EXCEPTIONAL CASE

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.
COVID-19 vaccine have been reported recently [5, 6]. Several cases of vasculitis and nephrotic syndrome following COVID-19 vaccine have been reported recently [5, 6]. Simi-
lar 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.

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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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