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Glomerulonephritis with Positive Anti-Glomerular Basement Membrane Antibodies following COVID-19 Vaccine

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Abstract

Presentation
A 78 year old female presented to the emergency department with a one day history of haemoptysis, cough, fever and shortness of breath. This was two days after the second dose of her Covid-19 mRNA vaccine.

Diagnosis
A diagnosis of vaccine-mediated anti-glomerular basement membrane antibody (anti-GBM) disease (or Goodpasture's Syndrome) was made after a vasculitic screen was sent for suspected glomerulonephritis.

Treatment
She was treated with IV Methylprednisolone 1000mg IV for three days, seven sequential sessions of plasmapheresis and pulsed IV Cyclophosphamide, with resolution of haemoptysis and kidney function.

Discussion
It is important to maintain a high index of suspicion and test for anti-GBM disease in patients receiving SARS-CoV-2 mRNA vaccination.

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) disease has caused a worldwide challenging and threatening pandemic (COVID-19), with extensive morbidity and mortality and major economic and health losses worldwide. Infection with SARS-CoV-2 has been linked to several presentations of kidney disease through a number of different pathophysiological mechanisms, including coagulopathy, microvascular injury, hemodynamic alterations, autoimmune molecular mimicry, sepsis, cytotoxic effects and collapsing glomerulopathy.[1,2] The development and rollout of novel COVID-19 vaccines, such as BNT162b2, mRNA-1273, Ad26.COV2.S, and ChAdOx1 nCoV-19, have shown promise in

altering the course of the pandemic. However, reports have documented vaccine-associated adverse effects, including cases of kidney injury, in some individuals following vaccination. Although rare, these vaccine-associated events warrant continued monitoring to better understand potential mechanisms of kidney injury linked to vaccination.

We present a case on the development of anti-glomerular basement membrane disease, starting two days after administration of the second injection of the BNT162b2 vaccine (Pfizer-BioNTech mRNA-based vaccine against SARS-CoV-2).

Case Report

A seventy-eight year old woman who developed positive anti-glomerular basement antibodies post COVID-19 vaccine. The patient presented with a one day history of fever, cough, haemoptysis and dyspnoea and was found to be in type one respiratory failure. She had received her second dose of the Pfizer-BioNTech (BNT162b2) Covid-19 mRNA vaccine two days prior to admission. The patients past medical history included crescendo transient ischaemic attacks, left carotid endarterectomy, hypertension, hyperlipidaemia and cholelithiasis. D-Dimers, full blood count, liver function tests, inflammatory marker and coagulation panel on admission were all within normal range. Serum creatinine was raised at 117umol/L, urea 14.9mmol/L.

She was initially treated as a lower respiratory tract infection. Following a further episode of haemoptysis, a vasculitic screen was sent. The patients' anti-GBM antibody was positive at 21 U/Ml and ANCA was negative. Urinalysis was negative for protein, glucose and blood. High resolution CT-Thorax showed three nodules in the right upper lobe but no definitive evidence of pulmonary haemorrhage. Obtaining tissue samples was considered at this point in the patients' admission. However, due to the invasive nature of the procedure and clinical improvement being seen, histology was deemed unlikely to guide further clinical intervention.

A diagnosis of vaccine-mediated anti-glomerular basement membrane antibody (anti-GBM) disease (or Goodpasture's Syndrome) was made and she was treated with IV Methylprednisolone 1000mg IV for three days, seven sequential sessions of plasmapheresis and pulsed IV Cyclophosphamide, with resolution of haemoptysis and kidney function.

Discussion

The clinical development and diagnosis of anti-GBM disease has been described under a variety of circumstances, including following the influenza vaccine and following SARS-CoV-2 infection.[3,4] Anti-GBM disease (also known as Goodpasture's disease) is a rare small vessel vasculitic autoimmune disorder, characterised by linear deposition of anti-GBM antibodies affecting the capillary beds of the lungs and kidneys, resulting in pulmonary haemorrhage and rapidly progressive glomerulonephritis.[5] Histology could provide valuable insights into

potential underlying pathophysiological mechanisms and may be seen as a limitation in the thorough evaluation of this case. In future cases, where clinically warranted, histological analysis may provide useful information for understanding vaccine-associated organ effects. Further research with histological data could enhance our understanding and contribute to broader knowledge in this area. Epidemiological studies suggest an incidence of 0.5 to 1 case per million population per year.[6] Treatment aims to rapidly remove the pathogenic autoantibody, typically with the use of plasma exchange, as seen in this case, along with steroids and cytotoxic therapy to prevent tissue inflammation and further autoantibody production. Retrospective studies have shown when aggressive treatment is commenced early in the disease process, the majority of patients have good renal outcome.[5]

Interestingly, a novel cluster of anti-GBM disease during the COVID-19 pandemic has been reported.[7] to the best of our knowledge, such occurrence has not previously been reported following the Pfizer-BioNTech or other COVID-19 vaccines. Nahhal et al describe a case of anti-GBM disease as a potential complication of COVID-19 infection. The mechanism underlying the disease development during COVID-19 infection is not yet well-defined, however, there is a suggestion for the possible role of inflammation unmasking certain epitopes in the basement membrane which permits access to Goodpasture antibodies.[4]

A case reported by Norton et al describes a case of double-seropositive (ANCA and Anti-GBM) vasculitis following the influenza vaccine. The aetiological mechanism underlying this association has been explored and several hypotheses have been postulated. Influenza vaccine contains inactivated immunogenic antigens representive of the influenza viruses. Therefore, molecular mimicry, whereby a foreign antigen shares structural similarities with self-antigens, may be a potential aetiological factor in the development of autoimmune disease post-vaccination.[3] The Pfizer-BioNTech mRNA vaccine is reported to induce robust T cell activation and cytokine release along with strong antibody responses, which similar to the influenza vaccine pathophysiology described, may have led to a “molecular mimicry” effect with anti-GBM antibodies, consistent with this observed clinical case.[8]

Our case provides support for a potential association between the BNT162b2 mRNA vaccine and onset of anti-GBM disease. Pharmacovigilance of COVID-19 vaccines will be important to determine the incidence of this potential adverse event.

Declaration of Conflicts of Interest:

None declared.

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