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COVID-19-Related Pneumonitis in Immunocompromised Patients: Reviewing Clinical Features and Management Approaches

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COVID-19-related Pneumonitis in Immunocompromised Patients: Reviewing Clinical Features and Management Approaches

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Abstract

In this case series, we explore persistent SARS-CoV-2 infection and its resultant pneumonitis within a cohort of immunocompromised patients. We elucidate the complex interplay between immunosuppression and COVID-19 by examining four patients who experienced prolonged viral shedding and recurrent respiratory failure due to their compromised immune systems. This series elucidates the clinical presentation, diagnostic challenges, and therapeutic strategies. We also summarize existing literature regarding persistent SARS-CoV-2 infection in immunocompromised individuals. Our findings support the use of a tailored treatment approach using a proposed diagnostic and management algorithm to standardize care and optimize outcomes.

Keywords: Covid-19, Pneumonitis, Immunocompromised

1. Introduction

A patient's immune status variably influences the presentation and outcomes of COVID-19, leading to a wide range of prolonged clinical courses and recurrent respiratory failure in immunocompromised individuals.[1] Immunity is essential for infection clearance; it can significantly affect viral kinetics, incubation period, symptom duration, disease severity, and viral shedding.[2] In immunocompetent individuals, SARS-CoV-2 PCR positivity in sputum samples may persist for weeks despite the absence of ongoing infection.[3] However, viral cultures reflecting virus viability tend to be negative within 10 days.[3] Generally, immunocompetent patients' symptoms resolve within 1−2 weeks, facilitated by an adequate immune response and the production of protective immunoglobulins (Ig).[1] However, impaired immune responses in immunocompromised patients can lead to persistent, active infection and ongoing viral replication. This has been observed with several different viruses, including SARS-CoV-2.[2]

The emergence of multiorgan post-COVID-19 sequelae and persistent SARS-CoV-2 infection in immunocompromised patients may indicate a "pandemic within a pandemic."[3–5] However, there is no consensus on the definitions of either condition. In their review article, Nalbandian et al. classify post-acute COVID-19 into two types: subacute COVID-19, where patients have persistent symptoms and/or abnormalities 4−12 weeks after acute infection and chronic COVID-19 where patients have symptoms/abnormalities extending beyond 12 weeks.[5] Persistent SARS-CoV-2 infection is a distinct entity in several case reports that presents almost exclusively among immunocompromised individuals as ongoing PCR positivity and positive viral cultures, with or without continuous COVID-19 symptoms.[6] Although criteria have been

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proposed, a universally accepted definition of persistent COVID-19 is elusive due to multiple challenges. For instance, symptoms and radiographic findings are inconsistent between cases; there can be discordance between the nasopharyngeal and lower respiratory viral cultures since the upper respiratory samples frequently have false negatives; and it is difficult to distinguish persistent RNA from active replication and infection.[6]

Although most radiographic changes associated with COVID-19 are reversible, fibrotic and non-fibrotic post-COVID-19 interstitial lung disease has been described in patients with persistent viral shedding as well as patients who recovered from SARS-CoV-2.[7–9] Although there is no consensus for a definition of post-COVID-19 interstitial lung disease, more than 10% lung involvement and persistent symptoms are strong indicators of the diagnosis.[7] Patients with prolonged viral shedding of SARS-CoV-2 may exhibit recurrent respiratory failure with evidence of pneumonitis, presenting in patterns of nonspecific interstitial pneumonia (NSIP) or organizing pneumonia (OP), but COVID-19 cases are rarely histologically confirmed as NSIP and OP.[10–12]

In our series of four cases, we share our experience with immunocompromised patients exhibiting low Ig levels in the context of rituximab use and prolonged SARS-CoV-2 positivity. These patients presented with respiratory failure and were diagnosed with pneumonitis in patterns of NSIP or OP. We outline management strategies for this subset of patients and review the literature to enhance understanding and management of this condition. Furthermore, we propose a diagnostic and management algorithm for such cases.

2. Cases

Case 1: A 53-year-old female with a significant medical history of follicular lymphoma, in remission after chemotherapy and rituximab nine months prior, presented with high spiking fevers and malaise. She had tested positive for COVID-19 three weeks before admission and had completed a course of three antibiotics and a 5-day course of remdesivir, to which she responded well. On presentation, a CT angiogram of the chest revealed diffuse ground-glass opacities (Image 1A). She was treated with antibiotics, remdesivir, and corticosteroids for another 10 days. Although her condition initially improved and she was scheduled for discharge, she experienced a deterioration marked by recurring fevers and increased oxygen requirements, prompting the initiation of prophylactic antibiotics. Repeat testing showed she remained COVID-19 positive.

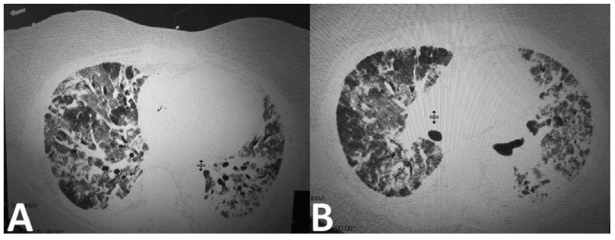

Image 1. Chest CT angiograms of a 53-year-old female (Case 1). A: Chest CT angiogram from an outside hospital after remdesivir and intravenous immunoglobulin shows bilateral ground glass opacities. B: Repeat CT angiogram shows persistent infiltrates and ground glass opacities bilaterally. This CT was done ten days after the first CT angiogram. In the interim, the patient had been treated with remdesivir, dexamethasone, and broad-spectrum antibiotics.

A repeat CT angiogram indicated pulmonary thromboembolism, bronchiectasis, worsening bilateral ground-glass opacities, and stable small pleural effusion (Image 1B). She was started on a heparin infusion. Flow cytometry demonstrated an absence of B-cells and significantly low immunoglobulin G (IgG) levels (394), confirming her immunocompromised status. Intravenous immunoglobulin (IVIG) therapy was initiated, leading to significant improvement over the next week with intravenous corticosteroids. She was subsequently discharged to a long-term acute care facility on a short oral corticosteroid taper, with plans for outpatient follow-up with Pulmonology. A repeat scan after three months showed marked improvement of bilateral infiltrates.

Case 2: A 66-year-old male with a 20-year history of Granulomatosis with polyangiitis (GPA), previously without lung or renal involvement, was on maintenance therapy with rituximab and mycophenolic acid. He was diagnosed with COVID-19 and initially presented to an outside hospital after experiencing a month-long worsening of nonproductive cough, fatigue, and dyspnea. He required Vapotherm, steroids, antibiotics, and three days of remdesivir, which was discontinued due to elevated liver function tests (LFTs). After a week of hospitalization, he was discharged home on 2L oxygen, nebulizers, and oral antibiotics.

Two days later, he presented with a syncopal episode, hypotension, and worsening dyspnea with increasing oxygen requirements, necessitating intubation. He tested positive for COVID-19 again. A CT angiogram of the chest revealed worsening ground-glass opacities (GGOs) indicative of COVID-19 pneumonitis and bilateral subsegmental pulmonary embolism (Image 2). He was started on steroids, broad-spectrum antibiotics, and therapeutic enoxaparin. A diagnostic bronchoscopy that day

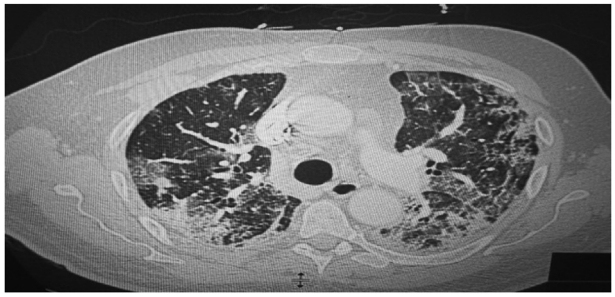

Image 2. Admission CT of a 66-year-old male (case 2) bilateral ground glass opacities and consolidations.

showed increasing sanguineous return on serial aliquots, suggestive of diffuse alveolar hemorrhage (DAH).

Lab workup was negative for any infectious etiology, but the autoimmune panel was positive for anti-PR3 antibodies and showed low levels of immunoglobulins. Following a Rheumatology consultation, he was started on IV immunoglobulins. His oxygen requirements gradually improved, leading to extubation to a high-flow nasal cannula. He was discharged home with supplemental oxygen, with his immunosuppression held until follow-up with Rheumatology, Pulmonology, and Pulmonary Rehabilitation.

Case 3: A 42-year-old female with a medical history of Raynaud phenomenon, Hashimoto's encephalopathy (treated with rituximab for five years), rheumatoid arthritis on mycophenolic acid, and recurrent pulmonary embolism presented with acute hypoxic respiratory failure. Over the past year, she had undergone multiple courses of steroids and antibiotics due to persistent fever and recurrent COVID-19 pneumonia, achieving only temporary improvement. Initially, she received IV dexamethasone and tocilizumab for persistent COVID-19 infection and showed improvement over 10 days, weaning to a baseline oxygen level of 2L. However, her condition deteriorated with worsening shortness of breath, leading to intubation. A CT angiogram of the chest revealed small multifocal segmental and subsegmental pulmonary emboli, along with diffuse bilateral alveolar opacities and air bronchograms, indicative of acute pneumonitis or diffuse alveolar hemorrhage (Image 3A and B). Despite remaining COVID-19 positive, further autoimmune workup detected only anti-nuclear antibodies. Her bacterial and fungal sputum cultures, along with tests for Nocardia and endemic fungi, returned negative. Diagnostic bronchoscopy showed normal bronchial mucosa and anatomy, but bronchioalveolar lavage tested positive for cytomegalovirus (CMV), corroborated by laboratory findings of CMV viremia. With low immunoglobulin levels noted, she received IVIG therapy. Despite improvements in respiratory status, antiviral therapy for CMV was withheld. She continued to improve, receiving three IVIG infusions, and within two weeks was extubated to 2L of supplemental oxygen. Discharged on a gradual six-month steroid taper, her follow-up CT chest scan showed nearly resolved ground-glass opacities and consolidations, yet persistent scarring suggested potential post-infectious fibrosis or non-specific interstitial pneumonia (NSIP) (Image 3C). She also demonstrated significant improvement in a 6-min walk test with reduced oxygen needs.

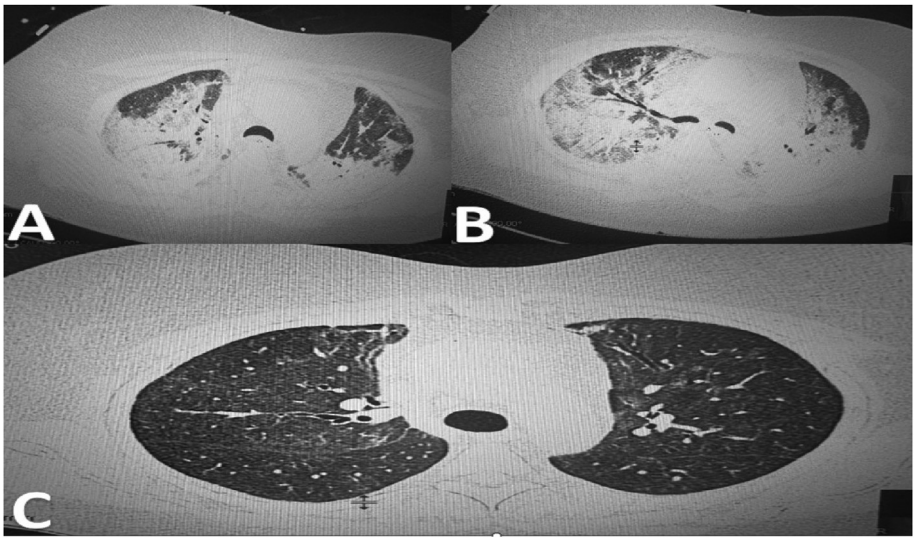

Image 3. Chest CTs of 42-year-old female (Case 3). A. Admission CT shows bilateral airspace opacities with air bronchograms. B. This is a different view of the same scan sequence and shows bilateral ground glass opacities. C. CT taken three months after discharge shows improved opacities bilaterally with some ground glass opacities remaining on the right.

Case 4: A 63-year-old male, previously diagnosed with mantle cell lymphoma and treated with bendamustine and maintenance rituximab following an autologous peripheral blood stem-cell transplant, presented with worsening dyspnea and cough persisting since his COVID-19 infection treated with nirmatrelvir/ritonavir five months prior. Despite initial mild symptoms, he experienced ongoing cough, fatigue, and weight loss. Imaging initially revealed waxing and waning bilateral ground-glass opacities (GGOs), indicative of an infectious or inflammatory process, possibly nonspecific interstitial pneumonia (NSIP) (Image 4A).

His COVID-19 PCR was positive on day 178 post-infection, indicating extended viral shedding, although a concurrent antigen test was negative, ruling out active infection. A bronchoalveolar lavage (BAL) revealed a lymphocytic predominance, and a transbronchial biopsy showed mild chronic lung inflammation. Subsequent cryobiopsy findings included lymphoplasmacytic inflammation in the interstitium without marked fibrosis, reactive type-II pneumocyte hyperplasia, and occasional early fibroblastic foci, suggestive of NSIP (Images 4C and D).

The patient's condition was further complicated by secondary hypogammaglobulinemia, with noted deficiencies in IgG and IgM. He was administered immunoglobulins and started on high-dose prednisone with a planned six-month taper. Despite an initial short course of prednisone and azithromycin, a follow-up CT scan 229 days post-infection showed disease progression. However, after initiating treatment with immunoglobulins and adjusting the steroid regimen, the patient demonstrated steady improvement.

3. Discussion

In this case report, we present four cases of persistent COVID-19 with prolonged viral shedding. Although viral cultures were not performed in any of our cases, our patients had persistent symptoms and responded to elimination strategies previously reported to have good results in similar cases.[13] Cases 1 and 3 were both cases of persistent COVID-19 presenting as OP with a lack of response to remdesivir and eventual response to IVIG due to hypogammaglobulinemia. Case 2 was a case of persistent COVID-19 in the context of low Ig presenting as acute respiratory distress syndrome. Case 4 was a case of NSIP with a lack of response to nirmatrelvir/ritonavir and an eventual response to IVIG.

The most commonly reported theme of immunosuppression is B-cell depletion or insufficiency secondary to a variety of conditions, such as hematological malignancies, anti-CD-20 monoclonal antibodies, and hematopoietic cell transplantation.[6] Although T-cells play an essential role in adaptive immunity against SARS-CoV-2 due to their vital interactions with B-cells, the B-cells are primarily responsible for adaptive immune responses against the virus due to the production of neutralizing antibodies.[14] Persistent SARS-CoV-2 PCR positivity in the context of T-cell depletion (for example, in AIDS patients) has also been described since T-cells play a role in differentiating B-cells and forming memory B-cells in viral infections.[15] All four of our patients were receiving anti-CD-20 monoclonal antibody (rituximab). The patient from case 2 was also on concomitant mycophenolate mofetil, while the patient from case 4

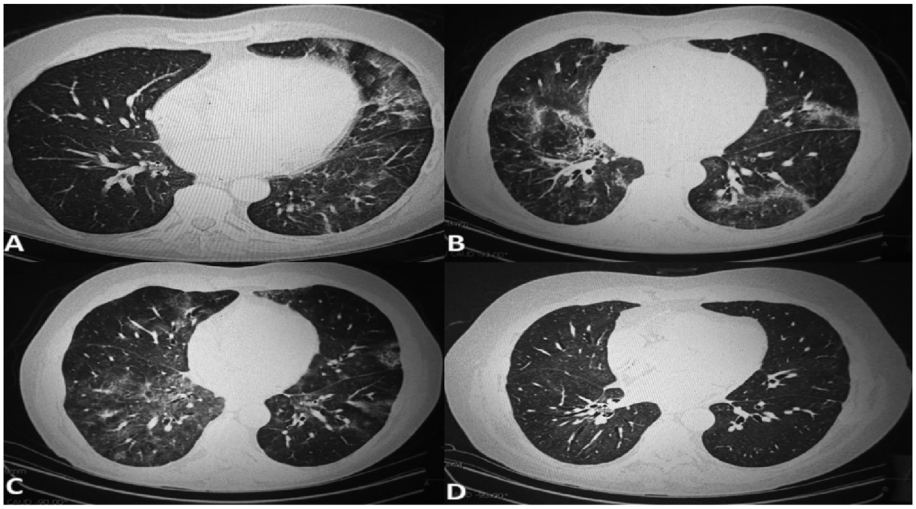

Image 4. Chest CTs of a 63-year-old male (Case 4). A. CT shows multifocal ground glass opacities concentrated on the left side of a two months after his first positive SARS-CoV-2 test. B. CT shows persistent findings two months after receiving a prednisone taper. C: CT chest scan after repeat steroid taper show reveals persistent bilateral multifocal ground glass opacities. D: CT after two doses of intravenous immune globulin shows markedly improved ground glass opacities.

was treated with bendamustine. Evidence suggests that lymphopenia related to bendamustine is limited mostly to T-cells, although combining rituximab and bendamustine can cause combined B-cell and T-cell lymphopenia.[16] We hypothesize that persistent viral replication and an inadequate response from antibodies during rituximab use led to prolonged recurrent respiratory failure in our patients. This can be compared to immunodeficiency, where recurrent infections and immune dysregulation can result in prolonged viral shedding and secondary pulmonary complications, such as OP.[17,18]

SARS-CoV-2 positivity lasted several weeks to months in our cases. This aligns with the findings of Hettle et al. who reported six cases with durations of SARS-CoV-2 positivity ranging from 58 to 305 days, with two patients testing positive until death.[13] Their literature review of 60 cases revealed that 80% had hematological malignancies, and 70% were treated with anti-CD-20 monoclonal antibodies, such as rituximab. Of those, 80% cleared viremia following treatment.[13]

All of our cases exhibited transient responses to initial elimination strategies: remdesivir for cases first 3 cases, nirmatrelvir/ritonavir for case 4, and IVIg serving as the definitive elimination strategy in all four patients (see Table 1). The literature suggests that treatment responses can vary, often showing transient improvements with therapies such as remdesivir and IVIg.[13] Persisting infection in immunocompromised patients may lead to viral mutations and thus may result in a resistance to remdesivir, as indicated by the mutation accumulation observed by Hettle et al.[13] This suggests that viral evolution might be driven more by the persistence of infection rather than by remdesivir, a notion supported by resistance analyses from the ACTT-1 trial and remdesivir monotherapy resistance cases reported by Brown et al.[13,19,20] Mutation accumulation likely occurred in our cases as well, though whole genome sequencing was not performed to confirm this.

In managing persistent COVID-19 among immunocompromised patients, various therapeutic approaches have shown efficacy. Trottier et al.'s successful treatment with remdesivir and nirmatrelvir/ritonavir in a chronic lymphocytic leukemia patient has set a precedent for subsequent successes.[21,22] Similarly, Maruki et al. and other case reports have documented sustained responses to combinations of antivirals and monoclonal antibodies, occasionally supplemented by IVIg in patients with low IgG levels.[23,24] Viral clearance following immune recovery post-rituximab treatment has been described by Overbeck et al., and studies by Wada et al. and Mikulska et al. have reported favorable outcomes using antiviral and antibody combinations, achieving an overall response rate of 82%.[25–27] Further evidence from Lanzafame et al. supports using nirmatrelvir/ritonavir in combination with sotrovimab, while the effectiveness of extended antiviral regimens and innovative treatments like virus-specific T-cells has also been highlighted.[28–33] Franceschini et al. emphasize a comprehensive approach using nirmatrelvir/ritonavir and the strategic use of IVIg in patients with low Ig levels.[34] On the other hand, recovery in many cases might be due to recovering humoral immunity over time.[35] Considering different patient comorbidities, potential drug interactions, and serum Ig levels, selecting a therapy should be tailored to individual patient profiles for managing persistent SARS-CoV-2 infection. This personalized approach ensures that treatment decisions are optimized for efficacy and safety and align with the patient's unique clinical situation. Prior discussions of different strategies to eliminate SARS-CoV-2 infections are summarized in Table 2.

In our case series, we also highlight various pneumonitis patterns in immunocompromised patients with persistent COVID-19. Some authors have divided patterns into inflammatory and fibrotic categories, although the lack of histological evaluation potentially leads to diagnostic inaccuracy.[7] Moreover, many of these changes are frequently reversible if followed over time.[7] SARS-CoV-2-related NSIP and OP have been reported previously, albeit rarely, in the context of persistent SARS-CoV-2.[9] NSIP and OP patterns have also been described in patients with HIV, pneumocystis pneumonia, and protracted SARS-CoV-2 infection.[36–39] In our

Table 1. Clinical summary of our cases highlighting persistent COVID-19 in immunocompromised patients.

Case #	Age (Years)	Sex	Immunosuppression	Initial Elimination Strategy	Final Diagnosis	Final Elimination Strategy
1	53	Female	FL/rituximab 9 months ago	Remdesivir	Organizing Pneumonia	IVIg
2	66	Male	GPA on MMF and rituximab	Remdesivir (3 days)	ARDS	IVIg
3	42	Female	HE on Rituximab	Remdesivir	Organizing Pneumonia	N/A
4	63	Male	MCL on Rituximab, S/P Bendamustine	Nirmatrelvir/ritonavir	NSIP	IVIg

FL: Follicular Lymphoma; GPA: Granulomatosis with Polyangiitis; MMF: Mycophenolate Mofetil; HE: Hashimoto's Encephalopathy; MCL: Mantle cell lymphoma; ARDS: acute respiratory distress syndrome.

Table 2. Summary of previously reported cases of persistent COVID-19 and different elimination strategies used.

Author	Age (years) and sex	Immunosuppression	Duration of Sars-CoV-2 positivity	Initial Elimination Strategy	Final Elimination strategy
Ford et al.[11]	40, male	B-cell ALL on RTX	Approx 5 months	RDV	NI/RI 20 day course
Ambati et al.[48]	25, male	B-ALL on CAR-T Therapy	Approx 8 weeks	RDV 10 days	RDV 18 days and COVID vaccination
Jung et al.[49]	59, female	FL on Ob and Bm	38 days	MU, RDV	RDV + En
Furuya et al. case 1[50]	76, male	MCL S/P Autologous SCT on Ib	73 days	MU, RSV, TCB, STB	En
Furuya et al. case 2[50]	78, female	DLBCL on CHOP + RTX + Intrathecal MTX and Cy	42 days	RDV, IVIg, STB,	En
Marangoni et al.[51]	73, male	FL on RTX and LND	69 days	NI/RI, CI/TI	MU + NI/RI
Wee et al. Patient A[52]	65, male	Good Syndrome	182 days	TI/CI, RDV	NI/RI
Wee et al. Patient B[52]	69, female	Good Syndrome on IVIg	Died day 98 of COVID infection	RDV, STB	RDV, TI/CI
Yang et al. Case 1[53]	Patient in 50s (age/sex not specified)	AML undergoing Allogeneic SCT	71 days	RDV + CP	Repeat RDV + CP
Yang et al. Case 2[53]	Patient in 70s (age/sex not specified)	S/P OHT/OLT on Tac/Sir/ Prednisone	Passed away day 31	RDV + CP	RDV
Carujo et al.[54]	73, male	DLBCL on RTX-CHOP	7 months	IVIg + RDV	None
Overbeck et al.[25]	64, female	RA on RTX	245 days	RDV + IVIg	CP + RDV + BCT
Villaseñor-Echavarri et al.[55]	45, male	DLBCL on multiple regimens	Passed away day 102	RDV, CP, BCT	CP
Bailly et al.[56]	23, male	ALL S/P Allogenic SCT, RTX for EBV reactivation recently	410 days	CP	REGN-COV2 (2 doses)
Montejano et al.[24]	30, male	DLBCL on multiple chemotherapeutic regimens	99 days	RDV, CP	STB
Trottier et al.[21]	64, male	CLL on Ob and VX	Almost 4 months	NI/RI, RDV, Beb	NI/RI + RDV
Cabañero-Navalon et al.[57]	22, male	CVID/GL-ILD on RTX/ AZA	Almost 3 months	IVIg	RDV/CP
Gandhi et al.[58]	70, female	NHL/lymphocytopenia and hypogammaglobinemia	164 days	RDV	Ca/Im
Martinez et al.[59]	44, male	GPA with secondary hypogammaglobulinemia	Almost 4.5 months	RDV, CP	Extended course RDV (30 days)
Colombo et al.[60]	67, female	NHL on RTX	Almost 2 months	RDV, IVIg	CP
Thronton et al.[61]	58, male	FL on RTX	202 days	RDV, IVIg, Bam	RDV, COVID vaccine

ALL: Acute Lymphoblastic Leukemia, AZA: Azathioprine, Bam: Bamlanivimab, BCT: Barcitinib, Beb: Bebtelovimab, Bm: Bendamustine, Ca/Im: Casirivimab-Imdevimab, CAR-T: Chimeric Antigen Receptor T-Cell therapy, CHOP: Cyclophosphamide, CI/TI: Cilgavimab/ Tixagevimab, CP: Convalescent Plasma, CVID: Common Variable Immunodeficiency, Cy: Cytarabine, DLBCL: Diffuse Large B-cell Lymphoma, Doxorubicin, EBV: Epstein–Barr virus, En: Ensitrelvir, FL: Follicular Lymphoma, GL-ILD: Granulomatous Lymphocytic Interstitial Lung Disease, GPA: Granulomatosis with Polyangiitis, HIV: Human Immunodeficiency Virus, Ib: Ibrutinib, Ino: Inotuzumab, LND: Lenalidomide, MCL: Mantle cell lymphoma, MMF: Mycophenolate Mofetil, MS: Multiple Sclerosis, MTX: MethotrexateH, MU: Molnupiravir, NI/RI: Nirmatrelvir/Ritonavir, Ob: Obinutuzumab, OHT: Orthotopic Heart Transplant, OLT: Orthotopic Lung Transplant, Prednisone, RA: Rheumatoid Arthritis, RDV: Remdesivir, RTX: Rituximab, SCT: Stem-Cell Transplantation, Sir: Sirolimus, STB: Sotrovimab, Tac: Tacrolimus, TCB: Tocilizuab, Vincristine, VX: Venetoclax.

patients, post-COVID interstitial lung disease presented as OP (cases 1 and 3) and NSIP (case 4).

A study on 40 patients undergoing bilateral orthotopic lung transplantation for post-acute COVID-19 syndrome revealed histopathological evidence of cellular and fibrous NSIP, with a median time from infection to transplant of 129 days.[40] Similarly, Konopka et al. discussed lung biopsy findings in 18 patients with persistent symptoms, identifying GGOs and interstitial thickening, with usual interstitial pneumonia being common but some showing NSIP-like patterns.[41]

In our series, the patient in case 3 had a positive CMV viral PCR of the bronchoalveolar lavage sample and recurrent episodes of SARS-CoV-2 infection. Although CMV pneumonitis can present with an organizing pattern, our patient responded to IVIg and did not require CMV-directed antiviral

therapy.[42] Post-COVID-19 OP is increasingly recognized, often emerging after acute infection resolution. Tiew et al. and Corvol et al. reported OP cases in immunocompromised patients responding to glucocorticoid therapy, despite initial treatment resistance.[8,37] Diagnosis often follows a period of symptom resolution, with GGOs evolving to consolidation. While oral corticosteroids are standard treatment, instances of steroid resistance and OP relapse exist.[9,43] Although immunotherapy-induced interstitial lung disease has been reported, lack of response to steroids with subsequent response to combination antivirals has been reported in patients with persistent COVID-19.[9] One of the patients in our case series had persistent COVID-19 patient with hypogammaglobulinemia and responded to IVIg and a higher dose of steroids. Tan et al. and others have successfully used prolonged steroid tapers for post-COVID-19 OP, underscoring the effectiveness of this approach.[44,45] Hong et al. reviewed 16 cases of OP, all responding to prolonged steroid therapy.[46] Although imaging findings of resolving acute COVID-19 pneumonia can persist for weeks, and a lag time of 10–12 weeks is recommended for follow-up imaging, the persistence of symptoms and response to steroids in our cases was consistent with post-COVID-19 OP.[47] Our findings align with the characteristic post-COVID-19 OP presentation and response to treatment, emphasizing the importance of timely diagnosis and management.

Based on our experience and review of existing literature, we propose a systematic, stepwise approach to treating patients recovering from acute SARS-CoV-2 infection who have persistent symptoms and PCR positivity. Previously, Dioverti et al. proposed clinical/virologic/radiographic criteria for the diagnosis of persistent COVID-19.[6] We propose a comprehensive algorithm and flowchart for the evaluation and management of recurrent respiratory failure in immunocompromised patients with persistent SARS-CoV-2 infection and suspected post-COVID-19 OP/NSIP (Supplemental Figure 1). This tool can facilitate decision-making through a structured approach, addressing both the identification of superimposed infections and the tailored therapeutic strategies, including antiviral and immunomodulatory treatments, for patients experiencing prolonged viral shedding and respiratory complications.

4. Conclusions

In our case series, we explored persistent SARS-CoV-2 infection and its management in immunocompromised patients. These cases highlight the complexity of prolonged viral shedding and recurrent respiratory failure. Through detailed clinical observations and treatment outcomes, we underscore the significance of individualized therapeutic strategies, emphasizing IVIg and antiviral therapies. Our findings highlight the necessity for personalized management plans and further research to optimize care for this vulnerable population. We advocate a multidisciplinary approach in tackling the challenges posed by persistent SARS-CoV-2 infection in immunocompromised individuals.

Ethics Statement

This study was conducted in accordance with ethical standards. As this study involved de-identified data and a review of previously published de-identified cases, individual consent was not required per journal requirements and IRB guidelines.

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Author contributions

Adeel Nasrullah: Conceptualization, Data curation, Writing – review & editing, Validation. **Muhammad Hassan Shakir:** Writing – original draft, Writing – review & editing. **Eiraj Khan:** Writing – original draft, Writing – review & editing, Data curation. **Muhammad Ibraiz Bilal:** Writing – review & editing, Data curation. **Abu Baker Sheikh:** Writing – review & editing, Supervision, Validation. **Khalid Malik:** Supervision, Validation, Visualization, **Tariq Cheema:** Supervision, Validation, Visualization, Writing – review & editing.

Patient consent

Patient consent for publication was obtained to ensure confidentiality standards.

Conflict of interest

The authors report no conflicts of interest.

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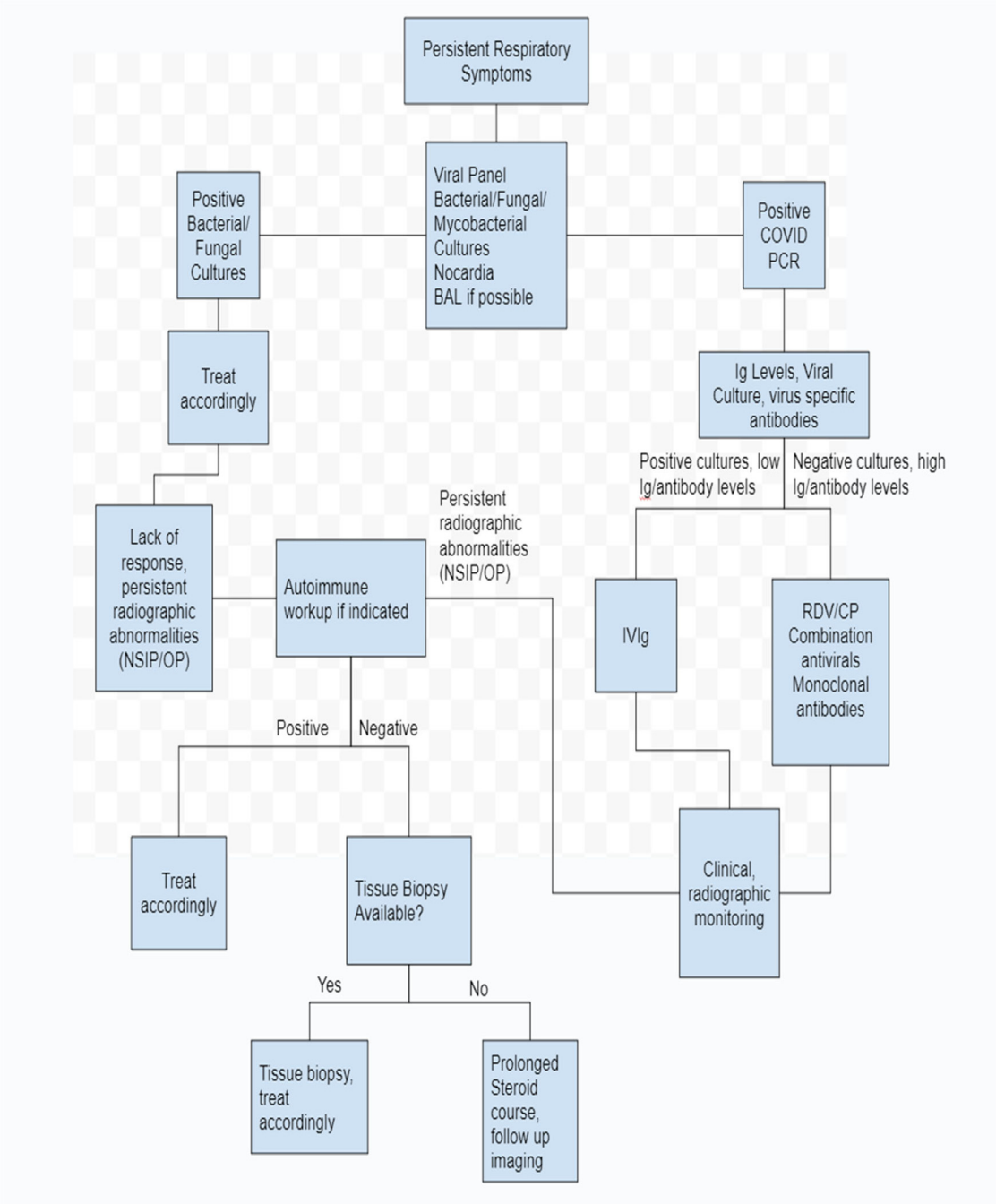
Supplementary Material.



Supplemental Fig. 1. Proposed Algorithm to approaching a case of suspected persistent COVID-19/persistent COVID-19-related interstitial lung disease. CP: convalescent plasma, NSIP: nonspecific interstitial pneumonia, OP: organized pneumonia, RDV: remdesivir.

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