Clinical Kidney Journal

Clinical Kidney Journal, 2022, vol. 15, no. 2, 357–359

https://doi.org/10.1093/ckj/sfab181
Advance Access Publication Date: 28 September 2021
Exceptional Case

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MPO-ANCA-associated vasculitis after the Pfizer/BioNTech SARS-CoV-2 vaccination

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ABSTRACT

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has demonstrated high efficacy at preventing coronavirus disease 2019 (COVID-19) and a favorable safety profile, however it has also been reported that COVID-19 vaccines may put increase of immune-mediated disease. We herein report a case of MPO-anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis following the mRNA vaccine BNT162b2 (Pfizer/BioNTech) for COVID-19. Although the causal relationship between vaccine and ANCA-associated vasculitis is uncertain, environmental and genetic factors may have set the stage for the development of vasculitis, and the vaccine may have triggered a domino effect.

Keywords: ANCA-associated vasculitis, focal necrotizing glomerulonephritis, MPO-ANCA, mRNA vaccine, SARS-CoV-2

BACKGROUND

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has demonstrated high efficacy at preventing coronavirus disease 2019 (COVID-19) and a favorable safety profile [1]. As of 9 September 2021, approximately 56% of the Japanese population had received two doses of vaccine (Pfizer/BioNTech and Moderna) [2]. It has also been reported that COVID-19 vaccines may put recipients at risk of immune-mediated disease [3]. Recently, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis following the COVID-19 vaccines has been reported [4, 5], although the causal relationship is uncertain. We herein report a case of MPO-ANCA-associated vasculitis following the mRNA vaccine BNT162b2 (Pfizer/BioNTech) for COVID-19.

CASE REPORT

An 84-year-old Japanese man came to our hospital with a 2-week lasting spike fever, malaise, and cough after receiving a second dose of BNT 162b2 (Pfizer/BioNTech). No abnormalities had ever been noted on urine tests, and the most recent urine test on 12 December 2019 was normal. The first and second doses of vaccine were provided on 22 May and 12 June 2021, respectively. Only a day after the second vaccination, he noticed a headache, low fever, malaise, and cough. Despite treatment with loxoprofen sodium, his fever did not resolve and lasted for 2 weeks. Cervical lymphadenopathy was also observed at admission. His medical history includes cerebral infarction without sequelae and early colon cancer, which was successfully treated with endoscopic mucosal resection 3 years before the presentation.

Received: 10.8.2021; Editorial decision: 20.9.2021

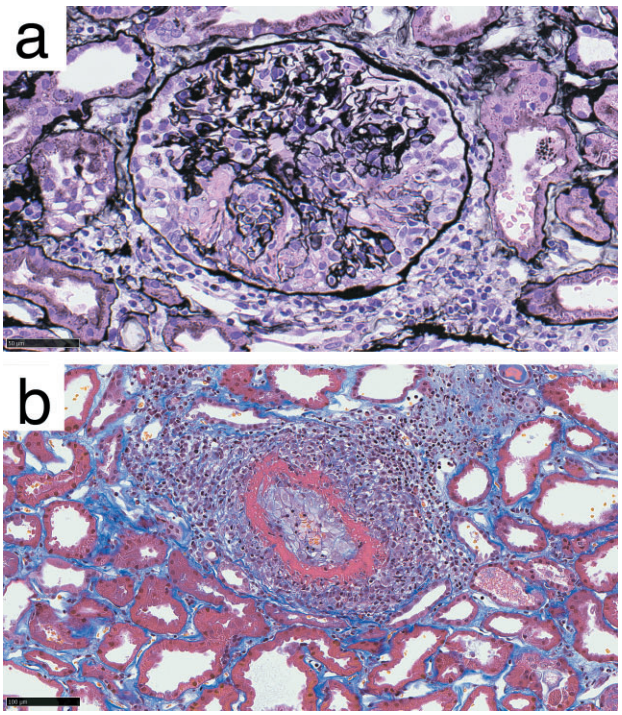

FIGURE 1: (**a**) Methenamine silver stain showing a glomerulus with a cellular crescent and segmental capillary necrosis. (**b**) Masson's Trichrome stain showing fibrinoid necrosis with marked endothelial swelling in the interlobular artery.

The initial laboratory tests revealed creatinine of 1.22 mg/dL (baseline 1.17 mg/dL, 3 years prior), blood urea nitrogen of 23.1 mg/dL, C-reactive protein (CRP) of 18.4 mg/dL, white blood cell count of 12,600/μL, and hemoglobin of 12.5 g/dL. Urinalysis showed protein 1+ (0.19 g/g/Cr) and blood 3+ [≥100 red blood cells (RBCs)/high-powered field]. Urine cytology showed RBCs, neutrophils and eosinophils, with no evidence of malignant tumors. The abdominal ultrasound demonstrated no signs of hydronephrosis. The chest computed tomography detected exacerbation of interstitial pneumonia affecting the lower lobes of the lungs, which was previously found 2 years previously. Two-week duration fever with worsening interstitial pneumonia and a new onset of kidney dysfunction led us to suspect ANCA-associated vasculitis (AAV). As a result, the titer of anti-myeloperoxidase (MPO)-ANCA was found to be positive with 112.8 U/mL. He underwent a renal biopsy.

A kidney biopsy revealed focal necrotizing glomerulonephritis with cellular crescents in 6 of 20 glomeruli (Figure 1a), and 3 of 20 showing glomeruli global sclerosis. Masson's Trichrome stain revealed fibrinoid necrosis with marked endothelial swelling all around the wall of the interlobular artery (Figure 1b). Immunofluorescence study confirmed pauci-immune type of glomerulonephritis. He was diagnosed with renal-limited MPO-AAV. On the next day of kidney biopsy, he was treated with 500 mg of methylprednisolone intravenously for 3 days followed by oral prednisolone 40 mg per day. At recent follow-up (8 weeks post initiation of treatment), serum creatinine was 1.35 mg/dL and his serum anti-MPO-ANCA titer 10.0 U/mL.

DISCUSSION

Several cases of vasculitis and nephrotic syndrome following COVID-19 vaccine have been reported recently [5, 6]. Similar to our case, MPO-AAV after administration of BNT162b2 (Pfizer/BioNTech) has been reported in the last few weeks [4]. To our understanding, this is the second report of a case of MPO-ANCA-associated vasculitis after BNT162b2 vaccine administration.

ANCA is produced by stimuli such as infections and drugs. Bacterial DNA recognized by dendritic cells (DCs) via Toll-like receptor (TLR)-9 prompts B-cell activation and subsequent antibody production [7]. Meanwhile, the mechanism of mRNA vaccines is not fully understood. RNA sensors in DCs and macrophages such as TLR-7 and pattern recognition receptors like retinoid-inducible gene 1 (RIG1) recognize mRNA, leading to the release of cytokines such as type 1-interferon [8]. These cytokines prime neutrophils, resulting in the formation of neutrophil extracellular traps (NETs) or the release of reactive oxygen species and lytic enzymes. NETs can be a double-edged sword. Although NETs play a significant role in host defense, aberrant regulation of NETs can contribute to angiopathy and production of ANCA. The disease susceptibility is thought to be due to abnormalities in the regulation of NETs and specific major histocompatibility complex-II types that tend to present MPO and PR-3 antigens [9].

The safety of mRNA vaccines has been widely shown, however in this case environmental and genetic factors may have set the stage for the development of vasculitis, and the vaccine may have triggered a domino effect. For instance, the patient may have a background of HLA that correlates with the disease, which may have triggered the vaccine to produce ANCA antibodies. We hope this case will help further elucidate the pathogenesis of AAV related to mRNA vaccine for COVID-19.

PATIENT CONSENT

The authors declared that they have obtained consent from the patient discussed in the report.

ACKNOWLEDGEMENTS

The authors thank Naoki Fujiwara and Hiroyuki Suzuki for their critical review of the article.

AUTHORS' CONTRIBUTIONS

S.O. and S.H. wrote the manuscript. S.O., M.Yamano and K.I. took care of the patient. M.Yanai contributed to the pathological data analysis. S.K. contributed to manuscript revision. All authors discussed and reviewed the article.

CONFLICT OF INTEREST STATEMENT

None declared.

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