. At this point, the correlation between the immunisation and FSGS is temporal, by exclusion, and in no way clearly established. To assess the actual prevalence of this potential vaccination adverse effect, we must wait for more reports of instances that are comparable to those already reported.

Keywords: nephrotic syndrome (NS), acute kidney injury (AKI), coronavirus 2019 (COVID-19), COVID-19 vaccine, focal segmental glomerular segmental sclerosis FSGS (collapsing variety) (FSGS).

INTRODUCTION

Over the past year, the coronavirus 2019 (COVID-19) pandemic has significantly increased morbidity and death across the globe. The introduction of innovative COVID vaccinations appears to be changing the course of events favourably at the moment. In addition to the numerous obvious advantages that immunisation programmes in many nations have, adverse effects from these vaccinations continue to be a worry that needs to be addressed. Significant adverse effects appear to be rare.

We describe the FSGS (collapsing variant) with nephrotic syndrome and acute kidney damage (AKI), which developed a few days after the initial Covaxin injection (Bharat Biotech's mRNA-based vaccine against SARS-CoV-2 is the coronavirus that causes severe acute respiratory syndrome).

The most recent virus on the list is COVID-19, which has been linked to FSGS (collapsing variant) and AKI in the past. To the best of our knowledge, there are no prior reports of such an event following Covaxin or other COVID-19 vaccinations. Compared to conventionally added protein and purified mRNA lipid nanoparticle-encapsulated or nucleoside-modified platforms are used in inactivated viral COVID-19 vaccines. These platforms result in much greater neutralising antibody titers and better antigen-specific CD4+ and CD8+ T-cell clusters in experimental mice, reactions and germinal centre B, and TH cell activation were greater. Proinflammatory cytokines such as V and interferon are produced by activated CD4+ and CD8+ T lymphocytes. We began to question if these immunizations would trigger or worsen immune-mediated glomerular disorders as a result.

FSGS (collapsing type) with nephrotic syndrome and AKI inevitably raises the question of whether the immunisation is coincidental with or causally connected to the occurrence. The occurrence of this trio and the COVID-19 immunisation, as stated in this article, can only be linked

by timing and by the elimination of other provoking elements, as no other definitive method to establish causation is currently available.

CASE REPORT

Following the onset of a headache, pedal edoema, and face puffiness, a 45-year-old previously healthy lady with a history of hypothyroidism on thyroxine 50 micrograms was taken to the hospital. She had gotten the Covaxin COVID-19 vaccine's first dose 10 days previously. At the injection location, she initially complained of discomfort. She started experiencing diarrhoea and stomach pain on the third day following the injection. He discovered the following day that he had lower extremity edoema that gradually got worse over the following 6 days. He arrived at the hospital on the eighth day following immunizations with a headache and anasarca. The patient refused to use NSAIDs or any other medicines either before or after the vaccine.

She had a blood pressure of 180/110 mmHg at the time of admission and was started on antihypertensives. Laboratory tests revealed haemoglobin of 12.7 gm/dl, TLC-8400/mm^3 and platelet of 3.5 lakh/mm^3, serum urea 33 mg/dl, serum creatinine 0.92 mg/dL, serum albumin of 2.4 gm/dl with total protein of 4.5 gm/dl, TSH was 4.69 IU/ml and urinalysis showed albumin of 4+, RBC-12/HPF and Pus cell 8-10/HPF, and UPCR of 7.3, and urine culture report was sterile. USG of the KUB region showed a right kidney of 10.4 cm and a left kidney of 10.8 cm with maintained corticomedullary differentiation and no features suggestive of hydronephrosis. COVID-19 by RT-PCR was negative. Her ANA by immunofluorescence was negative; C-ANCA and P-ANCA were negative; and her C3 and C4 levels were normal. She was managed conservatively with medication and antihypertensives, following which her blood pressure was controlled but her swelling did not decline. During hospitalisation, her creatinine increased to 3.92 mg/ dl and her serum albumin further decreased to 2.14 mg/dl within 5 days, and she has advised a renal biopsy and referred to our hospital. At our hospital, at the time of admission, both the blood pressure and heart rate were 140/90 mmHg. During a physical examination, pitting edoema in the lower limbs and facial puffiness were discovered. The abdomen was distended. She was further evaluated and had normal values for ESR and CRP. Viral markers (Hepatitis B, anti-HCV, and HIV) were negative. Serum creatinine increased to 3.88 mg/dl and serum albumin further decreased to 2 mg/dl. The lipid profile showed total cholesterol of 384 mg/dl, LDL of 126 mg/dl, HDL of 65 mg/dl, and triglyceride of 166 mg/dl. Urine analysis showed albumin of 3+, Pus cell of 10–15 mg/dl, and RBC of 12–15/HPF. The urine culture was sterile, and UPCR was 6.2. 2D-ECHO showed an ejection fraction of 60% and normal fundus evaluation. COVID-19 by RT PCR was repeated at our hospital, and it was negative and the chest X-ray was normal.

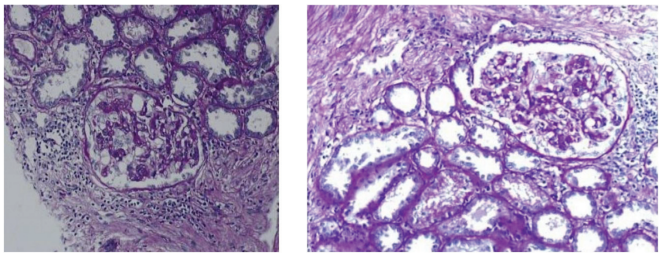

Figure 1. Showing glomeruli with FSGS (collapsing type).

A renal biopsy was done at our hospital. The results are shown in Figure 1.

A total of 26 glomeruli were detected, and 12 revealed segmental tufts along with focal intraglomerular foam cell changes. The neutrophilic infiltration and segmental collapse of the capillary tuft are associated with prominence/hyperplasia of overlying visceral epithelial cells around the collapsed capillary segment. Tubular atrophy and interstitial fibrosis are seen in 10% of the sampled cortex. There was a thickening of the GBM. Immunofluorescence revealed IgM (1+) segmental entrapment, with no staining for IgG and IgA C1q and negative for kappa and lambda chains.

Electron microscopic findings included diffuse effacement of visceral epithelial cell foot processes, and no electron-dense/organized deposits are seen in mesangial areas or GBM.

Post-biopsy period was uneventful. She was managed conservatively with antihypertensives and diuretics, following which her symptoms were relieved.

DISCUSSION

The relationship between the onset of nephrotic syndrome, AKI, and vaccine timing begs the issue of the underlying processes. The development of messenger RNA (mRNA) vaccines for the coronavirus illness of 2019 (COVID-19), which has been a highlight of the medical innovation process, has increased quickly. There is no risk of insertion-induced mutagenesis or infection since mRNA is a non-integrating, non-infectious platform [2]. Object: It is simple to add and delete immunogenic epitopes to swiftly adapt to a newly discovered virus or altered strain. They are anticipated to result in a greater antibody response compared to conventional vaccinations, as well as a stronger CD8+ T- and CD4+ T-cell response, including increased production of cytokines and chemokines [1, 3]. Result from the deregulation of factors related to permeability glomerulonephritis may occur. In this regard, it is appropriate to assume that there is a 4 crosslink between mRNA vaccination and relapse glomerulonephritis. As far as we are aware, relatively

few cases of COVID-19 vaccination-related relapsing and *de novo* glomerulonephritis have been documented by Rovin et al. Rahim et al. [6] reported that two instances of known IgA nephropathy experienced extensive hematuria after receiving the second dose of the Moderna vaccine. Lebedev et al., Maas et al., and Gutierrez et al. reported minimal change disease (MCD) following Pfizer-BioNTech m-RNA vaccinations [7, 8]. Clajus et al. found minimal change disease (MCD) with several vaccines, such as the DPT and influenza shots, which were documented by 10–12 years old. The question is if it is conceivable that the COVID-19 vaccination induces a cell-mediated response as soon as 6–7 days after its injection and might explain the initial suspected adverse effects of the vaccination, including the onset of gastrointestinal problems and peripheral edoema using the study of published publications on glomerulonephritis after immunisation from a clinical/observational perspective identifies a temporal window of 4 days to 4 months between the time of vaccination and the start of clinical symptoms. According to data from the perspective of immunology, a cellular immune response like T-cell activation can happen during viral infection in as little as 2–3 days [7, 8]. In most cases, virally vectored antigens generate a strong CD8+ T cell response vaccines [13], and mRNA vaccines should function similarly. Both viral-vectored vaccinations and mRNA vaccines have the benefit of eliciting balanced T cell and humoral immunity when compared to inactivated vaccines [14]. Although the immunological response of vaccine-induced protection against COVID-19 is poorly understood, both cellular and humoral immunity are probably to blame [15]. Immunity against cytotoxic CD8+ T cells helps protect against many viral respiratory illnesses 16 and robust T cell immunity may lower the chance of contracting SARS-CoV-2. Therefore, it would be ideal for normal practise to include T cell immunity testing to ensure appropriate vaccination responses.

As a result, we may assume that T cells may be quickly activated by the Covaxin to explain the onset of FSGS, indicating that the prospect of early T cell-mediated damage in response to the vaccination exists. Therefore, more research is required to fully understand the early immunological response to the vaccination, especially in regard to side effects, a job that is currently outside the purview of the current report.

Our case report raises the prospect of another serious adverse effect that, at this time, cannot be definitively linked to the COVID-19 immunisation, despite being an unusually life-threatening side effect like anaphylaxis of the COVID-19 vaccination. As a result, we recommend that patients who experience AKI and nephritic syndrome between days and weeks after receiving the COVID-19 vaccine undergo a kidney biopsy. If FSGS is identified, immediate administration of oral corticosteroids, such as prednisone at a dosage of around 1 mg/kg over a number of weeks, should be taken into consideration. This approach appeared to be successful in our case.

Covaxin side effects mainly include injection sitepain, headache, fatigue, fever, body ache, abdominal pain, vomiting, nausea, dizziness-giddiness, tremor, cold, cough, and injection site swelling [17] but glomerular disease has not been reported. This is possibly the first case of glomerular disease (FSGS) being reported after the COVID-19 vaccination.

The numerous COVID-19 vaccines that are already on the market, such as Covishield, Moderna, Oxford-AstraZeneca, Johnson & Johnson, Novavax, and Sputnik V, have already been given to millions of people throughout the world. We are awaiting further reports of instances that are comparable to assess the actual prevalence of this potentially serious side effect of the vaccination. The widespread usage of mRNA vaccines emphasises the need for research into their possible function as glomerular disease initiators. It is probably not safe to deliver second doses of the mRNA vaccine or upcoming boosters to patients who have glomerular illnesses, especially not to individuals who have started or relapsed with glomerular diseases. It is imperative that individuals with glomerular disorders receive special care during follow-up after receiving the COVID-19 vaccination.

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