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ORIGINAL ARTICLE

ANCA Glomerulonephritis after COVID-19 and post-COVID-19 vaccination – current state of knowledge

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Abstract

Introduction and Objective. In recent years, cases of secondary glomerulonephritis associated with anti-neutrophil cytoplasmic antibodies (ANCA-GN) have been reported following COVID-19 infection or vaccination against SARS-CoV-2. The aim of the study was to analyze publications related to this issue and to highlight both the benefits of vaccination and the potential for secondary immune responses to both infection and vaccination against COVID-19.

Review Methods. A literature review was conducted on sources available up to December 2023, utilizing databases such as PubMed, Cochrane, and Google Scholar. The analysis included cases of ANCA-associated glomerulonephritis (ANCA-GN) following SARS-CoV-2 infection and after COVID-19 vaccination.

Brief description of the state of knowledge. ANCA-associated vasculitis (AAV) is an inflammation of small and medium vessels affecting all systems, including the kidneys. Various causes contribute to the development of AAV, including pathogenic microorganisms and individual abnormal reactions to vaccinations, which can lead to autoimmunization. Since the Covid-19 pandemic, cases of ANCA-GN have been observed in patients without prior autoimmune diseases. The rapid progression of the COVID-19 pandemic led to a significant acceleration in the development of dedicated vaccines, thereby preventing a considerable number of deaths caused by the infection.

Summary. ANCA-associated glomerulonephritis post COVID-19 can be linked to both infection and vaccination, which may act as triggers for autoimmune responses. These mechanisms require further investigation. Vaccine-induced ANCA-GN following COVID-19 vaccination is rare, and vaccinations represent an appropriate strategy to combat this disease.

Key words

COVID-19, SARS-CoV-2 vaccination, ANCA-associated autoimmune glomerulonephritis, ANCA-associated vasculitis

INTRODUCTION

Anti-Neutrophil Cytoplasmic Antibody (ANCA)-associated glomerulonephritis is a severe form of glomerulopathy that can occur at any age. It is associated with systemic vasculitis linked to ANCA (AAV), involving renal glomeruli [1]. The disease progresses rapidly, often presenting with asymptomatic haematuria, proteinuria of varying severity, leading to acute renal failure. Renal biopsy typically reveals focal and segmental glomerulonephritis, as well as diffuse necrotizing and crescentic glomerulonephritis. The most crucial approach is rapid diagnosis and initiation of appropriate immunosuppressive treatment [2, 3].

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Various factors can trigger autoimmune reactions, including infectious agents and even vaccines, which may contribute to the development of AAV and autoimmunization [4]. Several cases of ANCA-associated vasculitis of the kidneys following COVID-19 illness and induced by the COVID-19 vaccine have been described in the literature [5].

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, began in December 2019 when the first cases of the disease were identified in Wuhan, Hubei province, China. The World Health Organization (WHO) recognized COVID-19 as a global public health threat [6, 7]. As of January 2024, the total confirmed case count is 773 million and continues to rise [8].

SARS-CoV-2 not only targets the respiratory system but can also affect other organs, and may be associated with the *de novo* development of autoimmune diseases [9]. A study by Cheng Y. and colleagues from the Nephrology Department

in Wuhan, China, determined that 44% of patients with COVID-19 developed proteinuria and haematuria, indicating the development of renal failure [10]. It has been established that SARS-CoV-2 infection is associated with various forms of renal involvement, causing injuries to renal tubules, interstitial nephritis, and glomerular diseases. Moreover, several cases of ANCA-associated glomerulonephritis (ANCA-GN) were observed post-COVID-19 infection, related to anti-neutrophil cytoplasmic antibodies (ANCA) [11 – 13].

The rapid increase in morbidity and mortality due to the SARS-CoV-2 pandemic led to a significant acceleration in vaccine development time from 10 – 15 years to 1 – 2 years, raising concerns among patients about the safety profile of these vaccines [14, 15]. We now know that vaccination, including the mRNA BNT162b2 (Pfizer-BioNTech) vaccine, has shown 95% efficacy against COVID-19 in individuals aged 16 and older. A favourable safety profile was observed during the first phase of the BNT162b2 study, confirmed in the phase 2/3 part of the trial, and was similar to that of other viral vaccines [16].

The aim of this study was to analyze publications related to secondary ANCA-associated glomerulonephritis (ANCA-GN) following COVID-19 illness or vaccination against SARS-Cov-2. Attention was paid to both the benefits of vaccination and the possibilities of secondary immune reactions to infection and vaccination against COVID-19. By highlighting this clinical issue, this study may contribute to faster diagnosis and the implementation of appropriate treatment.

MATERIALS AND METHOD

A literature review of publications from 2018 – 2023 was conducted using PubMed, Cronarche, and Google Scholar databases, without language restrictions. Articles were selected using the following key words: COVID-19, SARS-CoV-2 vaccination, ANCA-associated autoimmune glomerulonephritis, ANCA-associated vasculitis. The analysis included cases of ANCA-associated glomerulonephritis (ANCA-GN) related to anti-neutrophil cytoplasmic antibodies (ANCA) following SARS-CoV-2 infection and post COVID-19 vaccination, which were confirmed by biopsy.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Glomerulonephritis associated with Anti-Neutrophil Cytoplasmic Antibodies (ANCA-GN). ANCA-associated vasculitis is a group of autoimmune diseases characterized by necrotizing inflammation of small blood vessels, such as arterioles, venules, and capillaries, as well as medium-sized vessels, although the latter are less frequently involved in the disease process. The disease is marked by the development of autoantibodies against neutrophil leukocyte proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA) [17].

ANCA-associated vasculitis (AAV) is a rare disease, occurring at a frequency of about 20 cases per million population per year in Europe and North America, with a slight male predominance. Incidence increases with age, peaking in the 60 – 70 age group [18].

In AAV, involvement of all organ systems can occur. Besides the kidneys, AAV often affects the upper and lower respiratory tract, skin, and nervous system. Microscopic polyangiitis (MPA) is the most common disease involving the kidneys in AAV. About 90% of patients with MPA have renal involvement. Vasculitis limited only to the kidneys is a rare form of AAV. Renal biopsy typically reveals focal necrotizing glomerulonephritis with crescents, without deposition of immune complexes. Additionally, patients often present with microscopic haematuria with active urinary sediment, usually non-nephrotic range proteinuria, and elevated creatinine levels. Resistant hypertension is also common. There is a reduction in glomerular filtration and a decrease in GFR, even within a few days [3, 17, 19]. Changes progress at a rapid pace, leading to progression to end-stage renal failure if the disease is not recognized and treated early. Untreated patients have a very high mortality rate, reaching up to 90% [20]. The classification of primary vasculitides according to the 2012 Chapel Hill Consensus, is presented in Tab. 1 [21].

Table 1. Classification of primary vasculitides according to the 2012 Chapel Hill Consensus [21]

Primary Vasculitis Associated with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) [21].		
Granulomatosis with Polyangiitis (GPA)	Microscopic polyangiitis (MPA)	Eosinophilic granulomatosis with polyangiitis (EGPA)

Based on genetic and immunological studies, a different classification of ANCA-associated vasculitis (AAV) has been established: PR3-positive AAV (PR3-AAV), MPO-positive AAV (MPO-AAV), and in cases with the presence or absence of ANCA – respectively (ANCA+) or (ANCA–) [22]. The type of ANCA antibodies is one of the key factors determining the course of the disease and affects renal function, response to treatment, and the possibility of recurrence. In the case of PR3-ANCA antibody disease, there is often acute renal injury, with greater resistance to treatment and more frequent relapses. Patients with positive MPO-ANCA test results tend to have a milder form of the disease, with a tendency to progress to chronic renal failure [17, 18]. Table 2 presents a comparison of vasculitis depending on the type of antibodies [1].

Table 2. Comparison of vasculitis depending on the type of antibodies [1]

Characteristic for Comparison in Vasculitis	Type of ANCA Antibodies in Vasculitis	
	PR3-ANCA	MPO-ANCA
Area of prevalence	Northern Europe, Northern North America, and Australia	Southern Europe, Southern USA and Asia
HLA system	Genetic association with HLA-DP	Genetic association with HLA-DQ
Most commonly affected system	Upper respiratory tract	Kidneys
Type of inflammation	More characteristics of granulomatous inflammation	Fewer characteristics of granulomatous inflammation
Vascular features in biopsy	More characteristics of necrosis	More characteristics of sclerosis

The etiology and pathogenesis of ANCA-associated vasculitis (AAV) are multifactorial and not fully understood. Factors such as infections, drugs, vaccines, exposure to environmental antigens, and genetic predisposition may

contribute to increased immunization [21, 22]. There is insufficient knowledge about the primary cause of the autoimmune response that leads to ANCA production. Genome-wide association studies in patients with ANCA vasculitis have shown specific and different HLA associations with MPO-ANCA and PR3-ANCA vasculitis. It has been confirmed that genetic factors account for 20% of the risk of developing ANCA-associated vasculitis [23]. The human leukocyte antigen (HLA), PTPN22, CTLA-4, IL-10, and TLR9 are thought to be associated with the development of ANCA-positive vasculitis. Genome-wide association studies in eosinophilic granulomatosis and vasculitis reveal genetic subgroups: the MPO-ANCA+ subgroup strongly associated with HLA-DQ and the MPO-ANCA subgroup associated with regions such as GPA33 and IL5/IRF1 [24, 25].

In the genesis of ANCA autoimmunization, epigenetically-controlled increased expression of ANCA autoantigens plays a significant role. As a result of epigenetic dysregulation, MPO and PRTN3 genes in neutrophils and peripheral blood monocytes are over-expressed in patients with active ANCA vasculitis, compared to patients in remission and healthy individuals. Increased expression of MPO and PR3 genes likely influences the pathogenesis of the disease through two mechanisms – enhanced ANCA-induced neutrophil activation or stimulation of a pathogenic autoimmune response. These two processes may also occur simultaneously. However, it is known that both the acquired and innate immune systems are responsible for inducing ANCA vasculitis [1, 18]. Furthermore, in the pathogenesis of AAV, the loss of tolerance to neutrophil proteins has been proven, leading to activation, recruitment, and damage to neutrophils mediated by ANCA antibodies. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) also participates in this process [22]. Single nucleotide polymorphism in protein tyrosine phosphatase (PTPN22), Toll-like receptor 9, Fc gamma receptors, interleukin-10 and 2, are also associated with the occurrence of ANCA-associated vasculitis [3].

Single cases of vaccine-induced ANCA-associated vasculitis (AAV), specifically from influenza vaccination, have been described in the literature which, however, should not question the positive role of vaccinations. A research group led by Lisa S. Jeffs from the Institute of Medical and Veterinary Science in Adelaide, Australia, reported a case where a patient developed an excessive immune response and production of PR3-ANCA following an influenza vaccination with a vaccine containing viral ribonucleic acid. It is possible that the patient already had these antibodies before vaccination, and the procedure only initiated the immunological process and symptom [26]. This hypothesis is supported by a study by Huugen D. et al. on anti-myeloperoxidase IgG-induced glomerulonephritis in a mouse model, where pro-inflammatory stimuli intensified the development of glomerulonephritis [27].

The study by Lee et al. demonstrates the impact of HBV infection on the development of ANCA-associated vasculitis. It was observed that the initial disease was more severe and there was a higher frequency of relapses (RR 16, p 0.016?) compared to patients without prior HBV infection [28]. Iyoda et al. in their study demonstrated a link between severe Chlamydia pneumoniae infection and subsequent development of ANCA-associated glomerulonephritis. Positive Chlamydia pneumoniae IgM antibodies were found in 33% of the patients with MPO-ANCA-associated vasculitis [29]. Furthermore, numerous studies have been conducted to detect the relationship between chronic Staphylococcus aureus carriage in the pathogenesis of ANCA-associated vasculitis. A study by Stegeman and colleagues showed that chronic Staphylococcus aureus carriage is associated with an increased risk of relapse of this disease [4, 30]. In the study by Scott J. et al., various factors influencing the development of ANCA-associated vasculitis were summarized. It suggests that in addition to viral and bacterial infections, environmental contamination, UV radiation, and harmful working conditions can also contribute to the development of autoimmunization [4].

Treatment of ANCA-associated glomerulonephritis (ANCA GN) varies depending on the severity of the disease. The mainstay of treatment is immunosuppression. Standard therapy includes glucocorticosteroids in combination with cyclophosphamide and/or rituximab. Plasmapheresis is also popular for removing autoantibodies. After achieving remission, maintenance therapy is necessary. Patients are most commonly advised to continue with reduced doses of glucocorticosteroids combined with azathioprine or rituximab [3]. The optimal duration of maintenance therapy has not yet been established. According to the latest Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, therapy should last from 18 months to 4 years. Premature discontinuation of therapy increases the risk of disease relapse, while prolonged immunosuppression is associated with intensified side- effects [31].

Glomerulonephritis Associated with Anti-Neutrophil Cytoplasmic Antibodies (ANCA) (ANCA-GN) post-COVID-19 recovery. Initially, COVID-19 was recognized as an acute disease primarily affecting the lungs. It is now understood that the disease is more multifaceted, characterized by a wide range of symptom severity and affects people of all ages. Moreover, several organs are involved, but the kidneys are a particularly significant site of damage [12].

The exact pathogenesis of the development of this disease has not been fully elucidated. In patients with ANCA-positive vasculitis, a high level of circulating NETs has been documented in biopsy results. It is likely that extracellular neutrophil traps directly contribute to the development of vasculitis, damaging endothelial cells and activating the complement system, and indirectly through the production of PR3-ANCA and MPO-ANCA. This mechanism underscores the ability of SARS-CoV-2 to induce the autoimmunization phenomena, which can cause the occurrence or exacerbation of autoimmune renal vasculitis [11, 32, 33]. It is possible that COVID-19 masks the underlying genetic etiology and triggers an autoimmune process in genetically-susceptible patients [34, 35]. There are also mechanisms related to epitope spreading, leading to the induction of an immune response and consequently the production of ANCA antibodies and vasculitis [36, 37]. Furthermore, Cheng et al. confirmed this thesis in a prospective cohort study in which they observed that over 40% of hospitalized patients with Covid-19 had symptoms of kidney damage [10].

Since the COVID-19 pandemic, several cases of ANCA-positive vasculitis with renal involvement have been noted in the adult population without previous immunological disorders and following recent COVID-19 infections [38].

Banjongjit and others from the Nephrology Department at Vichaiyut Hospital in Bangkok, Thailand, published a

systematic review describing 23 cases of patients diagnosed with ANCA-associated glomerulonephritis (ANCA-GN) during hospitalization for SARS-CoV-2 infection, or a few months after COVID-19 infection worldwide. These patients were not previously vaccinated against COVID-19, ruling-out the possibility of vaccine-induced ANCA-GN. All patients presented with microscopic haematuria and proteinuria. Ten patients tested positive for myeloperoxidase (MPO)-ANCA, and seven showed positive results for proteinase-3 (PR3)-ANCA. One patient had mixed ANCA results. Five out of fourteen (36%) patients also had a positive antinuclear antibody (ANA) test; 14% of the patients had positive anti-glomerular basement membrane (anti-GBM) and p-ANCA antibodies, and 100% had a positive rheumatoid factor (RF) result. These patients showed varying degrees of elevated creatinine levels. Most of the patients demonstrated renal function improvement after immunosuppressive treatment. The authors concluded that there might be a link between SARS-CoV-2 infection and AAV and ANCA-GN, but they lacked sufficient research to make a definitive conclusion [13].

An important study by Chan L. from the Nephrology Department of the Icahn School of Medicine at Mount Sinai in New York, showed that 46% of 3,993 COVID-19 patients hospitalized in the USA developed acute kidney injury (AKI), and 19% required renal replacement therapy [39]. AKI is a common complication of COVID-19, with an incidence rate of up to 56.9% in cases involving renal involvement. The frequency of renal replacement therapy varies depending on the severity of AKI. However, there are few reported cases of COVID-19-associated vasculitis and even fewer of perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA)-associated vasculitis [40, 41]. Given the prevalence of AKI in COVID-19, determining the primary etiology of renal damage can be challenging [41].

Research is ongoing to elucidate the impact of COVID-19 infection on autoimmune or vascular physiology. The disease likely possesses properties similar to those observed in autoimmune diseases, particularly in the production of extracellular neutrophil traps (NETs) containing pro-inflammatory proteins [42, 43]. Table 3 presents selected cases of ANCA-associated glomerulonephritis (ANCA-GN) following COVID-19 infection.

Table 3. Characteristics of selected cases of ANCA-associated glomerulonephritis (ANCA-GN) following COVID-19 infection

Authors	Date of publication	Case Details
Nupur N. Uppal et al. [38].	2020	Two cases of pauci-immune glomerulonephritis (GN) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, showing clinical improvement after COVID-19 treatment and cautious use of immunosuppressive drugs.
T. Izci Duran et al. [11].	2021	Two instances of ANCA-associated vasculitis following COVID-19 infection, with acute kidney injury and renal biopsies revealing necrotizing glomerulonephritis.
M. Jalalzadeh et al. [44].	2021	A 46-year-old woman with systemic sclerosis experienced renal failure following a COVID-19 diagnosis. Renal biopsy showed glomerulonephritis.
Eduardo Briones et al. [45].	2022	Anti-GBM antibodies in a patient with glomerulonephritis and COVID-19 suggest a temporal association with pulmonary injury.
Jeong-Yeun Lee, H. Hwang [46].	2023	A case of ANCA-associated glomerulonephritis in a patient with COVID-19.
A. Pokharel et al. [47].	2023	COVID-19 may be associated with pauci-immune glomerulonephritis. ANCA tests can be falsely negative..
Tahir A. et al. [41].	2023	ANCA-associated vasculitis in an older male with no known history of autoimmune diseases, following recent COVID-19 illness. Tests revealed elevated myeloperoxidase antibodies (MPO-AB) and perinuclear ANCA (p-ANCA), with biopsy confirming focal crescentic glomerulonephritis.

Glomerulonephritis associated with ANCA following vaccination against SARS-CoV-2. Vaccines against SARS-CoV-2 (COVID-19) have proven beneficial in mitigating COVID-19 disease and preventing the spread of the virus. Rare cases of ANCA-associated renal vasculitis induced by the COVID-19 vaccine have been described in the literature. Collective reports on the rarity of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) raise concerns about its association with COVID-19 vaccination. Several case reports have described ANCA-associated pauci-immune glomerulonephritis (ANCA-GN) following COVID-19 vaccination [48, 49].

The molecular mechanisms of vaccine-induced ANCA-associated renal vasculitis are not well-defined. The pathophysiology of this process involves several factors. It is assumed that adjuvant molecules in the vaccine may trigger an autoimmune response [50]. Activation of the complement system, molecular mimicry, systemic inflammatory response, defective neutrophil apoptosis, and polyclonal activation of immune cells triggered by the formation of extracellular neutrophil traps and pro-inflammatory proteins may induce vasculitis in genetically susceptible individuals [32]. Reports suggest that COVID-19 vaccines, particularly mRNA vaccines, may potentially induce this disease. The vaccine may activate a cascade of pathways through dendritic and bone marrow cell stimulation, leading to autoinflammation [36, 50, 51]. Moreover, a series of cases showed that some patients developed dual-positive anti-GBM and MPO ANCA glomerulonephritis after mRNA COVID-19 vaccination, with outcomes varying from complete remission to dialysis dependence or death [5, 52].

A study by Laskova and colleagues suggests a potential link between COVID-19 vaccines and ANCA-associated glomerulonephritis, especially anti-MPO type, although further research is needed to confirm this [53]. There is also evidence suggesting that ANCA-associated vasculitis with pauci-immune crescentic glomerulonephritis may occur as a rare adverse effect following COVID-19 vaccination. In some cases, the condition was diagnosed after the second vaccine dose, and most cases achieved remission [48, 54].

Haoyue Cheng and others from the Department of Public Health and Department of Anaesthesiology at the Second Affiliated Hospital of Zhejiang University Medical School in China, in their latest meta-analysis of controlled clinical trials, confirmed the effectiveness of the COVID-19 vaccine in preventing disease and reducing severity. The safety profiles of COVID-19 vaccines were deemed acceptable. Furthermore, mRNA vaccines were considered the most effective, and the risk and severity of adverse events were minimal compared to severe symptoms caused by COVID-19. However, several cases of recurrent ANCA glomerulonephritis were recorded after COVID-19 vaccination [15].

An analysis of 29 cases by researchers from the Nephrology Department at Naresuan University in Thailand, led by Thammathiwat T., showed that ANCA-GN secondary to COVID-19 vaccination appeared more frequently in older women vaccinated with mRNA vaccines. The most common reported symptoms were abnormal urine sediment, fever, and general weakness. In over half of the studied cases, the following autoantibodies were confirmed: Coombs antibodies, ANA, and cryoglobulins. All patients responded well to treatment, with no fatalities. Most cases of ANCA GN after COVID-19 vaccination occurred after the second dose of the vaccine [48].

Billions of doses of COVID-19 vaccines have been administered worldwide, and ANCA-associated glomerulonephritis following this medical procedure is very rare. The benefits of COVID-19 vaccination outweigh the risk of potential autoimmune diseases. Thammathiwat and colleagues in their study emphasized the need to avoid unnecessary booster doses of COVID-19 vaccines in high-risk patients (carriers of HLA-DR4 or DRB4 alleles) [48, 55]. Renal vasculitis induced by the COVID-19 vaccine is rare, and mass vaccination against COVID-19 infection globally is the appropriate strategy to combat this serious viral disease [5]. Table 4 summarizes the published cases of ANCA-associated renal vasculitis after COVID-19 vaccination [55].

Table 4. Reported cases of renal AAV induced by vaccination against SARS-CoV2 [55]

Team Leader	Year	Case Description
Anderegg M.A. et al. [51].	2021	PR3-ANCA pauci-immune crescentic GN in an 81-year-old male after the second dose of mRNA-1273 vaccine.
Dube G.K. et al. [56].	2021	MPO-ANCA pauci-immune crescentic GN in a 29-year-old female, 16 days post-second dose of BNT162b2 mRNA vaccine.
Feghali E.J. et al. [57].	2021	ANCA GN associated with anti-PR3 in a 58-year-old male, 4 days after the second dose of mRNA-1273 vaccine.
Hakroush S. et al. [54].	2021	MPO-ANCA-associated vasculitis, pauci-immune crescentic GN in a 79-year-old female, 2 weeks post-second dose of BNT162b2 mRNA vaccine.
Ritter A.et al. [58].	2021	MPO-ANCA AAV with massive rhabdomyolysis and GN in a 69-year-old male, 33 days after the second dose of BNT162b2 mRNA vaccine.
Sekar A. et al. [50].	2021	PR3-ANCA pauci-immune necrotizing GN with crescents in a 52-year-old male, 2 weeks after the second dose of mRNA-1273 vaccine.
Shakoor MT. et al. [49].	2021	Renal-limited MPO-AAV in a 78-year-old female, 2 weeks after the second dose of BNT162b2 mRNA vaccine.
Willa M. et al. [59].	2021	Pauci-immune GN associated with P-ANCA in a 63-year-old male, 1 week after the first dose of ChAdOx1 nCoV-19 vaccine.
Al-Yafeai Z. et al. [60].	2022	PR3-ANCA-associated vasculitis in a 62-year-old female, 4 weeks after the first dose of BNT162b2 mRNA vaccine.
Cano-Gámez T. et al. [61].	2022	Rapidly progressive GN associated with MPO-ANCA in a 51-year-old female, after the third dose of ChAdOx1 nCoV-19 vaccine.
Christodoulou M. et al. [62].	2022	MPO-ANCA lung-renal syndrome and rapidly progressive GN in a 72-year-old female, 2 weeks after the second dose of mRNA-1273 vaccine.
Prabhahar A. et al. [36].	2022	PR-3 AAV GN with crescents in a 51-year-old male, 15 days after the first dose of ChAdOx1 nCoV-19 vaccine.
So D. et al. [63].	2022	MPA with elevated anti-MPO antibodies and GN in a 42-year-old male after the second dose of BNT162b2 vaccine.
Suzuki M. et al. [64].	2022	MPO-AAV with severe, pauci-immune crescentic GN in a 72-year-old male, 1 day after the second dose of BNT162b2 mRNA vaccine.
Kawamura T. et al. [65].	2023	MPO-ANCA, rapidly progressive GN in a 71-year-old female, 1 week after the second dose of BNT162b2 mRNA vaccine.

CONCLUSIONS

In summary, ANCA-associated glomerulonephritis can be linked to both infection and vaccination, and the underlying mechanism may involve autoimmune reactions. Scientific research indicates that COVID-19 can be a triggering factor for autoimmune reactions, including ANCA-associated glomerulonephritis, although these mechanisms require further investigation. This mechanism may cause the occurrence or exacerbation of autoimmune renal vasculitis. It is possible that COVID-19 masks the underlying genetic etiology and initiates an autoimmune process in genetically susceptible individuals in whom there is a complex interplay of various environmental and epigenetic factors. Genetic associations of vasculitis with HLA-DP and HLA-DQ systems have been found, depending on the type of ANCA antibodies, namely PR3-ANCA and MPO-ANCA, respectively. The occurrence of this condition as a side-effect of COVID-19 vaccines seems rare, and the benefits of vaccination generally outweigh the risk of such adverse effects. Billions of people have been vaccinated worldwide, and ANCA-associated glomerulonephritis following COVID-19 vaccination has occurred infrequently. Vaccination becomes a triggering factor for an autoimmune process mainly in genetically predisposed individuals, similar to infections. This suggests that the benefits of COVID-19 vaccination outweigh the risk of potential autoimmune diseases and ANCA-GN. Further research and years of observation are needed to draw significant conclusions.

There is a lack of data allowing direct comparison of the incidence of ANCA glomerulonephritis after COVID-19 and after COVID-19 vaccination. Available studies and case reports mainly focus on individual cases or small case series, not on statistical comparisons of incidence rates. Table 5 compares the current state of knowledge on ANCA glomerulonephritis after COVID-19 and after COVID-19 vaccination. Due to limited data, this table does not include specific numerical data because most available studies do not provide sufficient data to make a statistically reliable comparison. Additional detailed epidemiological studies are required to obtain accurate and comparable data.

Table 5. Summary of the current state of knowledge on ANCA glomerulonephritis after COVID-19 and after COVID-19 vaccination

Criterion	ANCA Glomerulonephritis Post COVID-19	ANCA Glomerulonephritis Post COVID-19 Vaccination
No. of published cases	Information on the number of cases is limited and often comes from individual reports or small case series.	Similarly, the information mainly comes from reports of individual cases, or small case series.
Incidence rate	There is insufficient data to determine the overall incidence rate	There is also insufficient data to determine the overall incidence rate.
Direct comparison of incidence	Direct comparison is not available in the scientific literature.	Direct comparison is not available in the scientific literature.

Source: prepared based on this article

Establishing a causal link between SARS-CoV-2 infection and renal involvement in ANCA-associated vasculitis also requires further research.

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