Clinical Kidney Journal, 2022, vol. 15, no. 5, 1010–1011

https://doi.org/10.1093/ckj/sfac026
Advance Access Publication Date: 27 January 2022
Letter to the Editor

LETTER TO THE EDITOR

COVID-19 vaccination precipitating *de novo* ANCA-associated vasculitis: clinical implications

Aaron Shengting Mai [1] and Eng-King Tan [2,3,4]

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [2]Department of Neurology, Singapore General Hospital, Singapore, [3]Department of Research, National Neuroscience Institute, Singapore, Singapore and [4]Duke-NUS Graduate Medical School, Singapore, Singapore

Correspondence to: Eng-King Tan; E-mail: tan.eng.king@singhealth.com.sg

We read with great interest the article by Fillon *et al.* [1] discussing a matter of arising importance—the precipitation of vasculitis associated with coronavirus disease 2019 (COVID-19) vaccination. Vaccination against COVID-19 remains the cornerstone in our battle against the pandemic and the need for herd immunity becomes increasingly important with the emergence of new variants. Despite having a good safety profile, post-marketing surveillance has demonstrated that COVID-19 vaccines may result in rare but severe adverse reactions, such as myocarditis and thrombotic thrombocytopaenia.

One major area of concern that has thus far received limited attention is the development of *de novo* autoimmune diseases following COVID-19 vaccination in previously well individuals. One such autoimmune condition, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), warrants particular interest because its presenting complaints can be very non-specific. AAV involves the inflammation of small blood vessels characterized by the presence of autoantibodies against the self-antigens in the cytoplasmic granules of neutrophils [2]. While the article by Fillon *et al.* [1] discusses four cases of relapsing AAV, another point of great interest that remains poorly studied is the precipitation of *de novo* AAV shortly after receipt of the COVID-19 vaccine.

To address gaps in knowledge regarding the association between COVID-19 vaccination and new-onset AAV, we reviewed published reports from January 2020 to January 2022 to investigate the clinical presentations, associations and outcomes of new-onset AAV precipitated by COVID-19 vaccination. Cases were included if the patients had symptom onset within 2 weeks of a previous COVID-19 vaccine dose, fulfilled the American College of Rheumatology diagnostic criteria for AAV [3–5], were previously undiagnosed with AAV and were treated with a reportable outcome. Our search found 13 cases fulfilling the criteria for *de novo* AAV occurring shortly after COVID-19 vaccination (Supplementary data, Table S1) [6–18].

Five cases presented with neurologic symptoms (such as headache, dizziness and even paraesthesia) [6, 8, 11, 16, 17], four cases with fever and flu-like symptoms [6, 7, 15, 16], four with weakness and fatigue [8, 11, 12, 16], three with nausea and vomiting [8–10] and three with haemoptysis [9, 14, 17]. With the exception of three patients [6, 16, 18], all remaining patients presented with acute kidney injury hallmarked by elevated serum creatinine, haematuria and proteinuria. Of interest, one patient presented with rhabdomyolysis [12], two presented with symptoms of neuritis [6, 18] and another presented with acute necrotizing granulomatous inflammation of the lungs [16].

Two cases were also observed to have underlying autoimmune risk factors: one patient had mild asthma [6], while another had seronegative arthritis and a 2-year history of undiagnosed vasculitis symptoms [8]. Eleven received a messenger RNA vaccine [6–13, 16–18], while two received a viral vector vaccine [14, 15]. AAV was precipitated in six patients after the first vaccine dose [7, 10, 14, 15, 17, 18] and in seven patients after the second [6, 8, 9, 11–13, 16].

Seven patients developed symptoms within 1 week after vaccination [6, 9, 13, 14, 16–18], with five developing them within 2 weeks [8, 10–12, 15]; the time to symptom onset was not reported for one patient [7]. All included cases were treated with steroid therapy; five patients were further treated with cyclophosphamide [7, 11, 12, 14, 15], five with rituximab [6, 8, 10, 16, 17] and two with both [9, 13]. All recovered without fur-

Received: 19.1.2022; Editorial decision: 24.1.2022

ther complications except for one patient who required chronic haemodialysis [11].

In conclusion, COVID-19 vaccination can be associated with the development of AAV in previously well patients, with the most common symptoms being fever, nausea and vomiting, non-specific neurological symptoms and malaise. The prevalence of post-vaccination new-onset AAV is comparable between the first and second dose and the prognosis is good following prompt treatment. Most importantly, physicians should have a high index of suspicion for AAV if patients develop the above-mentioned symptoms and screening for ANCA may be warranted.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Fillon A, Sautenet B, Barbet C *et al*. De novo and relapsing necrotizing vasculitis after COVID-19 vaccination. *Clin Kidney J* 2021; doi: 10.1093/ckj/sfab285
2. Nachman PH. ANCA glomerulonephritis and vasculitis. *Clin J Am Soc Nephrol* 2017; 12: 1680–1691
3. Calabrese LH, Michel BA, Bloch DA *et al*. The American College of Rheumatology 1990 criteria for the classification of hypersensitivity vasculitis. *Arthritis Rheum* 1990; 33: 1108–1113
4. Leavitt RY, Fauci AS, Bloch DA *et al*. The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. *Arthritis Rheum* 1990; 33: 1101–1107
5. Masi AT, Hunder GG, Lie JT *et al*. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990; 33: 1094–1100
6. Chan-Chung C, Ong CS, Chan LL et *al*. Eosinophilic granulomatosis with polyangiitis after COVID-19 vaccination. *QJM* 2021; 114: 807–809
7. Anderegg MA, Liu M, Saganas C *et al*. De novo vasculitis after mRNA-1273 (Moderna) vaccination. *Kidney Int* 2021; 100: 474–476
8. Davidovic T, Schimpf J, Sprenger-Mähr H *et al*. De novo and relapsing glomerulonephritis following SARS-CoV-2 mRNA vaccination in microscopic polyangiitis. *Case Rep Nephrol* 2021; 2021: 8400842
9. Feghali EJ, Zafar M, Abid S *et al*. De-novo antineutrophil cytoplasmic antibody-associated vasculitis following the mRNA-1273 (Moderna) vaccine for COVID-19. *Cureus* 2021; 13: e19616.
10. Shakoor MT, Birkenbach MP, Lynch M. ANCA-associated vasculitis following Pfizer-BioNTech COVID-19 vaccine. *Am J Kidney Dis* 2021; 78: 611–613
11. Sekar A, Campbell R, Tabbara J *et al*. ANCA glomerulonephritis after the Moderna COVID-19 vaccination. *Kidney Int* 2021; 100: 473–474
12. Hakroush S, Tampe B. Case report: ANCA-associated vasculitis presenting with rhabdomyolysis and pauci-immune crescentic glomerulonephritis after Pfizer-BioNTech COVID-19 mRNA vaccination. *Front Immunol* 2021; 12: 3957
13. Dube GK, Benvenuto LJ, Batal I. Antineutrophil cytoplasmic autoantibody–associated glomerulonephritis following the Pfizer-BioNTech COVID-19 vaccine. *Kidney Int Rep* 2021; 6: 3087–3089
14. Villa M, Díaz-Crespo F, José AP de *et al*. A case of ANCA-associated vasculitis after AZD1222 (Oxford–AstraZeneca) SARS-CoV-2 vaccination: casualty or causality? *Kidney Int* 2021; 100: 937–938
15. Yadav R, Shah S, Chhetri S. ANCA-associated vasculitis following Johnson and Johnson COVID-19 vaccine. *Authorea* 2021; doi: 10.22541/au.163578863.32575474/v1
16. Felzer JR, Fogwe DT, Samrah S *et al*. Association of COVID-19 antigenicity with the development of antineutrophilic cytoplasmic antibody vasculitis. *Respirol Case Rep* 2021; 10: e0894
17. Chen C-C, Chen H-Y, Lu C-C *et al*. Case report: Antineutrophil cytoplasmic antibody-associated vasculitis with acute renal failure and pulmonary hemorrhage may occur after COVID-19 vaccination. *Front Med (Lausanne)* 2021; 8: 765447
18. Takenaka T, Matsuzaki M, Fujiwara S *et al*. Myeloperoxidase anti-neutrophil cytoplasmic antibody positive optic perineuritis after mRNA coronavirus disease-19 vaccine. *QJM* 2021; 114: 737–738