Case Report

ANCA-associated vasculitis following Johnson and Johnson COVID-19 vaccine

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ABSTRACT

Introduction: Antineutrophil cytoplasmic autoantibodies associated vasculitis (AAV) is characterized by antibodies against antigens in cytoplasmic granules of neutrophils and predominantly affects small vessels. AAV after COVID-19 mRNA vaccination has been reported.

Case presentation: We report a rare case of AAV in a patient who presented with rapidly progressive glomerulonephritis (RPGN) after Johnson & Johnson COVID-19 vaccine administration.

Discussion: The temporal causal association between autoimmune manifestations like AAV and COVID-19 vaccines can be explained by hypothesized mechanisms like molecular mimicry, defective neutrophilic apoptosis, polyclonal activation, and systemic proinflammatory cytokine response. These mechanisms are likely to trigger autoimmune responses in genetically susceptible individuals. Still there are many research going on to fill the research gap on the development of ANCA associated with COVID-19 vaccines.

Conclusion: Increasing reports of rare adverse effects like AAV following COVID-19 vaccination warrants the further study and evaluation of immune responses induced by those vaccines. Considering the potential severity of COVID-19 and the rarity of the above-mentioned adverse effects, COVID-19 vaccination should not be withheld.

1. Introduction

As of early September 2021, there are 24 COVID-19 vaccines approved for SARS-CoV-2 prevention, while there are 140 other COVID-19 vaccine candidates in different phases of clinical trials. Approved vaccines have been granted emergency use authorization for the prevention of COVID-19, the ongoing global health pandemic. Although the short term and the common adverse effects of COVID-19 vaccines are well documented, the rare adverse effects are also more likely to be reported due to widespread mass immunization programs. The long-term sequelae of COVID-19 vaccines are yet to be witnessed in the future.

Vasculitis is the disorder characterized by the presence of mononuclear cells in vessel walls of different organs with reactive damage to mural structures. Antineutrophil cytoplasmic autoantibodies (ANCA) associated vasculitis (AAV) is characterized by antibodies against antigens in cytoplasmic granules of neutrophils and predominantly affects small vessels. AAV is associated with ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA) [1]. AAV can lead to renal failure by involving glomeruli. AAV after influenza vaccination has been previously reported. There are few case reports of AAV following COVID-19 vaccination (mRNA vaccines) [2,3]. Here, we report a rare case of AAV in a patient after Johnson & Johnson COVID-19 vaccine administration. This case report has been reported in line with the SCARE Criteria [4].

2. Case presentation

A 52-year-old female presented to our center with complaints of fever, joint pain, and weakness of all limbs. She developed symptoms 12 days after getting vaccinated with Johnson and Johnson COVID-19 vaccine in late July 2021. The fever occurred for 10 days, intermittent type, and associated with chills and rigor. The joint pain was for 3 days which was acute in onset involving small joints of hands and feet. The joints were tender making her bed ridden. Concurrently she also developed weakness of all four limbs with relatively more weakness in lower limb than upper limbs. She had more proximal weakness than distal weakness. She had hypertension for 12 years for which she was on

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medication with amldipine and enalapril. She had history of hysterectomy for uterine malignancy nine years back. She did not suffer from COVID-19 prior to presentation to our center. She is an ex-smoker and consumes alcohol occasionally. She had no drug allergy or use of illicit drugs.

On examination she was ill looking. She had no pallor, icterus, lymphadenopathy, clubbing, or cyanosis. Her blood pressure was 130/70 mm Hg, pulse rate of 84 beats per minute, respiratory rate of 24 breaths/min, and oxygen saturation of 95% in room air. Systemic examinations were grossly normal.

Peripheral blood smear revealed normocytic normochromic anemia with neutrophilic cytosis. Serologic evaluation was notable for increased lymphadenopathy, clubbing, or cyanosis. Her blood pressure was 130/70 mm of Hg, pulse rate of 84 beats per minute, respiratory rate of 24 breaths/min, and oxygen saturation of 95% in room air. Systemic examinations were grossly normal.

Laboratory parameters of the patient.

Table 1

| Laboratory parameters                  | Values               | Reference range |
|----------------------------------------|----------------------|-----------------|
| Hemoglobin                             | 9.5 gm%              | 12-18 gm%       |
| Packed cell volume                     | 28.4%                | 36-54%          |
| Total red blood cell count             | 330,000 cells/ mm³   | 450,000-550,000 cells/ mm³ |
| Mean corpuscular volume                | 86 fl                | 82-92 fl        |
| Mean corpuscular hemoglobin            | 28.79 pg             | 27-32 pg        |
| Mean corpuscular hemoglobin concentration | 33.45%              | 32-36%          |
| Total leukocyte count (TLC)            | 21,000 cells/ mm³    | 4000-11000 cells/ mm³ |
| Neutrophils                            | 92%                  | 45-75%          |
| Lymphocytes                            | 08%                  | 25-45%          |
| Monocytes                              | 0%                   | 2-10%           |
| Eosinophil                             | 0%                   | 1-6%            |
| Basophil                               | 0%                   | 0-1%            |
| Platelets                              | 223,000 cells/ mm³   | 150,000-400000 cells/ mm³ |
| Ferritin                               | 2 mg/ml              | 12-150 ng/ml    |
| Total iron binding capacity            | 208 mg/dl            | 240-450 mg/dl   |
| Urea                                   | 28.9 mmol/l          | 1.6-7.0 mmol/l  |
| Creatinine                             | 6.13 mg/dl           | 0.6-1.1 mg/dl   |
| Uric acid                              | 2.4 mg/dl            | 2.7-7.3 mg/dl   |
| Sodium                                 | 131 mEq/l            | 135-146 mEq/l   |
| Calcium                                | 1.7 mEq/l            | 2.1-2.6 mEq/l   |
| Potassium                              | 5.2 mEq/l            | 3.5-5.2 mEq/l   |
| Procalcitonin                          | 0.47 mg/ml           | <0.1 mg/ml      |
| Total protein                          | 63 gm/l              | 60-80 gm/l      |
| Albumin                                | 40 gm/l              | 38-49 gm/l      |
| Total bilirubin                        | 0.8 mg/dl            | 0.1-1.2 mg/dl   |
| Indirect bilirubin                     | 0.1 mg/dl            | 0.2-0.8 mg/dl   |
| SGPT                                   | 12 U/L               | <42 U/L         |
| SGOT                                   | 7 U/L                | <37 U/L         |
| Alkaline phosphatase (ALP)             | 66 U/L               | <128 U/L        |
| Prothrombin time                       | 12.4 seconds         | 10-12 seconds   |
| International normalized ratio         | 0.92                 |                 |

ANCA associated glomerulonephritis in the view of history of ANCA positivity (Fig. 1). She was discharged after 10 days of hospitalization.

3. Discussion

Local injection site reactions (swelling, itching, redness, tenderness) and systemic symptoms (fever, headache, fatigue, chills, myalgias, and arthralgias) are the most common adverse effects of all type of COVID-19 vaccines. The rare adverse reactions of COVID-19 vaccines like anaphylaxis, vaccine induced immune thrombocytopenia, thromboembolism (arterial thrombosis, cerebral venous sinus thrombosis), myocarditis, pericarditis, and Guillain-Barre-syndrome [5-7]. Minimal change disease is also reported with Pfizer Biotech vaccine [8,9]. Despite these adverse effects, COVID-19 vaccines are safe and effective as documented by large number of clinical trials.

Johnson & Johnson vaccine is an adeno virus vector vaccine which has human adenos virus type 26 (Ad26) vector. The vector expresses SARS-CoV-2 spike (S) antigen without virus propagation which elicits immune response to S antigen providing protection against COVID-19. Thrombotic complications associated with thrombocytopenia and Guillain-Barre syndrome are the rare reported adverse effect of Johnson & Johnson COVID-19 vaccine [10]. AAV has not been reported previously as the adverse reaction of this vaccine. Here, we report a newly onset renal limited AAV in a 52 year female after COVID-19 vaccination. She had normal renal function and laboratory parameters prior to vaccination, and this raises the suspicion of potential association between AAV and COVID-19 vaccine.

Genetic factors, infectious agents, some drugs, and environmental factors are thought to initiate the pathogenesis of AAV. There are studies suggesting the potential association between various infections and the occurrence of vasculitis [11]. However, whether the infections or vaccinations are the triggering factors for autoimmune conditions like vasculitides still lacks direct evidence. A study pointed out the increased level of ANCA in patients immunized with RNA based influenza and rabies vaccine [12,13]. Furthermore, there have been reports of AAV and other autoimmune conditions due to SARS-CoV-2 infections and vaccinations (mRNA COVID-19 vaccines) [14,15]. Interestingly, our patient developed AAV following adenovirus vector vaccine in contrast to the reports of AAV and glomerulonephritis following m-RNA COVID-19 vaccines [2,3]. The temporal causal association between autoimmune manifestations like AAV and COVID-19 vaccines can be explained by hypothesized mechanisms like molecular mimicry, defective neutrophilic apoptosis, polyclonal activation, and systemic proinflammatory cytokine response. These mechanisms are likely to trigger autoimmune responses in genetically susceptible individuals. Still there are many research going on to fill the research gap on the development of ANCA associated with COVID-19 vaccines.

There are only few case reports of AAV and ANCA glomerulonephritis developing after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) in the literature [2,5]. AAV following adenovirus vector vaccine has not been reported previously. We believe that this is the first case report of AAV that occurred following adenovirus vector COVID-19 vaccine administration. Our patient had been immunized with Johnson & Johnson COVID-19 vaccine and developed AAV 10 days after the immunization. There have been reports of several cases of vasculitis following different COVID-19 vaccines and cases of AAV after administration of influenza vaccine [13,16-18]. So, as a lesson learnt from the past, we can speculate the neutrophilic immune response to adenovirus vector present in Johnson and Johnson vaccines, to be a potential trigger for development of AAV. Derangement in the function and expression of MPO and PR3 present in neutrophil granules have been known to cause pauci-immune vasculitidis. Although this case does not conclusively clarify the causal relationship between adenovirus vector COVID-19 vaccine and AAV, further study in the future will insight the association.
4. Conclusion

Increasing reports of rare adverse effects like AAV following COVID-19 vaccination warrants the further study and evaluation of immune responses induced by those vaccines. Considering the potential severity of COVID-19 and the rarity of the above-mentioned adverse effects, COVID-19 vaccination should not be withheld. It is evident that the overall benefit of vaccination likely outweighs the risk of adverse side effects of COVID-19 vaccines including AAV for most individuals.

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