Journal of Cellular and Molecular Immunology

Romanello D, et al., J Cell Mol Immunol. 2025;4(1):11-13.

Commentary

Granulomatosis with polyangiitis triggered by SARS-CoV-2: Diagnostic challenges and clinical implications

Daniele Romanello[1,*], Sara Rotunno[1]

[1]Internal Medicine, Ospedale San Pietro Fatebenefratelli, Rome, Italy

*Author for correspondence:
Email: danieleromanello86@gmail.com

Received date: September 17, 2024
Accepted date: April 05, 2025

Introduction

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is an autoimmune vasculitis characterized by necrotizing inflammation of small- and medium-sized vessels, primarily affecting the lungs and kidneys. The most common symptoms include fever, persistent cough, epistaxis, and renal insufficiency. Diagnosing GPA is often challenging due to the overlap of its clinical manifestations with other infectious and autoimmune diseases. However, the presence of anti-neutrophil cytoplasmic antibodies (ANCA), combined with histological confirmation through biopsy, is crucial for the diagnosis [1,2].

In recent years, increasing attention has been directed towards the potential correlation between SARS-CoV-2 infection and the onset of GPA or other ANCA-associated vasculitides. The cytokine storm triggered by COVID-19, characterized by systemic inflammation and immune hyperactivation, has been suggested as a possible trigger for autoimmune diseases like GPA [3,4]. Several clinical reports describe cases of GPA arising during or shortly after SARS-CoV-2 infection, raising the possibility that the virus may act as an immunological trigger [4,5].

The aim of this commentary is to analyze the possible correlation between SARS-CoV-2 and GPA, providing an overview of the current evidence and evaluating how understanding this interaction could enhance clinical management and improve the pathophysiological knowledge of both conditions.

Article Summary

The article presents a case of a 41-year-old male diagnosed with GPA, a rare autoimmune vasculitis affecting small- and medium-sized vessels, which manifested following a SARS-CoV-2 infection contracted 3 months before. The patient initially exhibited persistent fever, cough, and fatigue, along with elevated inflammatory markers and a large solitary lung lesion identified via chest X-ray.

Despite initial treatment for pneumonia, the lack of response to antibiotics prompted further investigation. A definitive diagnosis of GPA was confirmed through lung biopsy and serological tests revealing c-ANCA (anti-proteinase 3)antibodies, a key marker for the disease. Notably, the patient had contracted a mild COVID-19 infection three months prior, raising the possibility of a correlation between the viral infection and the onset of GPA.

Treatment consisted of high-dose corticosteroids and rituximab, an immunosuppressive therapy aimed at controlling the autoimmune response. The case presented diagnostic challenges due to its atypical presentation, initially resembling a pulmonary infection or malignancy. However, early diagnosis and timely treatment improved the patient's condition.

The article highlights the increasing number of cases where patients develop autoimmune diseases such as GPA following SARS-CoV-2 infection. The authors suggest that the cytokine storm and immune hyperactivation caused by COVID-19 could serve as a trigger for autoimmune conditions, including ANCA-associated vasculitis [6].

Clinical Relevance Evaluation

This case report is highly relevant in the current clinical landscape due to its focus on the intersection of COVID-19 and GPA, an autoimmune disease rarely associated with viral infections. The article addresses an emerging area of concern where SARS-CoV-2 may act as a trigger for autoimmune conditions, a hypothesis supported by growing evidence of post-COVID-19 autoimmune sequelae. The ability to recognize potential links between SARS-CoV-2 infection and the onset of autoimmune diseases like GPA is crucial for early diagnosis and treatment, which can significantly improve patient outcomes. In this context, the report not only contributes to the evolving understanding of COVID-19's long-term effects but also reinforces the importance of vigilance for atypical disease presentations during the pandemic and post-pandemic periods.

Moreover, the case adds to the body of literature suggesting that the cytokine storm and immune dysregulation caused by SARS-CoV-2 may exacerbate or even initiate autoimmune responses, thus altering the course of diseases like GPA [4]. Understanding this relationship can lead to better management of autoimmune diseases in COVID-19 patients and inform therapeutic strategies aimed at modulating immune responses.

This case report focuses on a clinically important issue: the potential link between COVID-19 and autoimmune diseases. This case report underscores the necessity for healthcare providers to consider autoimmune conditions like GPA when patients present with persistent inflammation following SARS-CoV-2 infection. This insight is particularly valuable as it could lead to earlier diagnosis in similar cases, which is critical given the often rapid progression of GPA. The diagnostic process described in the article is thorough and systematic. The decision to pursue a lung biopsy after antibiotic failure and to perform serological testing for c-ANCA was pivotal for identifying the underlying cause of the patient's symptoms. This approach demonstrates clinical best practices in handling cases with atypical presentations, highlighting the importance of differential diagnosis when standard treatments do not yield expected results. The use of high-dose corticosteroids and rituximab for treatment aligns with current guidelines for managing GPA. This regimen is well-documented in the literature as effective for controlling disease activity in autoimmune vasculitis [7]. The report emphasizes the importance of early and aggressive treatment, which is a key factor in improving long-term prognosis for GPA patients.

While the article suggests a potential link between SARS-CoV-2 and GPA, the pathophysiological mechanisms underlying this relationship are only briefly touched upon. Further elaboration on how the cytokine storm and immune dysregulation caused by COVID-19 could specifically trigger or exacerbate GPA would strengthen the article. For instance, the role of Th17 cytokines, which are implicated in both COVID-19 and autoimmune responses, could be explored more in-depth [8].

The report could benefit from a comparison with other COVID-19-associated autoimmune cases. While the article mentions previous reports of vasculitis following COVID-19 infection, it does not provide a detailed comparison or analysis of how this case fits into the broader context of post- COVID-19 autoimmune phenomena. Including data from other case series or systematic reviews could help solidify the hypothesis that COVID-19 is a trigger for autoimmune diseases like GPA [3]. The article lacks a detailed discussion of the long-term follow-up of the patient. Given that GPA is a chronic, relapsing disease, it would be helpful to include information on the patient's condition several months after treatment, particularly regarding the effectiveness of rituximab in maintaining remission. This could provide valuable insights into the long-term management of COVID-19-associated GPA cases.

Future Research Directions

The case raises several important questions that warrant further research. Future studies should focus on elucidating the precise pathophysiological link between SARS-CoV-2 infection and the onset of autoimmune diseases like GPA. Although the cytokine storm and immune dysregulation are believed to play a role, further research is needed to identify specific pathways and immune mediators (such as Th17 cytokines or interferons) involved in triggering vasculitis in post- COVID-19 patients [7]. Investigating these mechanisms could also offer insights into why certain individuals develop autoimmune diseases after viral infections, while others do not. Large-scale epidemiological studies are required to determine the true incidence of COVID-19-associated autoimmune diseases, including GPA. These studies should examine the timing of onset, the severity of symptoms, and the prognosis of autoimmune conditions triggered by COVID-19 compared to traditional presentations of the same diseases. Understanding whether COVID-19 predisposes patients to more severe autoimmune manifestations or if certain subgroups (e.g., patients with genetic predispositions) are more susceptible to these outcomes could guide screening and preventive strategies.

Research into the long-term outcomes of patients with COVID-19-triggered GPA is crucial. Specifically, studies should investigate whether the disease course in these patients differs from those with idiopathic GPA. Understanding the relapse rates, treatment responses, and long-term organ damage in this subset of patients will help inform tailored therapeutic approaches.

Additionally, future research should evaluate the efficacy of immunomodulatory treatments, such as rituximab, in post-COVID-19 GPA, especially considering the immunosuppressive effects in the context of viral infections. As immunosuppressive therapy is the cornerstone of GPA management, it is critical to assess the risks and benefits of using drugs like rituximab and corticosteroids in patients with recent or concurrent COVID-19. Future clinical trials could evaluate the optimal timing, dosage, and combination of these therapies in COVID-19-triggered autoimmune diseases. These studies will help to define treatment protocols that minimize the risk of viral reactivation while effectively controlling the autoimmune response [8].

By addressing these areas, future research can improve the understanding of the interplay between viral infections and autoimmune diseases, ultimately leading to better diagnostic, preventive, and therapeutic strategies for patients with COVID-19-associated vasculitis and other autoimmune conditions.

Conclusions

This case report underscores the potential link between SARS-CoV-2 infection and the onset of granulomatosis with polyangiitis (GPA), adding to the growing body of evidence that COVID-19 may act as a trigger for autoimmune diseases. The patient's atypical presentation, initially mimicking pneumonia, emphasizes the importance of maintaining a broad differential diagnosis, particularly in post-COVID-19 patients with persistent inflammatory symptoms. Early recognition and appropriate treatment of autoimmune conditions like GPA are essential to improve outcomes and prevent irreversible organ damage.

References

1. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013 Jan;65(1):1-11.
2. Hoffman GS, Kerr GS, Leavitt RY, Hallahan CW, Lebovics RS, Travis WD, et al. Wegener granulomatosis: an analysis of 158 patients. Ann Intern Med. 1992 Mar 15;116(6):488-98.
3. Bastard P, Rosen LB, Zhang Q, Michailidis E, Hoffmann HH, Zhang Y, et al. Autoantibodies against type I IFNs in patients with life-threatening COVID-19. Science. 2020 Oct 23;370(6515):eabd4585.
4. Zacharias H, Dubey S, Koduri G, D'Cruz D. Rheumatological complications of Covid 19. Autoimmun Rev. 2021 Sep;20(9):102883.
5. Selvaraj V, Moustafa A, Dapaah-Afriyie K, Birkenbach MP. COVID-19-induced granulomatosis with polyangiitis. BMJ Case Rep. 2021 Mar 18;14(3):e242142.
6. Romanello D, Giacomelli M, Coccia I, Lido P, Rotunno S. An Unusual Presentation of Granulomatosis With Polyangiitis (Wegener's) After SARS-CoV-2 Infection. Cureus. 2023 Dec 6;15(12):e50088.
7. Guillevin L, Pagnoux C, Karras A, Khouatra C, Aumaître O, Cohen P, et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. N Engl J Med. 2014 Nov 6;371(19):1771-80.
8. Blanco-Melo D, Nilsson-Payant BE, Liu WC, Uhl S, Hoagland D, Møller R, et al. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. Cell. 2020 May 28;181(5):1036-45.e9.